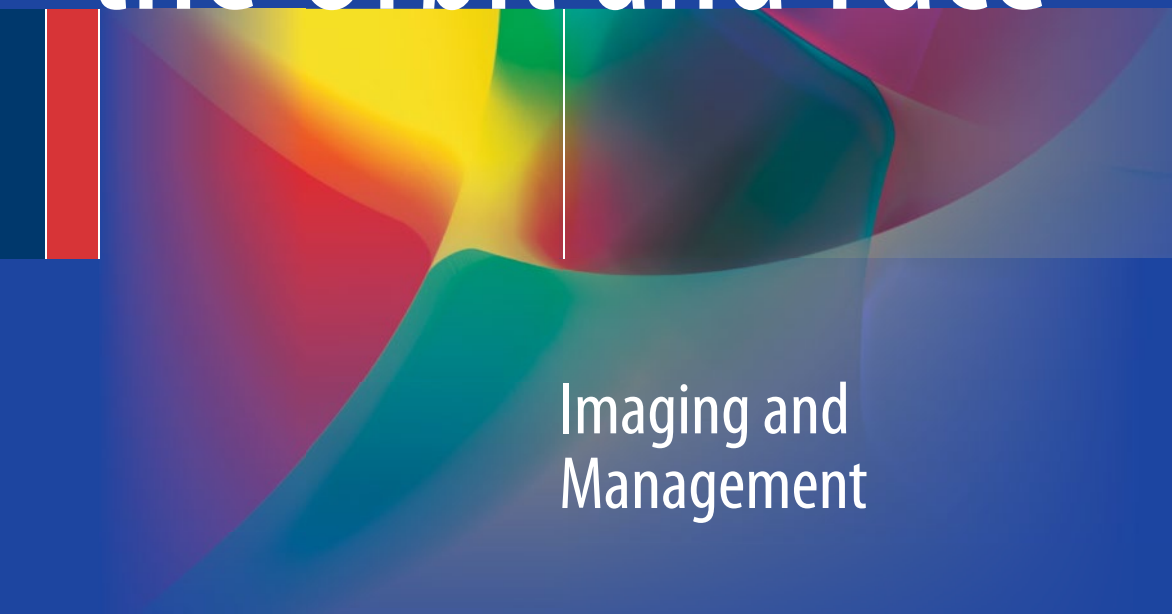
Michael T. Yen
Editor

Vascular Lesions of the Orbit and Face



Imaging and Management

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Dedicated to Kimberly, Ashley, Christopher, and Emily who fill my days with joy and inspiration.

Foreword

It is a privilege and honor to write a forward to this timely and excellent book by Dr. Michael T. Yen entitled *Vascular Lesions of the Orbit and Face*. Congratulations to Dr. Yen and the other authors for presenting the most comprehensive and up-to-date information for the diagnosis and treatment of these difficult and complex orbital and facial lesions. This textbook presents new information which is critical to managing these challenging vascular lesions which in the past have had many devastating functional and cosmetic outcomes. Much of this information was new to me as an "old expert" in the field. The authors are all experts in their field and present how the interdisciplinary management of these lesions greatly improves results. The new modulations discussed have led to paradigm shifts in our ability to diagnose and treat these lesions.

I recommend this book to all physicians involved in the treatment of vascular lesions including orbital surgeons, oculoplastic surgeons, ophthalmologists, pediatric ophthalmologists, facial plastic surgeons, dermatologists, and diagnostic and interventional radiologists. This book should be required reading for those training in these fields. I would like to thank Dr. Yen for his many contributions to oculoplastic surgery over the years. He taught me more as my fellow than I could teach him as a preceptor. I am very proud of Dr. Yen and his accomplishments, including this timely book.

Salt Lake City, UT, USA — Richard L. Anderson, M.D.

Preface

Orbital and facial vascular lesions have traditionally been challenging conditions to manage due to their varied presentation and limited available treatment options. However, as with much of medicine, technological advances and new treatments have significantly improved the ability to accurately evaluate and successfully treat these lesions with reduced complications. Some of these advances include new imaging modalities, endovascular and intralesional treatment approaches, photodynamic therapy, and additional medical therapies. Several of these advances, such as the use of oral propranolol for infantile hemangioma, have led to paradigm shifts in our understanding and management of vascular lesions of the orbit and face. With the rapid pace of advancement in this area of medicine, it is often difficult for the practicing physician to keep up with the medical literature on these new treatments, devices, and techniques.

This text provides a consolidated yet comprehensive source for the classification, evaluation, diagnosis, and management of vascular lesions of the orbit and face. As is evident by the diverse backgrounds of the contributing authors, many of the advancements in the area of orbital and facial vascular lesions are the result of interdisciplinary collaborations and interactions with multiple specialties of medicine. While the ophthalmologist, pediatric ophthalmologist, or orbital specialists are often involved with the initial evaluation of the patient, optimal management often requires the expertise of diagnostic and interventional radiologists, dermatologists, and oculoplastic surgeons. For this text, experts in these specialty fields have written structured in-depth chapters that can also serve as a reference guide for the clinician. The text is an excellent resource for not only those in training but also the seasoned practitioner wanting to be updated on the newest diagnostic and treatment techniques for orbital and facial vascular lesions. Even I did not realize quite how much my own knowledge base needed updating until I read through these chapters.

I am extremely grateful and indebted to all the authors for their contributions to the text. A special thanks to Rick Anderson who not only wrote the foreword to

the text but has been a wonderful mentor and friend. The editors and staff at Springer also deserve special recognition, especially Sverre Klemp, Rebekah Amos, and Karthik Periyasamy, for their assistance in bringing this manuscript to completion.

Houston, TX, USA Michael T. Yen

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Chapter 1
Classification of Orbital Vascular Anomalies

Preeti J. Thyparampil and Michael T. Yen

1.1 Introduction

Vascular lesions of the orbit comprise a significant portion of orbital pathology, accounting for 7 % in one review of 4000 orbital lesions [1]. A straightforward and functional classification of orbital vascular anomalies is important to aid clinicians in diagnosing these lesions and in planning treatment.

Current classification systems organize vascular lesions of the orbit based on histopathological features (tumors vs. malformations) and based on hemodynamic properties (no-flow, low-flow, or high-flow lesions). Additionally, current systems characterize vascular anomalies based on anatomic location or depth and complexity. While these various classification systems aid greatly in understanding vascular orbital anomalies, the nomenclature of some lesions remains confusing. For example, the cavernous hemangioma is better characterized as a venous flow (or low-flow) malformation as opposed to a hemangioma or tumor [2]. However, it behaves quite differently than the other venous malformations of the orbit. Another example of a lesion with unclear classification is the low-flow dural carotid cavernous fistula (CCF). Unlike the high-flow CCF which is believed to be a fistula which has formed due to trauma, the dural CCF is due to connections to small branches of the internal and external carotid arteries and may be true acquired fistulas or may be the result of preexisting malformations [3].

While existing organizational systems do not eliminate all confusion in the classification of orbital vascular lesions, they nonetheless are very helpful for categorizing lesions and guiding treatment based on histopathological origin, clinical presentation, and radiographic imaging.

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1.2 Tumors/Neoplasms vs. Malformations

One classification system distinguishes vascular lesions as either tumors or malformations. Orbital vascular tumors, the most common of which is the infantile hemangioma (Fig. 1.1), are characterized histopathologically by proliferating endothelial cells, while vascular malformations do not have proliferating endothelium, but rather dysplastic vessels [4]. Neoplasms can grow in vitro, while malformations cannot. In addition, malformations are generally considered to be present from birth and do not undergo spontaneous regression. While present from birth, not all malformations may be clinically apparent at birth and may grow in response to hormonal changes or concurrent illnesses. Malformations may be composed of vascular elements, lymphatics, or both. Radiographically, neoplasms tend to appear as well-circumscribed, lobular masses that are hyperintense with contrast administration, while malformations have less distinct margins with patchier hyperintensity with contrast and may have focal areas of calcification within the lesion. The effect on adjacent structures also varies between the two types of lesions. Whereas tumors tend to infiltrate adjacent structures or cause mass effect, malformations tend to cause distortion of adjacent structures by becoming incorporated into the vasculature of the nearby bone and soft tissue [5]. The International Society for the Study of Vascular Anomalies (ISSVA) also characterizes lesions into the broad categories of tumors and malformations. A summary of key differences between vascular tumors and malformations is shown in Table 1.1.

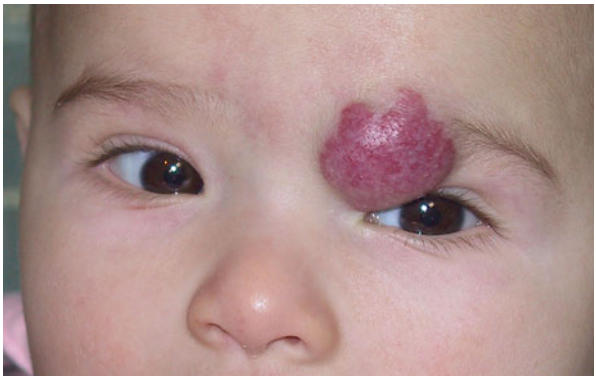

Fig. 1.1 Large infantile hemangioma of the left orbit and upper eyelid

Table 1.1 Tumors vs. malformations

Tumors	Malformations
Not present from birth	Present from birth
Can grow in vitro	Cannot grow in vitro
Proliferating endothelium	Dysplastic vessels without proliferating endothelium
Well-circumscribed lobular masses on imaging	Less well circumscribed on imaging
Infiltrate adjacent structures or cause mass effect on imaging	Distortion of adjacent structures on imaging by becoming incorporated into the vasculature of the nearby bone and soft tissue

1.3 Classification of Malformations Based on Hemodynamics

The Orbital Society further advises classification of malformations based on flow characteristics. In this classification system, malformations can be characterized as either no-flow lesions, low-flow (venous,) lesions, or high-flow (arterial) lesions [6]. Characterizing lesions based on flow aids in identification using clinical and radiologic features and also helps to guide treatment. Both clinical and radiographic features can be used to characterize the hemodynamic properties of vascular malformations. Clinical characteristics include change in lesion appearance with body position, Valsalva maneuver, or concurrent illness and presence of bruit or pulsatility. Enlargement of a lesion with Valsalva followed by rapid shrinkage is indicative of large outflow channels and distensibility, while slow growth and deflation suggest small outflow channels [2]. Imaging characteristics include signal intensity on contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography and flow patterns on venography, arteriography, or intralesional dye injection. Dynamic imaging can be performed by having the patient perform the Valsalva maneuver during acquisition of a contrast-enhanced CT or MRI scan. Successful Valsalva can be confirmed by visualizing dilation of the superior ophthalmic vein (Fig. 1.2a, b). Intralesional injection of the lesion with contrast can be used to guide treatment of the lesion with gluing or sclerotherapy. Venography through a distal venous access can also be helpful to visualize the

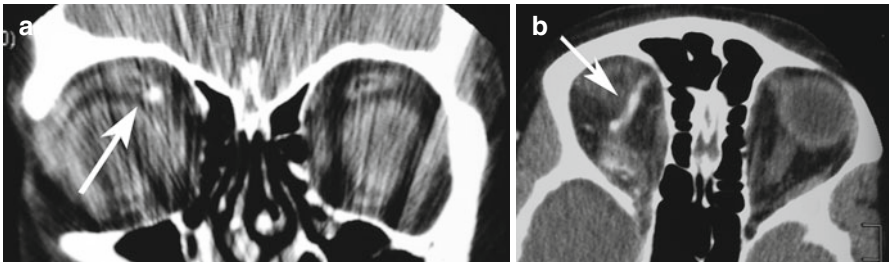

Fig. 1.2 (**a**) CT scan demonstrating dilated superior ophthalmic vein (*arrow*) in the right orbit. (**b**) Axial view of the same CT scan showing the dilated superior ophthalmic vein (*arrow*) in the right orbit

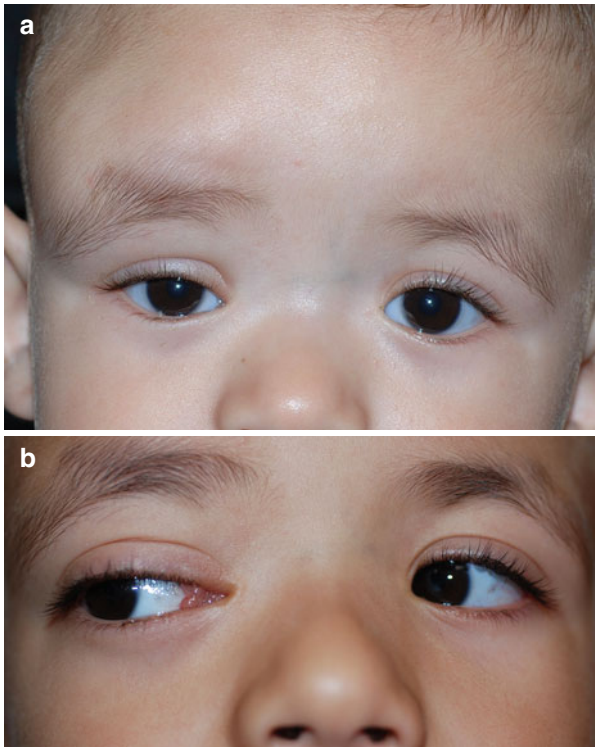

Fig. 1.3 (**a**) Extensive lymphangioma of the right forehead, brow, and orbit. (**b**) With anterior orbital extension, the lymphangioma may appear as a collection of cystic lesions in the conjunctiva

lesion and can rarely be used to guide treatment via thrombogenic coiling. This technique has limited utility, however, as the vessels often recanalize and can cause significant pain due to thrombosis [2].

Based on these physical and imaging features, malformations can be characterized into three types. Very low or no-flow lesions are primarily lymphatic lesions and include venous lymphatic malformations or lymphangiomas (Fig. 1.3a, b). The second category is low-flow lesions, which are venous in origin, and includes venous malformations. These lesions are noted on physical exam and radiography to expand with increased venous pressure. Finally, high-flow lesions have an arterial component with a direct connection between the arterial and venous components of the lesion. Arteriovenous malformations are an example of this type of lesion [5].

Additionally, malformations can be classified based on anatomical location. Superficial lesions usually involve just the eyelid or conjunctiva. Deep lesions are typically orbital without external visible components. Combined lesions have both superficial and deep components. Finally, complex lesions can be multifocal including orbital, intracranial, and systemic components and can be seen with multisystemic syndromes [5]. A summary of the classification of vascular lesion based on hemodynamics is shown in Table 1.2.

Table 1.2 Classification of malformations based on hemodynamics

Low or no flow (lymphatic malformations)	Low flow (venous malformations)	High flow (arterial malformations)
Purely lymphatic Combined venous lymphatic Lymphatic dominant Nondistensible i.e., lymphangiomas Venous dominant Distensible	Large connections to normal venous circulation Small connections to normal venous circulation i.e., cavernous hemangiomas	Direct connection from arterial side to venous side i.e., arteriovenous malformations i.e., congenital arteriovenous fistulas

1.4 Very Low or No-Flow (Lymphatic) Vascular Malformations

These lesions derive embryologically from the venous system and undergo differentiation into a primarily lymphatic lesion. The ISSVA classification divides lymphatic lesions into microcystic, macrocystic, and mixed lesions. These malformations can also be characterized as purely lymphatic malformations and combined venous lymphatic malformations. Some combined lesions are lymphoid dominant, while others are venous dominant. Venous dominant lesions tend to be distensible, while lymphoid dominant lesions are not distensible and are commonly referred to as lymphangiomas. The deeper orbital portions of these mixed lesions tend be more venous. Venous dominant lesions tend to present at an earlier age (average 6 years), while lymphatic dominant lesions tend to present later (average age 13 years). Histopathological features of these vascular malformations include lymphorrhages, hemorrhages, lymphatic vessels, dysplastic venous channels, and smooth muscle [2].

Lymphatic malformations and venolymphatic malformations vary in clinical appearance based on anatomic location. Superficial lesions of the conjunctiva may appear as clear cystic structures filled with xanthochromic material. Under the skin, they may appear bluish in color. These superficial lesions can usually be removed by surgical excision. These are typically considered solid, microcystic lymphangiomas. Direct excision can usually be performed without significant bleeding, but the lesion margins can be difficult to determine. Deep lesions can present with sudden proptosis due to hemorrhage or sudden increase in size related to concurrent illness. Sudden bouts of hemorrhage are due to capillary tufts present within macrocystic walls in the lesion. This is common with lymphatic dominant venolymphatic malformations (lymphangiomas). Management of these lesions may be warranted if sudden hemorrhage causes orbital congestion and compressive optic neuropathy, for ocular exposure secondary to proptosis, or for disfiguring appearance. Interventional treatment methods include simple aspiration and surgical excision. Surgical excision is more difficult with combined lesions and may require concomitant carbon dioxide laser treatment, gluing with fibrin or cyanoacrylate, or circumferential panorbitotomy [5]. Intralesional sclerotherapy has also shown recent

promise in the treatment of these lesions. Combined lesions may have features of both superficial and deep vascular malformations. These malformations are usually more defined in their anterior aspect and more irregular posteriorly. The posterior aspect may be more firmly adherent. Often the more superficial lymphatic portion of combined lesions can be excised, whereas the deeper part is more venous and may require clipping or gluing of the outflow tract with excision. Combined lesions are more likely to be extensive, even extending sometimes into the intracranial space via the superior orbital fissure. Complex lesions can involve other parts of the body as well, and if a lesion extends beyond the eyelids, the remainder of the face including the cheek and mouth should be checked for vascular malformations [2].

1.5 Low-Flow (Venous) Vascular Malformations

Venous flow lesions can have large connections to the normal venous circulation or smaller connections. Large connections result in distensibility of the malformation, whereas smaller connections do not result in distensibility. The less expandable lesions have more sluggish blood flow and therefore are more likely form clots or hemorrhages. There can be variation in the anatomic location of expandable venous flow malformations. Superficial lesions appear as dilated venous structures visible on the lid or subconjunctival surface. Deeper lesions may expand based on body position or Valsalva and may result in intermittent proptosis, hemorrhage, or enophthalmos due to atrophy of orbital fat. Thrombosis may occur and phleboliths may be present on imaging with peripheral enhancement around the clot [5]. Combined and complex lesions may additionally involve intracranial or systemic structures. On imaging, these lesions can appear distended especially during dynamic CT or MRI, where the patient is asked to Valsalva during the study. One study showed that 60 % of distensible venous malformations show enlargement with Valsalva clinically, while the remaining 40 % show distension on imaging (Fig. 1.4) [2]. Venography or direct intralesional injection would show a dilated mass of vessels flowing into normal outflow veins or into aberrantly shaped venous channels. Surgical excision of expandable venous malformations is difficult because the abnormal vessels are thin and prone to bleeding. Approaches to limit bleeding include ligation or glue embolization of outflow channels prior to excision of the lesion [5]. Intralesional coiling has been performed but often results in recanalization and the resultant thrombosis can cause significant pain [7]. Sclerotherapy with alcohol has been used although this is generally avoided intraorbitally because of the subsequent inflammatory response. Less inflammatory sclerosing agents such as bleomycin and doxycycline have also been used [8]. Indications for intervention include pain due to thrombosis, cosmesis, significant enophthalmos, or severe hemorrhage. Most hemorrhage can be observed for resolution, while thrombosis may take a long time to resolve [2].

Venous flow malformations which have smaller outflow channels, and which are therefore not as distensible, are clinically similar to lymphangiomas with both

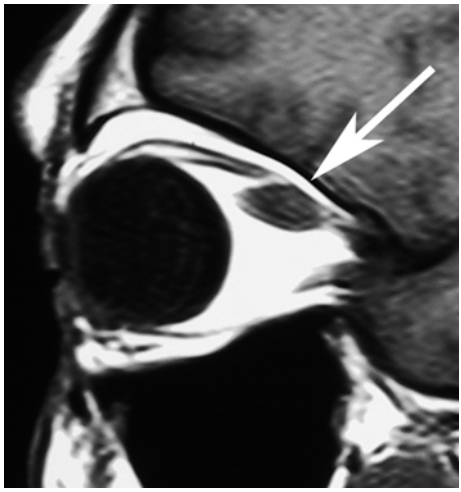

Fig. 1.4 MRI scan demonstrating a large venous malformation in the superior orbit (*arrow*)

lesions having low or no flow. Lymphangiomas, especially the more superficial portions, are filled with clear lymph fluid, whereas nondistensible venous malformations have blood-filled vessels. On histopathology, lymphangiomas have both lymph-filled and blood-filled endothelially lined vessels, whereas varices have just venous, blood-filled channels. Unless undergoing sudden growth in the setting of an upper respiratory tract infection, lymphangiomas can present clinically very similarly to a varix with episodes of sudden pain or proptosis due to bleeding or thrombosis. Both lesions are likely of similar venous origin, with lymphangiomas having undergone further differentiation to lymphatic vessels. Imaging of nondistensible venous flow malformations appears as a cystic mass due to the presence of a pseudocapsule. The treatment of nondistensible venous malformations involves removal of thrombosis and the related hemorrhagic cystic lesion [5].

The cavernous hemangioma is the most frequently diagnosed orbital vascular malformation (Fig. 1.5). It is typically considered a vascular hamartoma but is actually more appropriately characterized as a venous flow vascular malformation with low flow. They typically present as slow-growing, discrete masses that may present with gradual proptosis but often few other manifestations. On CT or MRI scan, the lesion may appear as a well-demarcated mass that enhances with contrast administration. Contrast filling may be uniform or patchy. Angiography may show focal early filling followed by gradual filling in the venous stage which is consistent with the low-flow inflow and outflow connections of the malformation. Ultrasonography shows medium reflectivity within the lesion and high reflectivity along the edges. Typically, these lesions are encapsulated and well demarcated but can often have vessels or nerves associated with the capsule. Histopathologically, thrombosis and neovascularization have been seen, suggesting slow growth over time. Cavernous hemangiomas usually do not need to be excised unless there is pain, excessive proptosis, or optic nerve compression. The lesions are very unlikely to cause acute changes [2].

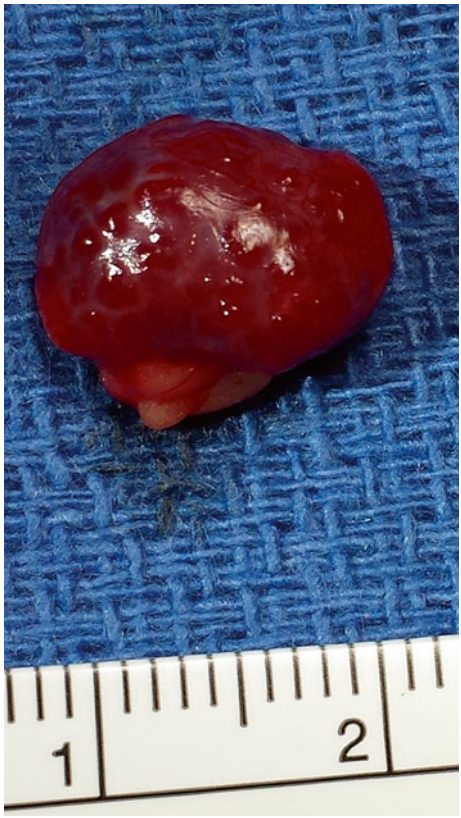

Fig. 1.5 Cavernous hemangioma after excision from the posterior orbit

1.6 High-Flow (Arterial) Vascular Malformations

These lesions are arteriovenous malformations with a direct connection from the arterial side to the venous side of the lesion. Clinically, this results in proptosis with pulsatility. A bruit may be present. The lesion may enlarge with Valsalva. There may be episodes of hemorrhage or thrombosis which can result in the acute onset of pain, proptosis, and bruising. These clinical signs are the result of the altered blood flow patterns within the lesion. Arteriovenous malformations get larger with time as they slowly come to involve more arterial inflow vessels [2, 5] If the lesion is peri-orbital, it may cause shunting of blood flow from the orbit causing ischemic changes to the orbit [9]. On CT or MRI scan, these lesions appear as large, irregular masses which enhance with contrast. Ultrasonography would show high flow through the lesion. Angiography would show a rapid transit from the dilated arterial portion of the malformation through the lesion into the venous portion. Treatment of these lesions can be preceded by identification and embolization or ligation of the arterial portions of the lesion to minimize bleeding during subsequent surgical excision of the central portion [2, 5]. Other treatment modalities include alcohol sclerotherapy,

intralesional injection of the malformation, or ablative laser treatment. Another example of a high-flow arteriovenous malformation is the congenital fistula [2].

1.7 Summary

Classification systems such as the ISSVA classification system and a hemodynamically based system have aided in the organization of vascular lesions into categories which facilitate diagnosis and treatment. However, the terminology of some lesions, however, may remain confusing [10]. Current classification systems are useful for characterizing lesions based on clinical and radiographic features and provide a useful structure for guiding treatment. However, a completely integrated classification system has yet to be developed.

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Chapter 2
Imaging Vascular Lesions of the Orbit and Face

Jed Poll, Michael T. Yen, and Suresh K. Mukherji

Imaging can be crucial in establishing a diagnosis of any mass or lesion. This is especially apparent with orbital lesions where direct physical examination can be limited. The aim of this chapter focuses on describing radiographic features of various vascular lesions and malformations commonly found in the orbit and face. Logically, a good basis of understanding of various imaging modalities, especially magnetic resonance (MR) imaging, is critical in appreciating the features highlighted in the representative images.

Interpretation of MR images can be complicated; however, the basics of MR imaging can be readily adopted and utilized by an experienced clinician. On T1-weighted images, fluid is dark (hypointense), fat is bright (hyperintense), and soft tissues tend to be gray depending on the intrinsic water and fat content of the respective tissues. T1-weighted images usually show normal anatomy but can also be useful demonstrating pathology, especially after contrast administration. On T2-weighted images, fluid is bright (hyperintense). Many pathologic processes cause edema that increases water content making the T2-weighted images of the lesions brighter. More sophisticated sequences and techniques can add value to an imaging study and aid in bringing out pathologic features.

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2.1 Hemangiomas

Hemangiomas are common vascular tumors involving the head and neck. While oftentimes the diagnosis can be made on clinical observation, imaging modalities such as MR can be important in confirming the diagnosis. Furthermore, understanding the typical radiographic appearance of hemangiomas can guide us in identifying and distinguishing them from other vascular malformations.

Classic hemangiomas have a typical bimodal course in clinical observation, characterized by rapid growth followed by slow resolution during which the vascular tumor is replaced by a fibroadipose deposition. This pattern is also reflected in the appearance of hemangiomas on MR imaging. During the proliferative, biologically active phase, they have a characteristically different appearance than during the involuting phase [1].

The radiographic appearance of a hemangioma in the proliferative phase is characterized by a lobulated, solid mass with uniform, robust enhancement and the presence of intralesional flow voids (Fig. 2.1a). Flow voids are an MR equivalence of high flow, characteristic of arterial flow seen in various arterial

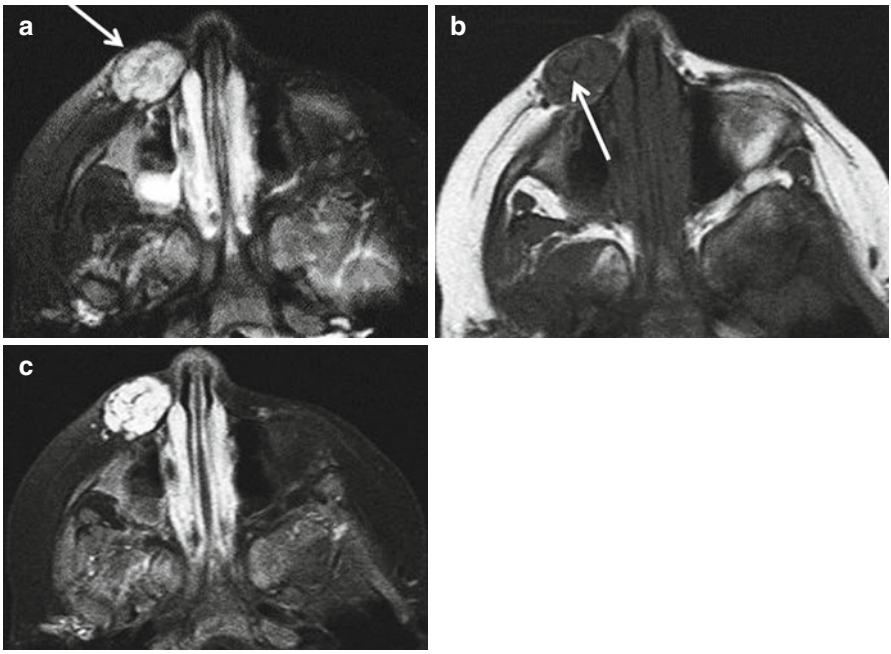

Fig. 2.1 Hemangioma: (**a**) axial T2-weighted MRI shows a lobulated high-signal mass (*arrow*) located in the right nasolabial fold. (**b**) The lesion has intermediate signal on the non-contrast T1-weighted image. The *arrow* demonstrates a serpiginous area of low signal within the hemangioma that is characteristic of a "flow void" indicating a "high-flow" vascular lesion. (**c**) Axial T1-weighted image performed after contrast administration and with fat-suppression shows that the mass avidly enhances which also increases the conspicuity of the dark flow voids

malformations and proliferative hemangiomas. On MR imaging, flow voids are dark spots within the lesion, readily identifiable in bright T2-weighted images and post-contrast enhancement T1-weighted images. On T1-weighted imaging, hemangiomas are dark, lobulated masses that then enhance with contrast with the intralesional flow voids (Fig. 2.1b). T2-weighted images of hemangiomas show a bright, high signal, lobulated mass with dark flow voids. Robust enhancement of hemangiomas is also characteristic on computed tomography (CT) imaging [2–4] (Fig. 2.1c).

During the involuting phase, hemangiomas transition to a low-flow vascular lesion. As a consequence, the dark flow voids are absent on imaging. Involuting hemangiomas maintain a characteristic lobulated appearance and continue to show robust, uniform enhancement on post-contrast T1-weighted images. The presence or absence of flow voids not only indicates activity of the hemangioma but also can guide treatment options [5, 6].

2.2 Vascular Malformations

Capillary malformations consist of birthmarks or port wine stains. They are typically seen in the V1 or V2 distribution of the face. Secondary to the benign nature of the lesion, imaging is not often indicated. On MR imaging, capillary malformations are characterized as very thin or linear and serpiginous. Capillary malformations are low flow and therefore do not exhibit flow voids. On T2-weighted images, capillary malformations display bright, thin, linear flow confined superficially to the skin [7] (Fig. 2.2).

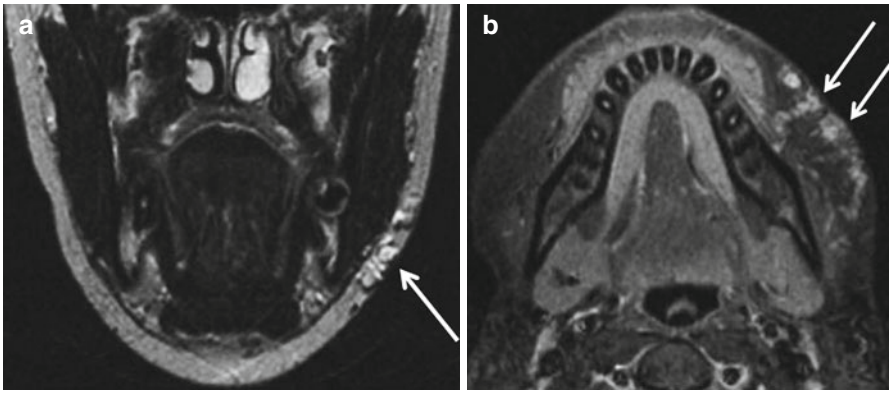

Fig. 2.2 Capillary malformation: (**a**) coronal T2-weighted image performed through the oral cavity illustrates subtle increased T2 signal involving the cutaneous and subcutaneous tissue overlying the left mandible (*arrow*). There is no deep extension into the deep musculature. (**b**) Axial T2-weighted MRI obtained through the same region shows thin serpiginous enhancement in the dermis and subdermal region (*arrows*). The enhancement is due to the increased capillary component of this type of low-flow vascular malformation

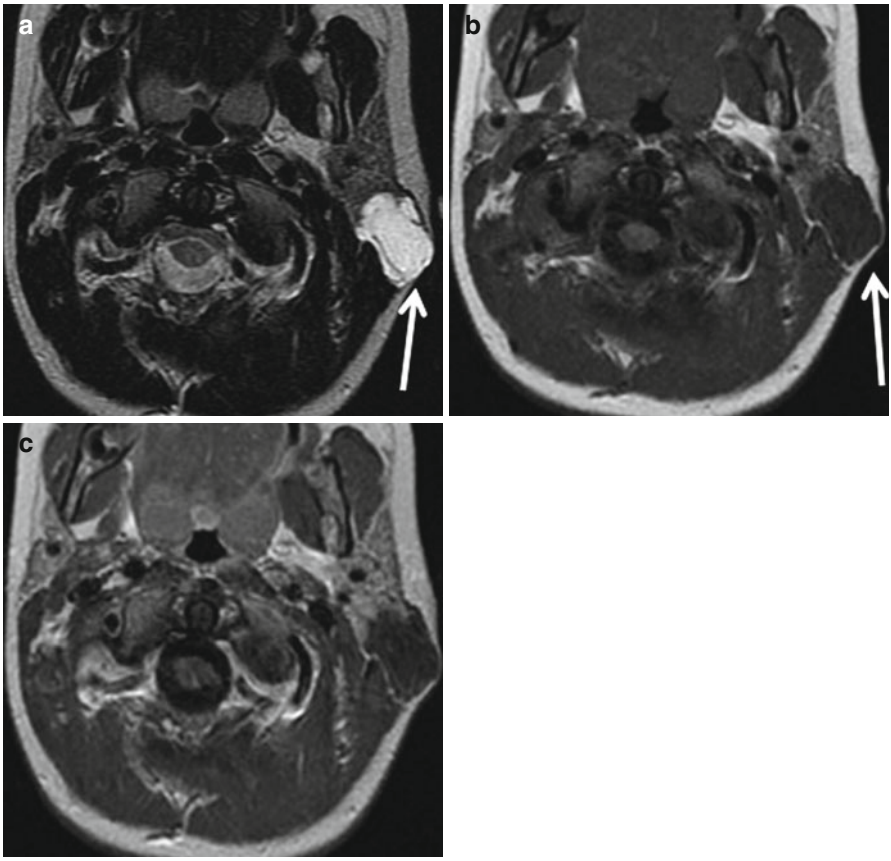

Fig. 2.3 Lymphatic malformation: (**a**) axial T2-weighted imaged demonstrates a high-signal mass (*arrow*) involving the posterior aspect of the parotid gland extending posteriorly and abutting the anterior aspect of the sternocleidomastoid muscle. (**b**) Non-contrast axial T1-weighted images show that the mass is low signal (*arrow*). The presence of high T2 and low T1 signal indicates that the mass is cystic. (**c**) The contrast-enhanced T1-weighted images show that the mass does not enhance indicating there is no vascular solid component, thereby confirming the clinical suspicion of a lymphatic malformation

Lymphatic malformations, formerly known as lymphangiomas or cystic hygromas, have a very classic MR appearance. Similar to hemangiomas, lymphatic malformations are characterized by a lobulated mass with a high signal on T2-weighed images and low signal on T1-weighted images (Fig. 2.3a, b). However, unlike hemangiomas, there is no post-contrast enhancement, and because this is a low-flow lesion, flow voids are naturally absent. Lymphatic malformations are essentially a sack of fluid, but there can be multiple septations which also do not exhibit enhancement on imaging (Fig. 2.3c). The soft, pliable nature of these malformations allows them to involve multiple anatomical locations and displace normal structures [8].

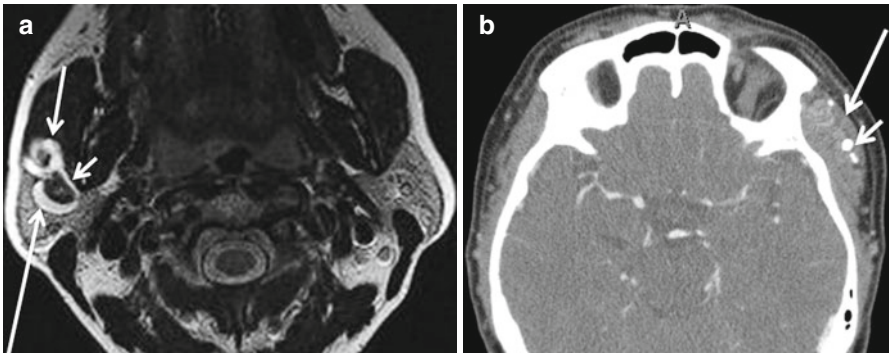

Fig. 2.4 Venous malformation: (**a**) axial T2-weighted image shows heterogeneous mass in the right parotid gland. (*large arrow*) The mass is predominantly increased T2 signal and extends into the right masseter muscle indicating an intramuscular component. (*intermediate arrow*) The high-signal mass contains focal areas of low signal (*short arrow*) that is due to clot within the venous malformation. (**b**) Contrast-enhanced CT in a different patient show enlargement of the left temporalis muscle. (*long arrow*) There are focal areas of increased attenuation due to calcified phleboliths indicating a venous malformation involving the left temporalis muscle. (*short arrow*)

Venous malformations, formerly known as cavernous angiomas, are the most common vascular malformations. Like their lymphatic counterparts, MR imaging of a venous malformation usually shows a lobulated mass with a high T2-weighted signal (Fig. 2.4a). Again, because venous malformations are low-flow lesions, flow voids would be absent. Distinguishing features of venous malformations are a classic intramuscular location and the presence of phleboliths (Fig. 2.4b). Phleboliths represent calcifications within the malformation. With any intramuscular lesion with a high T2-weighted signal, a venous malformation would be a high likelihood diagnosis. However, a venous malformation elsewhere in the soft tissues would make the diagnosis difficult to distinguish from a lymphatic malformation. A key difference would be the presence of phleboliths and the presence of slow, post-contrast enhancement of the venous malformation. Because there is low venous flow, the diagnosis can be confirmed with ultrasonography. Also, because there is slow flow in the venous malformations, clots can develop which appear as low signal densities with the mass on T2-weighted images [9, 10].

True arterial malformations are a rare diagnosis. The classic example is that of a carotid-cavernous fistula. Images with MR or contrast-enhanced CT would demonstrate considerable enlargement of the superior ophthalmic vein (Fig. 2.5). CT angiography would better define the anatomic details; however, conventional angiography is the diagnostic test of choice, especially if endovascular treatment is being considered [11].

Mixed versions of malformations exhibit features of their components. Arteriovenous malformations are characterized by large flow voids owing to high, arterial flow encountering slow, venous flow. Time resolved angiography or direct angiography can be beneficial in distinguishing venous from arterial in these malformations. Venolymphatic malformations appear as a lobulated lesion with internal

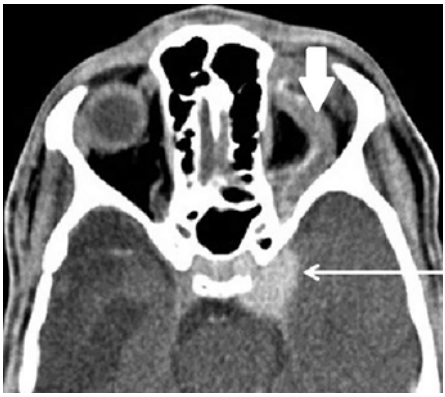

Fig. 2.5 Cavernous-carotid fistula (CCF): axial contrast-enhanced CT show an enlarged and asymmetrically enhancing left cavernous sinus. (*long arrow*) This is associated with a markedly enlarged and tortuous super ophthalmic vein. (*short arrow*) The enlarged vein is due to "reversed" arterialized flow from the direct CCF

blood-fluid levels. Again, because both components are low flow, flow voids are absent. Capillary lymphatic malformations look like lymphatic malformations but do exhibit post-contrast, linear enhancement characteristic of capillary malformations. With mixed vascular malformations, there are three or more components. Diagnosis is aided by identifying key elements such as enhancement, flow voids, and phleboliths [12].

2.3 Summary

Imaging of hemangiomas and vascular malformations is oftentimes crucial in establishing a proper diagnosis and guiding treatment options. The presence or absence of flow voids is especially important from a therapeutic standpoint as high-flow malformations demonstrating flow voids are typically treated endovascularly. Low-flow malformations, without flow voids, can be treated with direct injection or sclerotherapy. Future chapters will further address these lesions with their respective treatments.

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Chapter 3
Vascular Malformations of the Retina and Posterior Segment of the Eye

Nora Khatib and Robert E. Coffee III

3.1 Macular Telangiectasia

Macular telangiectasia, also known as idiopathic juxtafoveal telangiectasia, is a vascular abnormality that affects the capillaries in the posterior pole. There are two types of macular telangiectasia: type 1, which is a congenital unilateral vascular anomaly and may be a part of the spectrum of Coats disease, and type 2, which is typically bilateral with onset in middle or older age. Macular telangiectasia is a rare vascular condition, and the incidence of macular telangiectasia type 2 ranges from 0.0045 to 0.1 % [1, 2]. Visual disturbances are typically mild, usually consisting of mild metamorphopsia or a scotoma [3, 4]. Visual acuity may decline with progression of the disease, but visual acuity less than 20/200 is rare [5, 6]. The earliest sign is a loss of temporal retinal transparency, or a grayish discoloration, followed by dilation of temporal parafoveal capillaries [5, 6]. Abnormal capillaries can be noted to make a right-angle turn diving deeper into the retina. Later on, retinal pigment epithelium migration and hyperplasia along abnormal capillaries can be noted as well as retinal atrophy [5, 6]. Perifoveal crystalline deposits may be seen (Fig. 3.1). The diagnosis can be made with fundus autofluorescence imaging, which reveals a loss of the hypofluorescent center of the macula due to the depletion of macular pigment. This change is one of the earliest signs and is diagnostic of the disease [7]. Fluorescein angiography shows telangiectatic capillaries, beginning temporal to the macula, with late staining [6]. Optical coherence tomography shows an early enlargement of the temporal side of the foveal pit followed by

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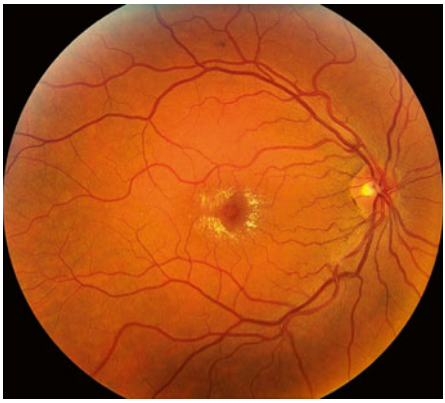

Fig. 3.1 Perifoveal crystalline deposits in macular telangiectasia type 2

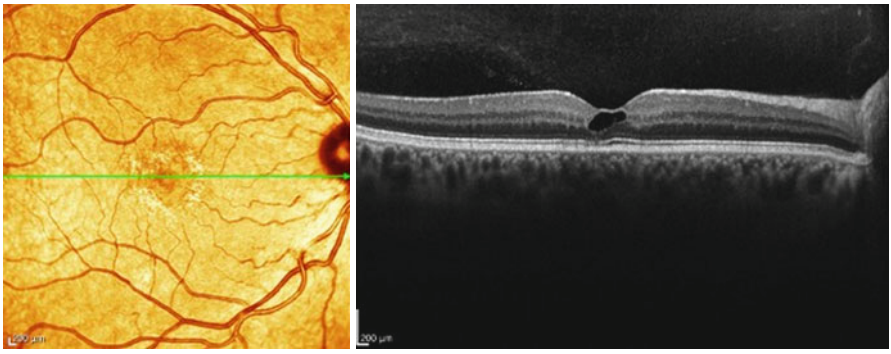

Fig. 3.2 Optical coherence tomography of the macula in macular telangiectasia type 2 showing pseudocystic spaces in the fovea caused by loss of tissue

disruption in the outer retinal and photoreceptor layers (Fig. 3.2). The development of retinal cavities and hyporeflective spaces at times leaving only the overlying internal limiting membrane, without corresponding leakage on fluorescein angiography, occurs with disease progression due to loss of retinal layers [7]. The most feared complication is the development of retinal neovascularization. Currently, there is no effective treatment of the disease. In cases of retinal neovascularization, the mainstay of treatment is intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF). The visual prognosis is good with 50 % maintaining visual acuity 20/32 or better [8].

3.2 Retinal Arterial Macroaneurysm

Retinal arterial macroaneurysms (RAMA) are fusiform outpouchings or dilatations of retinal arterioles, commonly at retinal bifurcations or arteriovenous crossings. Acquired RAMAs are generally associated with atherosclerosis and

hypertension and tend to occur in the sixth and seventh decade of life [9–12]. The location is usually in the posterior pole within the first three orders of arterial bifurcation, and 90 % are unilateral (Fig. 3.3). RAMAs can be associated with lipid exudation and hemorrhage in the subretinal, intraretinal, and preretinal space and can result in visual decline when involving the macula [13]. Fluorescein angiography demonstrates early arterial filling of the RAMA with a variable amount of late leakage (Fig. 3.4). If hemorrhage is present, the RAMA and surrounding leakage may be obscured on fluorescein angiography. Optical coherence tomography can delineate subretinal hemorrhage and intraretinal fluid and exudation. Treatment is not always necessary, because RAMAs can thrombose and spontaneously involute with clearance of associated lipid exudation [9]. When the macula is involved, treatment options include laser photocoagulation of the RAMA, pneumatic displacement for submacular hemorrhage, and vitrectomy for vitreous hemorrhage [14–16].

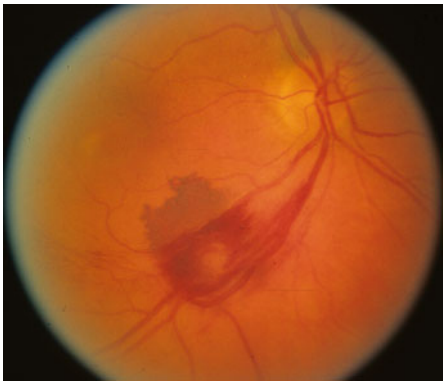

Fig. 3.3 Retinal arterial macroaneurysm surrounded by retinal hemorrhage (Image courtesy of Richard A. Lewis, M.D.)

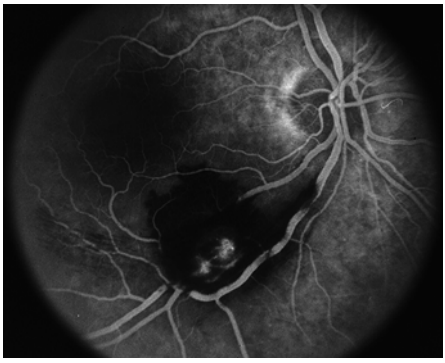

Fig. 3.4 Fluorescein angiography showing blockage owing to retinal hemorrhage and hyperfluorescence with late leakage from the aneurysm itself (Image courtesy of Richard A. Lewis, M.D.)

3.3 Coats Disease

Coats disease was originally described in 1908 by George Coats as an idiopathic condition with telangiectatic vessels and associated lipid exudation [17]. It affects males three times more frequently than females and is unilateral in 80–95 % of cases [18–20]. The average age of diagnosis is 5 years of age. Children most frequently present with decreased visual acuity, and in some cases, strabismus, leukocoria, heterochromia, nystagmus, or asymptomatically [19]. On fundus examination, telangiectatic vessels, subretinal lipid exudation, exudative detachments, retinal hemorrhage, retinal macrocyst, and optic disc neovascularization can be present (Fig. 3.5). Coats disease is typically slowly progressive. A staging system proposed by Shields et al. is summarized in Table 3.1 [19]. Fluorescein angiography reveals telangiectatic vessels and aneurysms with early and progressive leakage, peripheral retinal nonperfusion, and areas of capillary dropout. Coats disease must be differentiated from retinoblastoma, in which children can also present with leukocoria and exudative retinal detachments. Ultrasound sonography, computed tomography, and magnetic resonance imaging can aid with differentiating the two entities. Treatment of Coats disease consists of laser photocoagulation to leaking telangiectatic vessels in early stages of the disease [21–23]. Cryotherapy can also be used for peripheral lesions and lesions

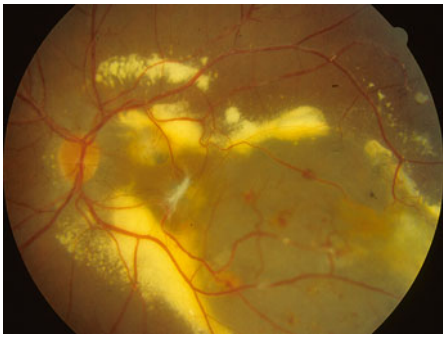

Fig. 3.5 Coats disease with telangiectatic vessels in the temporal macula leading to an exudative retinal detachment (Image courtesy of Richard A. Lewis, M.D.)

Table 3.1 Staging of Coats disease

Stage	Ocular findings
1	Retinal telangiectasias without exudation
2a	Retinal telangiectasias with extrafoveal exudation
2b	Retinal telangiectasias with subfoveal exudation
3a1	Subtotal exudative detachment, extrafoveal
3a2	Subtotal exudative detachment, involving the fovea
3b	Total exudative detachment
4	Exudative detachment with glaucoma
5	End stage

with a poor response to laser photocoagulation [24]. Treatment is often performed under anesthesia with multiple treatment sessions over the course of several months [25]. Intravitreal triamcinolone acetonide and anti-VEGF alone or in combination have also been reported to be effective in treating subretinal fluid and macular edema [26–32]. In severe cases, vitrectomy and subretinal drainage may be necessary [33–36]. Despite treatment, visual prognosis is poor due to damage to the macula. In one series, 47 % of cases had visual acuity ranging from hand motions to no light perception and another 29 % ranging from 20/200 to counting fingers [25].

3.4 Familial Exudative Vitreo-Retinopathy

Familial exudative vitreo-retinopathy (FEVR) is a bilateral ocular disease due to a genetic mutation that results in incomplete formation of the retinal vasculature. It is inherited in an autosomal dominant pattern, although X-linked transmission has been reported. The retinal findings can vary in severity, with earlier onset associated with more severe disease. On examination, ocular findings range from straightening of the retinal vessels and peripheral retinal nonperfusion to more severe forms with peripheral neovascularization, lipid exudation and subsequent exudative retinal detachments, and tractional retinal detachment as neovascular membranes contract. Treatment involves laser photocoagulation to peripheral avascular retina and vitrectomy for management of tractional retinal detachment.

3.5 Norrie Disease

Similar to FEVR, Norrie disease is due to a genetic mutation that results in incomplete development of the retinal vasculature. It is inherited in an X-linked recessive manner and can be associated with hearing loss and mental retardation. Retinal findings include peripheral retinal neovascularization, lipid exudation, and tractional retinal detachment. Treatment involves laser photocoagulation to peripheral avascular retina and vitrectomy for management of tractional retinal detachment.

3.6 Retinal Cavernous Hemangioma

Retinal cavernous hemangioma is a rare vascular hamartoma consisting of clumps of saccular aneurysms in the inner retina or on the optic nerve head (Fig. 3.6). It is typically unilateral and 1–2 disc diameters in size. The size typically does not change over time. There is no clearly visible feeding vessel, and

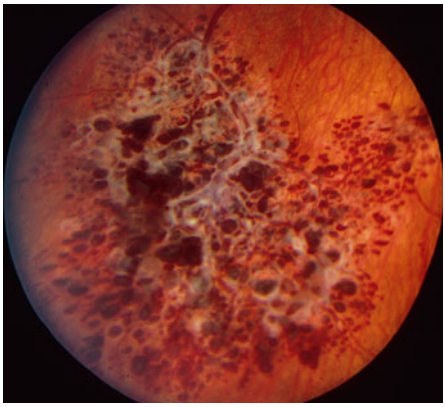

Fig. 3.6 Retinal cavernous hemangioma with grapelike clusters of malformed vessels (Image courtesy of Richard A. Lewis, M.D.)

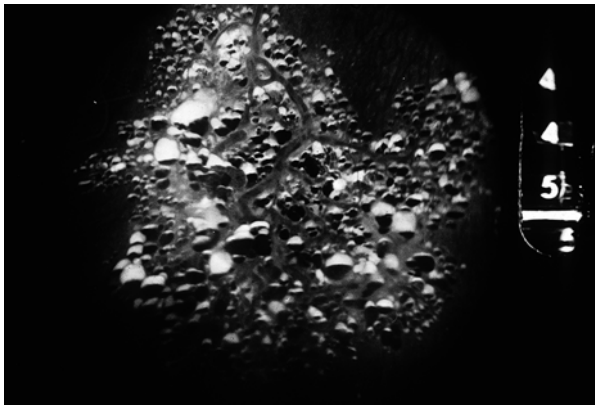

Fig. 3.7 Fluorescein angiography of the cavernous hemangioma showing the laying of dye in the saccular malformations (Image courtesy of Richard A. Lewis, M.D.)

the lesion is usually located over a vein. The aneurysms are usually filled with dark blood, giving the appearance of a "cluster of grapes." Retinal cavernous hemangioma is typically asymptomatic but has been reported to cause mild visual disturbance if located in the macula or if vitreous hemorrhage occurs [14]. Lipid exudation is rare due to the slow circulation through the aneurysms. Red blood cells can layer inferiorly within the aneurysm resulting in a plasma-erythrocyte separation. In some cases, retinal cavernous hemangiomas can be associated with cutaneous and central nervous system angiomatous lesions. Fluorescein angiography demonstrates an incomplete and slow filling of the aneurysms, with fluorescein often accumulating in the superior portion of the aneurysm while inferior accumulated red blood cells cause blockage (Fig. 3.7). Retinal cavernous hemangiomas typically do not require treatment. If vitreous hemorrhage occurs, the hemangioma can be treated with laser photocoagulation or cryotherapy.

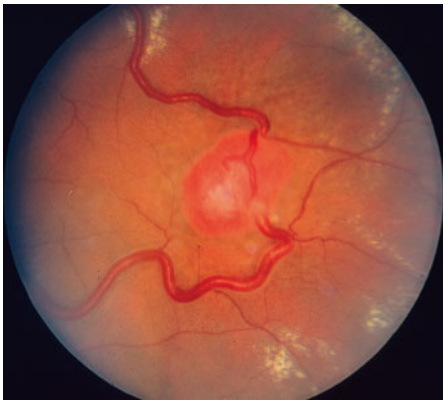

Fig. 3.8 Retinal capillary hemangioma in von Hippel-Lindau disease showing dilated feeder vessels and surrounding lipid exudate (Image courtesy of Richard A. Lewis, M.D.)

3.7 Retinal Capillary Hemangioma

Retinal capillary hemangioma is a vascular tumor that occurs as an isolated ocular lesion or part of a systemic condition known as von Hippel-Lindau disease, an autosomal dominant disorder with multiple benign or malignant lesions that occur in the retina, central nervous system, and visceral organs. Retinal capillary hemangiomas begin as small lesions, typically in the peripheral retina, that progressively enlarge over time with dilation of blood vessels to and from the lesion (Fig. 3.8). Lipid exudation from the lesion can result in an exudative retinal detachment. Late fibrosis of the lesion can cause a tractional retinal detachment [37]. Decreased vision occurs secondary to exudation in the macula and development of exudative and tractional retinal detachment. The diagnosis is made clinically, but ancillary testing can aid in diagnosis. Fluorescein angiography shows early leakage from the hemangioma that may persist or decrease with time. Ocular coherence tomography reveals the extent and amount of exudation. Treatment includes laser photocoagulation to smaller lesions and cryotherapy for larger, peripheral lesions [38–41]. Exudative and tractional retinal detachment can be managed with vitrectomy [42]. Photodynamic therapy, radiation therapy, and systemic anti-angiogenic agents have been used with limited success [43–49].

3.8 Retinal Arteriovenous Malformation (Racemose Hemangioma)

Retinal arteriovenous malformation is also known as racemose hemangioma. This is a vascular malformation in which direct anastomoses occur between the retinal arterial and venous circulation with dilation of retinal vessels (Fig. 3.9). It is nonhereditary and is associated with ipsilateral vascular malformations of the midbrain in Wyburn-Mason syndrome. There is typically no lipid exudation and no leakage on fluorescein angiography. The Archer classification scheme separates the vascular

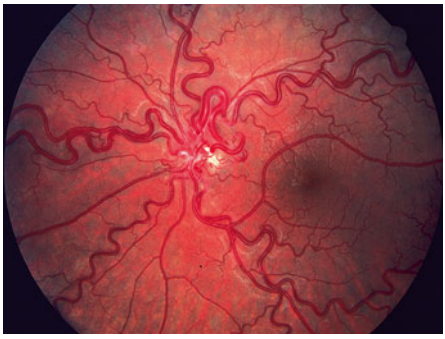

Fig. 3.9 Dilated and tortuous retinal vessels in the setting of Wyburn-Mason syndrome (Image courtesy of Richard A. Lewis, M.D.)

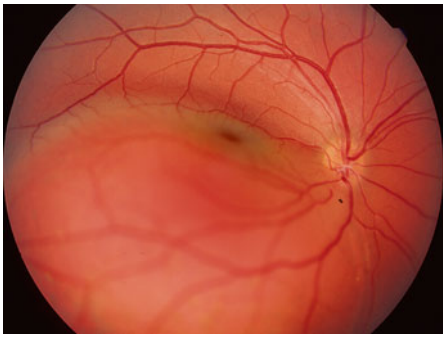

Fig. 3.10 Large choroidal hemangioma in a Sturge-Weber patient resulting in a serous retinal detachment affecting the macula (Image courtesy of Richard A. Lewis, M.D.)

malformations into 3 groups. Group 1 consists of an abnormal arteriovenous communication with an intervening capillary plexus and is typically asymptomatic. Group 2 is defined as a direct arteriovenous communication without intervening capillary vessels and with few visual symptoms. Group 3, the most severe form, consists of a complex arteriovenous communication with dilated and tortuous vessels commonly with associated visual loss [50]. Approximately 30 % of cases with retinal findings will have lesions in the central nervous system [51]. Racemose hemangioma does not require treatment.

3.9 Encephalofacial Hemangiomatosis

Encephalofacial hemangiomatosis (Sturge-Weber syndrome) is a nonhereditary disorder characterized by congenital hamartomas of the eye, brain, and skin. The most common central nervous system finding is a diffuse leptomeningeal hemangioma ipsilateral to the facial hemangioma or nevus flammeus (port-wine stain) [52]. Ocular findings include dilated epibulbar vessels, glaucoma, tortuous retinal vessels, retinal pigmentary changes, and diffuse choroidal hemangioma that results in a "tomato-catsup" fundus appearance. Diffuse choroidal hemangioma can lead to a total retinal detachment and secondary neovascular glaucoma (Fig. 3.10) [14]. On

B-scan ultrasonography, the choroidal lesion demonstrates high echogenicity. Choroidal hemangiomas that are minimally elevated can be observed. Refractive changes should be monitored closely to prevent amblyopia. Large tumors with elevation and retinal detachment can be treated with oral propranolol, photodynamic therapy, or external beam radiation [53].

3.10 Summary

Vascular malformations of the eye and retina are important to be recognized. Ocular findings can aid with the diagnosis and management of systemic disease. These disorders often require close monitoring to prevent or detect complications, and prompt treatment is required in some cases to preserve or improve vision.

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Chapter 4
Infantile Hemangiomas of the Eyelids and Orbit

Mohamed A. Hussein and Kimberly G. Yen

4.1 Introduction

Infantile hemangiomas are benign vascular tumors that typically appear in the first few weeks of life, with about one-third being present at birth [1, 2]. They occur more commonly and seem to grow larger in female patients and have a predilection to occur in the head and neck area [4]. Prematurity is another risk factor for hemangioma development [5].

Hemangiomas are felt to result from hamartomatous proliferation of vascular endothelial cells [2]. Typically, these tumors grow in two phases: a proliferative and an involutional phase [2]. During the proliferative phase, generally during the first year of life and most notably the first 3–6 months, the lesion will grow rapidly [1, 2]. The next phase, involution, is characterized by regression of the hemangioma, which frequently occurs spontaneously between 1 to 5 years of age [6, 7]. Approximately 50 % of the tumors will be gone by age 5 [1, 4], and over 75 % resolve completely and spontaneously by age 7 [8]. Regression of the lesions may sometimes be associated with soft tissue or bone deformities [9].

Periocular hemangiomas can appear as a classic strawberry nevus, subcutaneous with dark blue or purple coloration, and as deep orbital lesions [5]. The pathogenesis of hemangiomas is not well understood. It is felt that the tumors may be angiogenesis dependent due to angiogenic molecules, which are tightly regulated by inhibitors of endothelial cell growth. These angiogenic molecules may initiate formation of capillary networks [7].

When these tumors are located in the periocular region, they can interfere with proper visual development in the involved eye, leading to amblyopia. Most

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commonly, this occurs by obstructing the visual axis or by causing astigmatism through distortion of the cornea [3, 10]. The lesions can also be cosmetically disturbing. Orbital hemangiomas can cause strabismus from globe compression or can extend in the retrobulbar space causing optic nerve atrophy [3]. Although a small and slowly growing tumor can be observed, large tumors may require early treatment [1].

4.2 Patient Evaluation

Amblyopia is the most common ocular complication from periocular infantile hemangiomas and generally occurs from anisometropia, visual deprivation, or a combination of both etiologies [1]. All patients require a comprehensive dilated exam including assessment of fixation behavior (if preverbal), visual acuity assessment, and cycloplegic refraction. Evaluation of motility and pupils is also important as orbital lesions can compress the optic nerve or impinge on the extraocular muscles, affecting motility.

Amblyopia has been found to occur in up to 46 % of patients with periocular infantile hemangiomas [1]. Because patients with periocular hemangiomas often present in the first several months of life when the visual system is developing, amblyopia is a major concern. Anisometropia occurs from the indentation the mass can cause on the globe causing anisometropic astigmatism, leading to amblyopia; deprivational amblyopia can result if the tumor causes the eyelid to obstruct the visual axis. As expected, larger, more diffuse hemangiomas, especially those greater than 1 cm, are associated with a greater risk of amblyopia. Nasal location of the lesions on the upper eyelid also increases the risk of amblyopia [5].

At initial evaluation, if the child has a clear visual axis and symmetric refractive state, observation may be initiated, although the child should be examined at regular intervals during the growth phase. Presence of significant astigmatism and anisometropia warrants treatment. It is important to educate families of children who undergo treatment to reduce the size of the hemangioma that astigmatism may persist, even after the lesion has been treated. Continued management of the amblyopia is imperative, even after the cosmetic appearance of the lesion has improved.

Treatment of amblyopia induced by hemangiomas generally involves prescribing glasses to correct the refractive error. Treating and monitoring the amblyopia until visual maturity is reached is necessary. Patching or other penalization treatment may need to be initiated. In patients who have orbital lesions, neuroimaging may be required to delineate the mass and confirm diagnosis.

4.3 Systemic Associations

Patients with lesions of the eyelids and orbit may have hemangiomas elsewhere as well [9]. In these patients, the PHACES syndrome should be considered; approximately 2 % of patients with hemangiomas meet the criteria for PHACES syndrome

[11]. PHACES is an acronym for *P*osterior fossa brain malformations, *H*emangiomas of the face, *A*rterial cerebrovascular anomalies, *C*ardiovascular anomalies, *E*ye anomalies, and *S*ternal defects [12]. Any patient with a large facial lesion should be evaluated for PHACES. This evaluation may include a cardiac echocardiogram as well as MRI/MRA of the brain and the chest [13].

About 16 % of patients with PHACES syndrome can have associated ocular abnormalities including Horner's syndrome, retinal vascular abnormality, optic nerve atrophy, iris vessel hypertrophy, iris hypoplasia, congenital cataracts, sclerocornea, lens coloboma, strabismus, choroidal hemangiomas, congenital third nerve palsy, morning glory deformity, and peripapillary staphyloma [12]. The hemangiomas in PHACES syndrome are often described as segmental, meaning that the lesions are large and plaque-like, covering a large cutaneous area. These patients also frequently have structural malformations of the central nervous system, especially cerebrovascular abnormalities as well as nonspecific neurologic sequelae such as developmental delay and seizures [12].

4.4 Treatment

The main goal of the treatment of periocular hemangiomas is to decrease the size of the lesion and clear the visual axis removing the effects of the pressure from the globe [13]. Studies have demonstrated worse visual outcome in hemangiomas that occlude the pupil [14]. Reduction in the size of the hemangioma has been demonstrated to reduce the amount of anisometropic astigmatism [14]. Earlier treatment, especially before the age of 6 months, has also been demonstrated to reduce the risk of residual amblyopia. Treatment of these hemangiomas, therefore, should be aimed at both treating the amblyopia and anisometropia as well as reducing the size of the lesion, especially in the situation of pupillary occlusion [14].

Corticosteroids have long been the mainstay of treatment for hemangiomas with various modalities of treatment that include topical, intralesional, and systemic steroids, all with variable success [3, 15–21]. Each modality, however, is associated with its own risks.

Local steroid injections require, in many cases, general anesthesia for the injections and can be associated with serious adverse effects such as central artery occlusion, resulting in vision loss [9, 18, 20]. Other complications include subcutaneous fat atrophy, depigmentation of the skin, adrenal suppression, orbital cellulitis, and Cushingoid effects [3, 9, 13, 18]. Full-thickness eyelid necrosis has also been reported [3]. Intralesional injection of a new compound of glucocorticoids preparation, Diprospan, a combination of short-acting and long-acting betamethasone, has been most recently reported to successfully treat small-sized infantile hemangiomas of the face and the neck [22]. Side effects included local atrophy, ulcer, and Cushingoid manifestations; however, all the side effects were reported to regress [22].

Systemic steroids are associated with serious systemic side effects, such as hypertension, adrenal insufficiency, immunosuppression, and gastrointestinal bleeding [3]. The use of these steroids requires close monitoring by pediatricians [23].

Even when used on a short-term basis, complications can include Cushingoid facies, changes in personality, and gastric irritation, as well as growth retardation [23].

Interferon alpha 2a has also been used, both primarily and in lesions that have failed corticosteroid treatment, with varying degrees of success [24]. This treatment has generally been reserved for life- or sight-threatening lesions [3]. These injections are often performed on a daily basis over a few months and can be associated with hepatotoxicity, neurotoxicity, and myelosuppression [3, 9]. Imiquimod—an imidazoquinoline amine—has also been shown to be useful in the treatment of infantile hemangioma [25]. Argon laser therapy has been used as a second-line treatment and can be successful in reducing the size of the lesion; however, it leaves residual tumor [8]. Scarring, pigmentation changes, and intralesional hemorrhage are some of the complications that can occur from laser treatment [8].

Simple surgical excision of the tumors plays an important role in the treatment of well-circumscribed hemangiomas or as an adjunct in patients in which pharmacologic treatment has not provided adequate response [13, 26, 27]. In some cases, debulking rather than full resection is all that is possible. In situations in which the tumor is not well encapsulated, the surgery can be difficult and significant bleeding can occur [27]. Identifying the anatomic landmarks, especially the levator muscle, is important, and imaging prior to surgery allows the surgeon to evaluate the extent of the lesion [13]. As with any surgery, the inherent risks of anesthesia and surgery exist.

4.5 The Role of Propranolol

Propranolol is a nonselective beta-blocker, indicated for use in hypertension, arrhythmias, and migraine [28]. The first report of the use of propranolol in the treatment of infantile hemangioma use was by Leaute et al. in 2008 as an incidental finding in two patients who were being treated with propranolol for hypertrophic cardiomyopathy [3, 29]. In these children, the growth of the hemangiomas regressed significantly; nine additional patients with hemangiomas that obstructed their airways were treated similarly, again with significant decrease in the size of the hemangiomas [28]. Unlike with the use of systemic steroids, the hemangiomas showed no rebound growth after the propranolol was stopped [30]. Successful treatment with oral propranolol as a first-line therapy has subsequently been reported with a dosage of 2–3 mg/kg/day given in two or three divided doses [29].

Other reports of the use of oral propranolol in the management of ocular infantile hemangioma have followed in multiple specialties, all with similar positive results [28, 30–35]. Propranolol demonstrated rapid and significant reduction in the size of the hemangiomas in most cases. This medication has been used to treat hepatic hemangiomas and hemangiomas of other locations as well [33]. Additionally, oral propranolol appeared to be safe with no reported serious systemic complications in these reports.

4.6 Choice of Patients

Candidates for treatment with propranolol include infants with large hemangiomas, rapidly growing hemangiomas, orbital hemangiomas, or cosmetically unappealing hemangiomas. Hemangiomas that obstruct the visual axis or cause astigmatism, putting the patient at risk of amblyopia, are good candidates for treatment as well. Propranolol has also been found to be effective in patients who failed treatment with systemic corticosteroids [32].

Propranolol should not be used in infants who have any contraindications to the use of beta-blockers. Examples include infants with a history of bronchial asthma or known cardiac problems, specifically cardiac conduction defects [32]. Additionally, infants may not be able to be treated with propranolol if they have known systemic vascular associations, as in infants with PHACES syndrome. Patients with suspected PHACES syndrome require imaging of the cerebral blood vessels as these patients can be at risk for cerebral ischemia and brain blood perfusion [32].

4.7 Protocol for Treatment

There is still no standard protocol for treatment; however, clearance from the patient's pediatrician is recommended. Careful evaluation of the patient is important prior to initiating treatment with propranolol. Many institutions will coordinate care with primary care physicians, cardiologists, and dermatologists due to the concern of systemic side effects.

In general, most infants will require a baseline EKG and cardiac evaluation prior to beginning treatment. Evaluation of the patient's vital signs and glucose is also necessary. PHACES syndrome or a high index of suspicion for visceral lesions should be raised if the patient has large segmental hemangiomas or multiple lesions [3]. Parents should be educated to recognize signs and symptoms of side effects, such as lethargy, poor feeding, bronchospasm, and bradycardia.

If the cardiac evaluation and EKG are normal, infants can be started on oral propranolol at a dose of 1 mg/kg/day in four divided doses that can be titrated gradually to 3 mg/kg/day. Treatment with propranolol at a dose of 3 mg/kg/day for 6 months has been shown to result in a significantly higher success rate as compared with placebo [36].

Treated infants may be followed monthly for the first 3 months and then every 2–3 months. At each exam, external photographs should be taken to evaluate the size of the tumor. In addition, visual fixation, ocular motility, and pupillary responses should be tested. Cycloplegic refraction and dilated fundus examination should be performed prior to treatment and then every 3 months after treatment. Glasses and amblyopia treatment should be provided as indicated in patients who meet the standard criteria.

Laboratory investigations to assess for side effects of propranolol should be done on a routine basis. Suggested labs and clinical assessments include measurement of glucose levels from finger-prick blood samples; physical examination, including pulmonary auscultation, liver palpation, and assessment of vital signs; assessment of neurodevelopment (normal or abnormal); and electrocardiography [36].

Treatment is generally stopped when it is felt that the infant has had stable reduction in the size of the tumor or stable refraction. In older infants, treatment is generally stopped when the tumor is felt to have entered into the involutional phase. Treatment can be reinstituted if the tumor is found to increase in size after cessation of treatment.

4.8 Response to Treatment

A treatment effect can be seen as early as the first week after initiating treatment. The initial effect is seen mostly in the form of decreased tension and firmness of the tumor before the tumor starts decreasing in size. Up to 60 % of hemangiomas are expected to have complete resolution by week 24 from starting treatment, with 88 % showing some improvement by week 5. Approximately 10 % of hemangiomas have poor response to the treatment [36]. Tumors in all different anatomical locations have been reported to respond favorably to oral propranolol including eyelid, periorbital, and even large orbital infantile hemangiomas [37, 38] (Figs. 4.1 and 4.2). Studies that have evaluated the decrease in astigmatism have demonstrated reduction of the amount of astigmatism in 60–83 % of patients after the use of propranolol treatment [3].

4.9 Adverse Effects

Side effects of propranolol include allergy, hypotension, bradycardia, and bronchospasm; however, these complications seem to be infrequent at the dosage that is used for treatment of infantile hemangioma [28]. Bronchospasm generally occurs as an exacerbation in patients with known reactive airway disease, and a history of this should be obtained prior to initiating treatment [34]. Heart-rate decreases have been reported and typically have occurred within 1 h after dose administration [36]. Propranolol also has been reported to mask the clinical signs of hypoglycemia in infants, a risk that is probably a greater consideration during the first week of life [34]. The risk of hypoglycemia may be minimized with proper education of parents or guardians about the importance of administering propranolol as prescribed (i.e., during or right after feeding) [36].

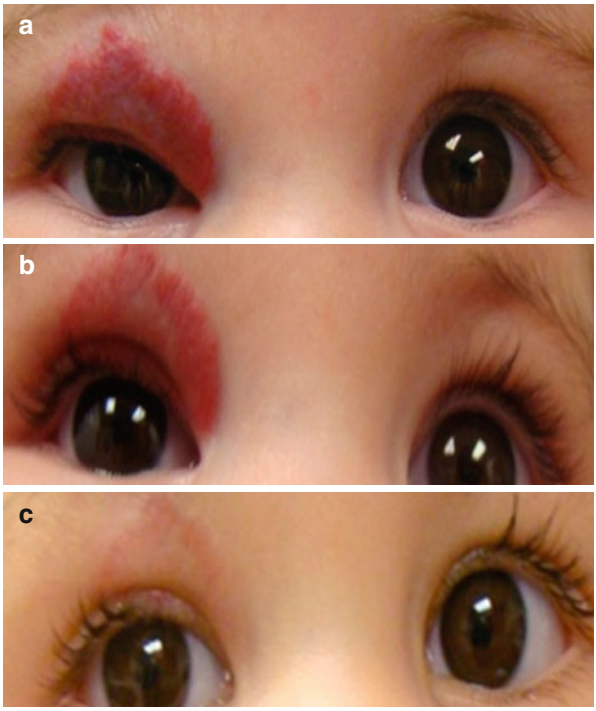

Fig. 4.1 (**a**) Eyelid hemangioma prior to treatment with propranolol. (**b**) One month after treatment. (**c**) Three months after treatment

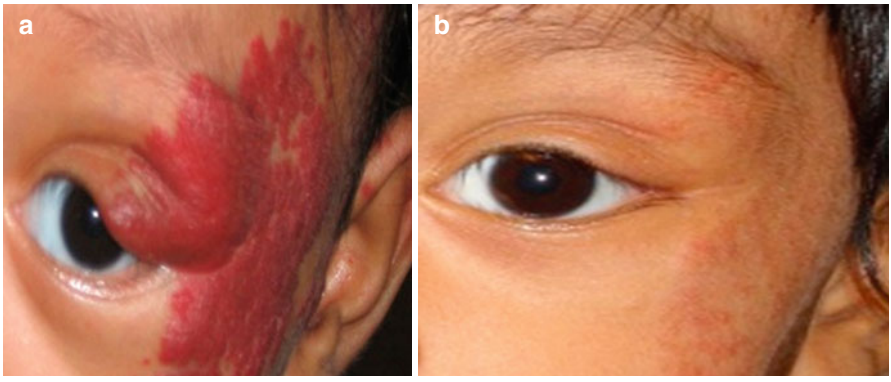

Fig. 4.2 (**a**) Facial hemangioma in PHACES syndrome prior to treatment with propranolol. (**b**) Appearance 15 months after treatment with propranolol

Systemic hypotension may require cessation of treatment, but this has been found to be rare, as most patients who experience hypotension become normotensive spontaneously while on treatment [3]. Other systemic side effects include sleep disturbances and gastrointestinal discomfort, cold hands and feet, somnolence, decreased appetite, bronchitis, and bronchiolitis [3, 36].

There have been reports of treatment failure in patients who initially responded to the propranolol but then developed regrowth of the lesions while still on therapy [3, 39]. In these patients, intralesional steroid injections were added to the treatment regimen with successful reduction of the lesions [39]. A combination therapy consisting of a short-term course of oral steroids followed by oral propranolol treatment has been found to cause a significantly faster initial reduction in the size of the hemangioma, as compared to monotherapy with oral propranolol alone, and may be a potential alternative in larger hemangiomas [40].

4.10 Other Oral Beta-Blockers

Atenolol is a cardioselective beta-blocker that may have fewer adverse events. It has been used successfully in the management of infantile hemangioma. The results appear to have been as equally effective as propranolol in a small series of patients [41].

4.11 The Role of Topical Beta-Blockers

Topical beta-blockers have been suggested as a safe and effective treatment for superficial hemangiomas with reduced systemic side effects. Ni et al. treated seven patients with superficial periocular hemangiomas; none of the patients had any previous treatment, and all were treated using timolol maleate 0.5 % solution [3]. The solution was spread over the lesion two times a day. The authors found the hemangiomas had reduced in size by 55–95 % over 1–6 months [42]. None of the patients developed local or systemic side effects, and all patients showed fading of the hemangioma over time [42]. The authors also reported reduction of the average astigmatism from 2.5D to 1.0D in their patients [42].

This experience has been duplicated in other reports that have showed regression or arrested growth in lesions using timolol gel. Timolol gel 0.25 or 0.5 %, rather than the solution, can be applied topically twice daily as an alternative to the drops [3, 42, 43].

4.12 Mechanism of Action

The mechanism of action in reducing the size of infantile hemangiomas is not clear. Various theories have been suggested, but none seem to fully explain the effect, and few have been scientifically and properly studied. The immediately visible color changes, associated with a palpable softening of the hemangioma, lead to the suggestion that vasoconstriction and decreased release of nitric oxide may be involved [3].

Decreased expression of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF*)* genes through the downregulation of the RAF-mitogen-activated protein kinase pathway has been suggested [7]. Triggering of apoptosis of capillary endothelial cells has also been proposed [44].

It has been shown more recently that proliferating hemangiomas can also respond to angiotensin II. Angiotensin II is known to induce VEGF secretion. Beta-blockers decrease activation of the rennin-angiotensin-aldosterone system, which leads to decreased angiogenic signaling [3].

4.13 Conclusion

Periocular and orbital hemangiomas are an important cause of amblyopia in pediatric patients. Although there have been traditionally different modalities for managing infantile ocular hemangiomas, the use of oral propranolol has revolutionized the management of these lesions. This treatment appears to be a safe alternative to other modalities of treating infantile hemangiomas with reduced systemic side effects. Monitoring and treating these patients for anisometropia and amblyopia is critical.

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Chapter 5
Surgical Approaches to the Orbit

Seongmu Lee

5.1 Introduction

Surgery of the orbit entails a firm understanding of complex bony and soft tissue anatomy, as the orbit consists of important neurovascular structures that are compressed into a small, confined space with often challenging visualization. Vascular lesions of the orbit are numerous, and careful consideration of clinical features and imaging characteristics, particularly with respect to anatomic location, is critical for surgical planning. Approaches are numerous and are governed by the lesion, size, location (anterior, mid-orbit, apex), and relationship to adjacent soft tissue and bone.

5.2 Anterior Orbit

5.2.1 Superior Orbit: Medial, Central, and Lateral

Lesions in the superior orbit that are anterior to the trochlea may be approached with a curvilinear subbrow or eyelid crease incision. The latter approach begins through the skin, followed by dissection in the suborbicularis plane, identification of the preaponeurotic fat pad, and incision of the orbital septum. If the lesion involves the bone beneath the periosteum, dissection superiorly to the periosteum of the orbital rim should be performed, followed by an incision into periosteum anterior to the arcus marginalis.

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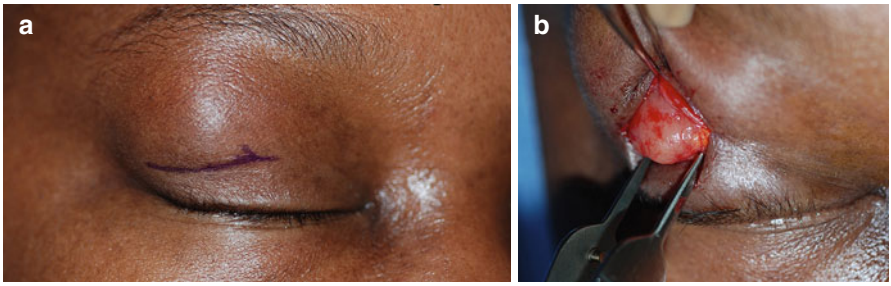

Fig. 5.1 (**a**) A lateral lid crease incision can be utilized to access the central and lateral anterior orbit. (**b**) A lacrimal gland lesion is shown, accessed through the lateral eyelid crease incision. (Images courtesy of Michael T. Yen, MD)

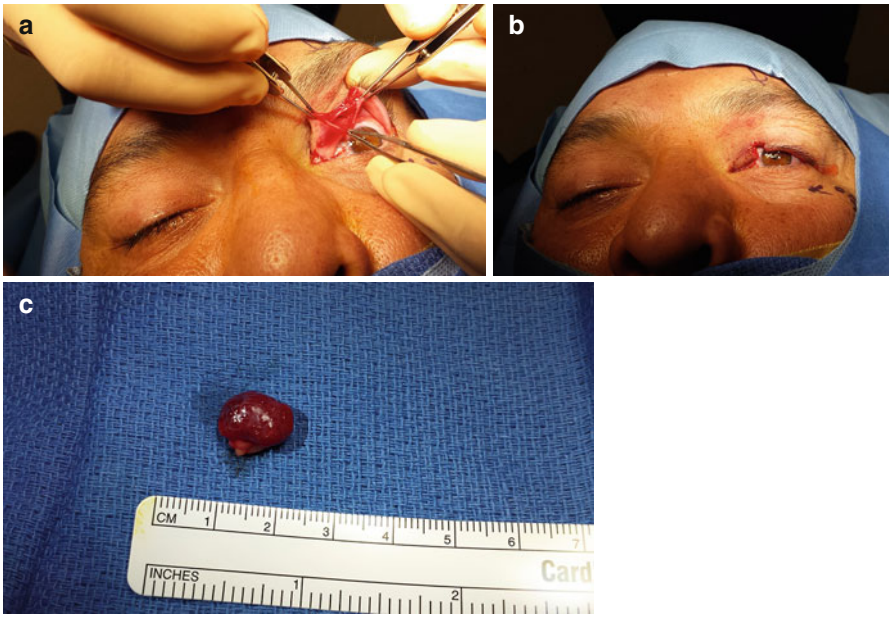

Fig. 5.2 (**a**) A full-thickness vertical lid split incision (perpendicular to the lid margin) can provide excellent operative space and visualization of the anterior orbit. (**b**) The external appearance of the vertical lid split orbitotomy after dissection is relatively small and easily closed. (**c**) Large orbital lesions, such as this venous malformation, can be excised through the vertical lid split incision (Images courtesy of Michael T. Yen, MD)

A direct or modified Lynch incision, conjunctival (with dissection through Tenon's capsule) incision, or a coronal incision may be necessary to approach the area in the superomedial orbit posterior to the trochlea, the latter in situations where there is a large lesion extending over the brow or intracranially. Exposure with distraction of the superior oblique tendon or elevation of the periosteum and trochlea may be necessary based on the lesion location and its relationship to the bone or

adjacent sinus. With a conjunctival approach, an incision is made through Tenon's capsule around the area of the equator of the globe, allowing access to the superomedial orbital tissue.

The eyelid crease incision can be utilized in most instances to approach the central and lateral superior orbit (Fig. 5.1a, b). Dissection is performed in the suborbicularis plane in front of the preaponeurotic fat pad, followed by incision through the orbital septum.

A subbrow approach may be more useful for deeper lesions posterior to Whitnall's ligament, particularly for supraperiosteal lesions. The space between the levator and superior rectus may be approached via a conjunctival approach. For further deeper lesions, a lateral orbitotomy or vertical lid split orbitotomy may be necessary.

In the vertical lid split technique, a full-thickness vertical incision (perpendicular to the lid margin) is made at the junction of the medial and central thirds of the upper eyelid. The skin, orbicularis, and tarsal plate are cut, extending superiorly through the palpebral conjunctiva into the superior fornix. Blunt dissection is then utilized to enter the orbit (Fig. 5.2a–c).

5.2.2 Inferior Orbit: Lateral and Central

Lesions of the central and lateral inferior orbit may be approached via a transconjunctival swinging eyelid technique. Preseptal lesions may be approached directly via a subciliary incision, although this results in a visible scar and may increase the risks of lid retraction. An inferior fornix/transconjunctival approach can be utilized to reach the inferior orbit in the majority of cases, with an adjunctive lateral canthotomy and inferior cantholysis swinging eyelid approach for further exposure (Fig. 5.3a, b). The transconjunctival incision can be extended medially utilizing a transcaruncular incision to provide further access inferomedially.

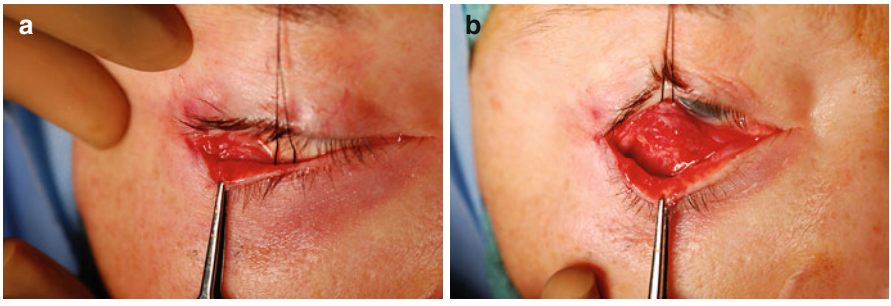

Fig. 5.3 (**a**) A transconjunctival swinging eyelid orbitotomy incision is created with a lateral canthotomy and inferior cantholysis to provide access to the inferior orbit. (**b**) The conjunctiva and lower eyelid retractors are retracted superiorly, exposing an inferior orbital lesion (Images courtesy of Michael T. Yen, MD)

5.2.3 Medial Orbit

A transcaruncular approach can be utilized to approach the medial orbit. In this technique, an incision is made in the caruncle and extended superiorly and inferiorly. Careful attention is paid to avoid injury to the canalicular system. Curved tenotomy scissors are then inserted, and gentle, blunt dissection is performed over the posterior lacrimal crest, thereby exposing the periosteum of the medial orbital wall. The anterior and posterior ethmoidal vessels serve as useful landmarks.

A direct cutaneous incision above/lateral to the medial canthal tendon or a standard dacryocystorhinostomy incisional approach may be needed for lesions posterior to the lacrimal sac. Disinsertion of the medial canthal tendon, followed by elevation of the ligament and periosteum overlying the anterior rim of the lacrimal crest, can be used to obtain access to this particular space.

5.3 Mid-orbital Lesions

5.3.1 Superior Orbit: Medial, Central, and Lateral

Access to the mid-orbit involves extensions of techniques utilized to approach the anterior orbit. The superomedial orbit can be accessed via a modified Lynch incision, subbrow incision, or an eyelid crease incision. A coronal approach may be necessary for approaches requiring access to the frontal bone/skull or involving extension intracranially.

Access to the lateral mid- and posterior orbit may require a lateral orbitotomy. A coronal incision may also be utilized for complicated lesions involving the frontal bone of the intracranial space. A lateral orbitotomy incision begins with a direct lid crease or lazy-S incision. Once the frontozygomatic process and the upper margin of the zygomatic arch are identified, an incision is extended laterally from the lid crease to slightly superior to the lateral canthal tendon. Dissection is performed to expose the periosteum of the frontozygomatic arch. An incision is then made through the periosteum and the periosteum elevated onto the anterior orbital rim anteriorly and posteriorly to detach the temporalis muscle. A bony incision is then made just above the zygomaticofrontal suture line and inferiorly along the superior margin of the zygoma utilizing an oscillating bone saw. The periorbita can then be incised to access the lateral orbit.

5.3.2 Inferior Orbit, Lateral

Access to the inferior and inferolateral mid-orbit can be obtained by utilizing a swinging eyelid technique, where a lateral canthotomy and inferior cantholysis are performed to disinsert the eyelid, followed by extension of the incision

centrally and medially via a transconjunctival approach. The incision can be further extended medially via a transcaruncular incision to provide further exposure.

5.4 Apical Lesions

5.4.1 Medial Orbit

Access to lesions in the posterior third of the orbit medially can be obtained by a transcaruncular approach, a conjunctival/semilunar fold incision (with or without disinsertion of the medial rectus), or a direct cutaneous incision/lynch incision. A direct cutaneous approach may be useful for lesions of the medial orbit with involvement of the ethmoid sinus. A collaborative transcranial approach with neurosurgery may be necessary for apical lesions superior to the optic nerve.

5.4.2 Superior, Lateral, and Inferior

A lateral orbitotomy may be utilized to access the area inferior and lateral to the optic nerve. The lateral orbitotomy may need to be extended posteriorly with removal of the bone up to the superior and inferior orbital fissure. Involvement of the intracranial cavity may necessitate a collaborative transcranial approach with neurosurgery.

5.5 Conclusion

Surgery of the orbit requires a firm foundation of orbital anatomy and an understanding of the clinical disease process. Meticulous preoperative planning with attention to the location of pathology, nature of the disease process and its effects, objectives of surgery, and anticipated alterations in anatomy is critical.

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Chapter 6
Combined (Hybrid) Operations for Orbital Venous Malformations

Hunter K. Yuen, Emmy Y. Li, and Tommy C. Chan

6.1 Introduction

Orbital vascular malformations encompass a wide spectrum of diseases, and the management of orbital vascular malformations is a significant challenge to clinicians and surgeons despite the various treatment options available. These lesions are usually present at birth and continue to expand over time. The indications for treatment include physical disfigurement, profuse hemorrhage, hemorrhage or thrombosis leading to pain, or complications related to the mass effect of the lesion such as visual loss from compressive optic neuropathy or diplopia from ocular misalignment. A number of treatments have been described, including sclerotherapy, laser photocoagulation, embolization, and surgical resection. Outcomes are variable and depend on the channel (lymphatic, venous, or arteriovenous) and the flow characteristics (low flow, combined flow, or high flow) of the lesions. Sclerotherapy and laser photocoagulation have been used for low-flow vascular malformation [1] but requires multiple treatment sessions and may result in sclerosant-induced inflammation and swelling [1, 2]. Sclerotherapy is more effective in lymphatic malformation but less effective for venous malformation. Laser therapy has been described useful in superficial venous malformations, although it carries a high rate of recurrence [1]. Surgical excision is theoretically the most definitive treatment for venous malformation, yet it remains technically demanding and often dangerous due to the risk of profuse intraoperative hemorrhage, lack of well-defined resection margin, and in some cases, close proximity or even infiltration to important ocular or cranial structures.

Preoperative or intraoperative venography and fluoroscopy have been proposed to assist the surgical excision of orbital venous malformations [3, 4]. However, limitations in interventional radiology support and intraoperative visualization

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technology are the major obstacles for a safe and complete surgical removal. Similarly, embolization with N-butyl cyanoacrylate ("N-BCA") prior to surgical resection has been described to reduce intraoperative blood loss. N-BCA helps to solidify the vascular malformation and thus provides a better demarcation between the vascular malformation and surrounding healthy tissue [5]. Accidental dissection into a solidified venous malformation would not result in collapse of the lesion. Initial results on safety and efficacy were encouraging [5–8]. Early studies mainly describe delayed surgical resection (between days to weeks) after preoperative embolization and sclerotherapy, with one study demonstrating the benefits of same-stage preoperative embolization at the interventional radiology suite followed by surgical resection in the operation theater [5].

Hybrid procedure refers to embolization with N-BCA glue followed immediately by surgical resection in the same setting at the endovascular operating room (EVOR) without the need of patient transfer. EVOR has been used successfully for diagnostic and therapeutic vascular procedures in cardiovascular and cerebrovascular surgeries [9, 10]. It is a hybrid operating theater-angiography suite, which meets the stringent requirements of an operating theater while harboring the facilities of an interventional radiology room [11]. With the biplane digital subtraction angiography in place, intervention radiologist is able to perform real-time imaging, three-dimensional reconstruction of the images, as well as roadmapping via contrast injection; these sophisticated imaging capabilities greatly facilitate simultaneous radiological and surgical interventions with multidisciplinary collaboration for complex vascular lesions.

6.2 Technique

The EVOR used in our center is set up with a biplanar digital subtraction angiographic system (BDSAS) (Artis zee biplane system, Siemens, Erlangen, Germany) installed in a standard operating theater with positive pressure airflow, standard sterilization protocols, infection control standards, a full range of supporting staff, and surgical instruments available. The procedure is performed under general anesthesia. Preoperative assessment and counseling are performed at the multidisciplinary vascular anomaly clinic. Patients would have contrast-enhanced magnetic resonance imaging (MRI) or computed tomography (CT) and Doppler ultrasound study when necessary, to confirm the diagnosis of venous malformation and evaluate the extent.

At the beginning of the session, angiogram/venogramusing BDSAS is performed to confirm the extent and the draining pattern of the venous malformation by interventional radiologists. Access into the venous malformation is performed either by transcutaneous puncture or direct puncture after surgical dissection with a 21-G or 23-G butterfly needle, depending on the site and vessel characteristics of the venous malformation. Catheters' position is confirmed with free back flow of blood in the case of direct puncture, and digital subtraction angiography is done

after contrast injection. Pretreatment venogram of the venous malformation is useful to further delineate the extent of the lesion and flow pattern, especially the presence and location of intracranial vascular communication. The BDSAS pictures are digitally captured with color adjustment and used as a "roadmap" for subsequent sclerotherapy. The N-BCA (B. Braun Surgical SA, Rubi, Spain)/Lipiodol (Guerbet, Roissy CdG, France) "glue-dye" mixture is prepared, with its concentration adjusted according to the location, size, and presence of draining vessels of the lesion. The mixture is introduced into the venous malformation under fluoroscopic guidance until complete filling, with the needle or catheter removed on completion. There is real-time control of the glue location, and the location of the glue can be ascertained when the image is overlaid onto the previous "roadmap." External compression to the draining veins would be given if necessary. For deep-seated venous malformation, surgical dissection can be performed to expose the lesion first before direct puncture venogram to enhance the accuracy and safety of the procedure. The glue will solidify as a glue cast shortly after injection, and surgical resection is then performed in the same setting without the need of patient transfer. The aim is complete macroscopic removal while preserving vital structures. Dynamic CT may be performed intraoperatively to guide complete resection. For multiloculated lesions, supplementary venogram and glue injection can be added during the procedure to further facilitate surgical excision of the previously unglued portion of the lesion and to achieve a more complete removal of the lesion. For the smaller lesions, imaged-guided sclerotherapy can be done at the same setting.

6.3 Case Illustration

6.3.1 Case 1

A 69-year-old woman was referred for left orbital mass involving the upper and lower eyelids. Over the last few decades, she received multiple interventions including embolization and surgical resection. However, the lesion recurred and increased in size over years. She suffered from left mechanical ptosis and severe periorbital pain and discomfort, resulting in psychological disturbance. Contrast CT and MRI of the orbit showed a low-flow infiltrative vascular lesion of both upper and lower lids suggestive of a venous malformation. Operation was carried out in the EVOR. The lower lid venous malformation was managed by injecting sclerosant into the lesion guided by BDSAS. The upper lid lesion was excised through a transverse skin incision after embolization guided by the BDSAS. Multiple injections were needed because of the multiple loculations in the venous malformation. Histology confirmed a multiloculated venous malformation. At 18 months' follow-up, the patient had no discomfort and no recurrence of ptosis. She was satisfied with the surgical outcome (Fig. 6.1).

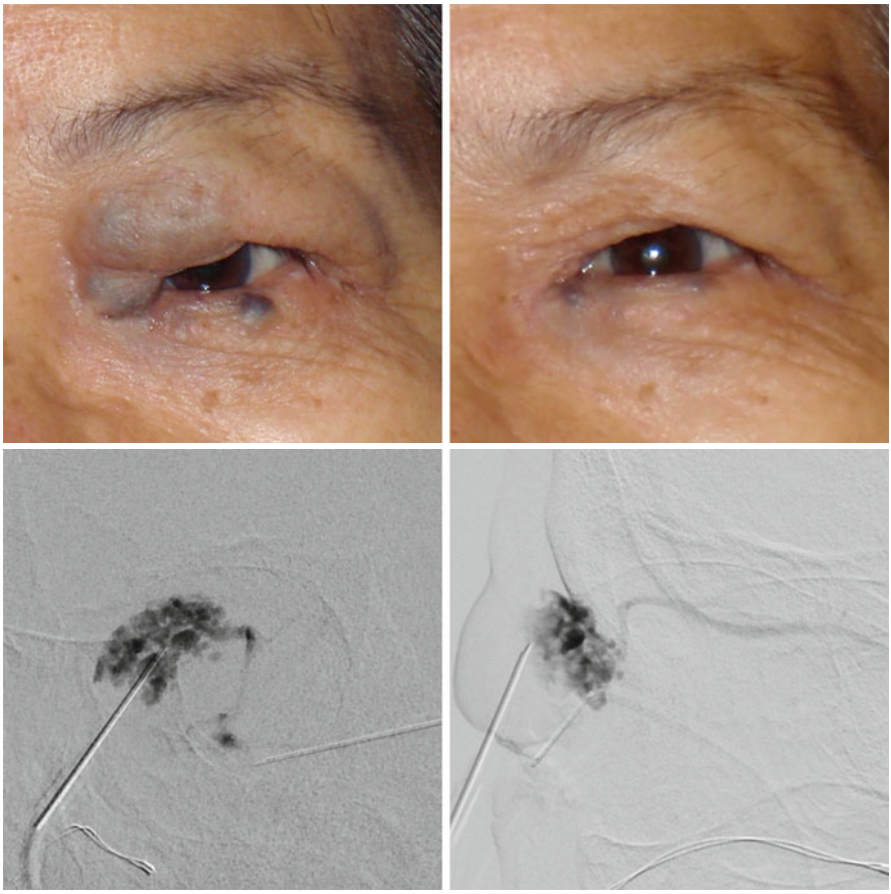

Fig. 6.1 Clinical photos of Case 1. (*Top left*) Preoperative appearance of the patient showing the left upper lid venous malformation. (*Top right*) Postoperative appearance of the patient. (*Bottom left*) Injection of tissue glue and contrast mixture was visualized and localized with the anterior-posterior view under the biplanar digital subtraction angiographic system. (*Bottom right*) The corresponding lateral view under the biplanar angiographic system

6.3.2 Case 2

A 23-year-old woman described a progressive swelling in her left upper lid over a 2-year period. This was associated with marked cosmetic blemish and mild discomfort. Her vision and ocular motility remained normal. A contrast-enhanced CT scan showed a venous malformation extended from the left upper lid to around the trochlear region. Her symptoms gradually increased, and she underwent surgical excision of the venous lesions at the EVOR. Intraoperative direct puncture venogram and embolization were performed by interventional radiologists. This was followed by sub-brow skin incision over the lesion. With the aid of BDSAS-guided embolization, the vascular lesion was excised as much as possible up to the trochlear region, preserving the superior oblique muscle tendon. Histology showed ectatic

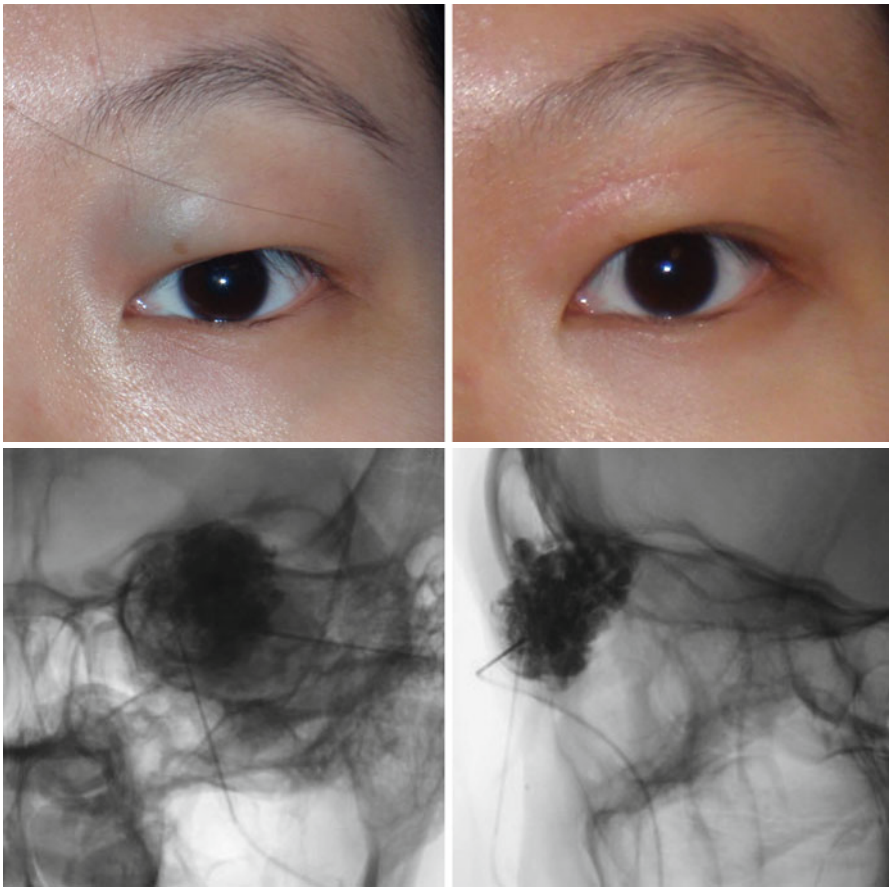

Fig. 6.2 Clinical photos of Case 2. (*Top left*) Preoperative appearance of the patient showing the left upper lid venous malformation. (*Top right*) Postoperative appearance of the patient. (*Bottom left*) Injection of tissue glue and contrast mixture was visualized and localized with the anterior-posterior view under the biplanar digital subtraction angiographic system. (*Bottom right*) The corresponding lateral view under the biplanar angiographic system

thin-walled vascular channels consistent with venous malformation. She was free of pain, and there was no evidence of recurrence at the follow-up at 18 months (Fig. 6.2).

6.3.3 Case 3

A 38-year-old woman was noted to have a left upper lid vascular lesion since the age of 24. She received partial surgical excision of the lesion 10 years ago in China; histology at that time showed dysplastic venous channels. Subsequently she was noted to have progressive proptosis, ocular dysmotility, and compressive optic

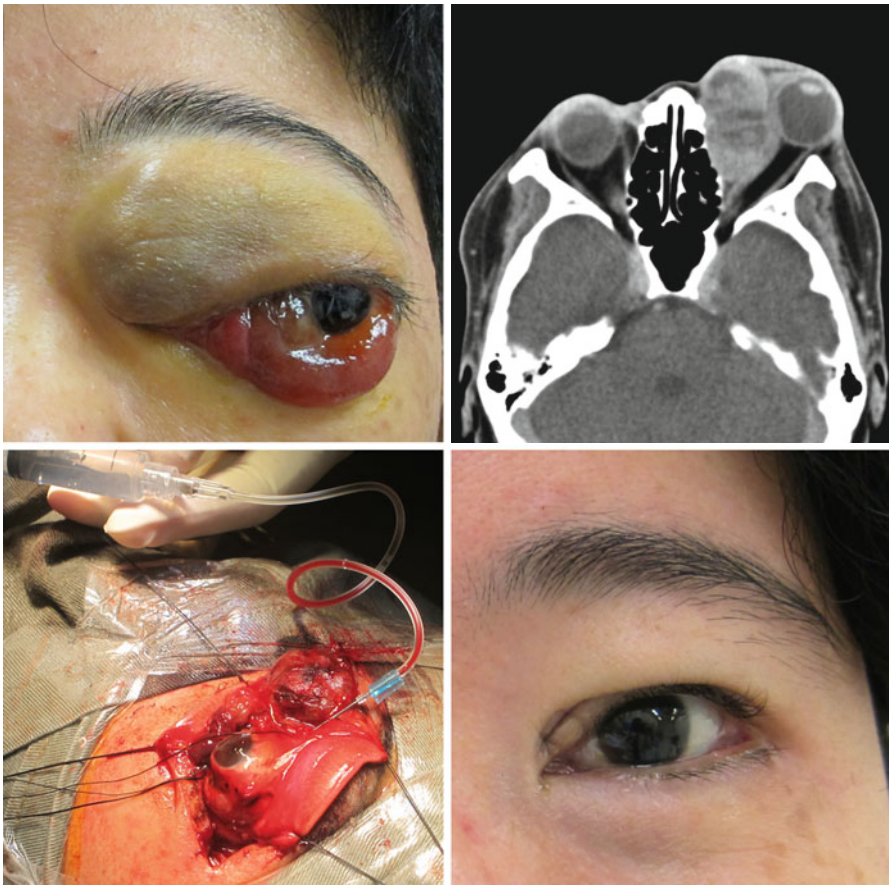

Fig. 6.3 Clinical photos of Case 3. (*Top left*) Preoperative appearance of the patient. (*Top right*) Computed tomography showing a large contrast-enhancing lesion with posterior orbital extension. (*Bottom left*) Intraoperative photo showing excision of the glued mass via a panorbitotomy approach under supplementary direct puncture venogram and embolization guided by the biplanar angiographic system. (*Bottom right*) Postoperative appearance of the patient

neuropathy. MRI of her orbit showed a contrast-enhancing extraconal mass at the anteromedial aspect of her left globe. It displaced the left medial rectus muscle and the globe laterally. She received sclerotherapy to her left orbital venous malformation, but the clinical response was transient. In view of the progressive deterioration in vision, surgical excision was repeated in the EVOR. BDSAS-guided glue embolization was done with direct transcutaneous needle puncture, the lesion was then excised via panorbitotomy combining lateral canthotomy and inferior cantholysis, and transconjunctival and transcaruncular and vertical eyelid splitting incisions were made to allow excision of the lesion. The solidified part of the vascular lesion was excised with clear delineated dissection plane, yet the deeper part of the lesion did not take up sufficient glue with the initial superficial puncture. In view of the extensive lesion size, repeated venogram with additional glue injection under

BDSAS guidance was supplemented. Complete macroscopic excision was achieved, and the follow-up orbital CT performed at 18 months after excision did not reveal any recurrence. Despite prolonged optic nerve compression by the lesion and established optic atrophy, her vision improved from hand movement to 6/60 after operation. There was mild limitation in left eye abduction, but patient has no diplopia, and there was no clinical recurrence with satisfactory cosmetic outcome (Fig. 6.3).

6.3.4 Case 4

A 22-year-old gentleman had a left conjunctival vascular lesion since 10 years old. He noted the mass was gradually increasing in size and causing significant cosmetic disfigurement. On MRI of the orbit, a multiloculated intraconal lesion was noted at the inferomedial aspect of the left orbit. The lesion extended anteriorly to the preseptal space involving the inferior eyelid and posteriorly to the intraconal orbital space with features suggestive of a slow-flow orbital venous malformation. The lesion was managed in the EVOR collaboratively by radiologists, vascular surgeons, and ophthalmologists. Contrast injection followed by embolization under BDSAS guidance was performed through insertion of catheter to the inferior lid lesion. The glued venous malformation together with the feeder vessels was excised via a transconjunctival approach. The lesion was noted to have infiltrated the inferior rectus muscle, and the latter was preserved. A small portion of the most posterior intraconal component was left in place in view of surgical risk outweighing the benefits. Histopathology showed dysplastic venous channels with lymphatic components. There was no clinical recurrence noted 2 years after the operation although a small residual intraconal venous malformation was noted in follow-up MRI. His visual acuity remained good with no ocular dysmotility and disfigurement (Fig. 6.4).

6.3.5 Case 5

A 35-year-old gentleman was presented with an intermittent left upper lid mass for 6 months. The mass increased in size after Valsalva maneuver and caused mechanical ptosis and periocular discomfort, but there were no proptosis and ocular dysmotility. He had left ruptured eyeball repaired over 10 years ago, with subsequent poor visual acuity. In view of the cosmetic disfigurement and discomfort, surgical resection at EVOR was performed. Dynamic contrast CT of the orbit showed a lobulated nodular lesion in the preseptal compartment of the left orbit enlarging on prone Valsalva maneuver. Superficial dissection was performed through a lid crease incision until the venous malformation was exposed, followed by direct puncture venogram and embolization of the lesion under BDSAS surveillance to avoid spillage from the superior ophthalmic vein into the cavernous sinus. After completed embolization, the lesion was removed completely en bloc. Histopathology of the specimen

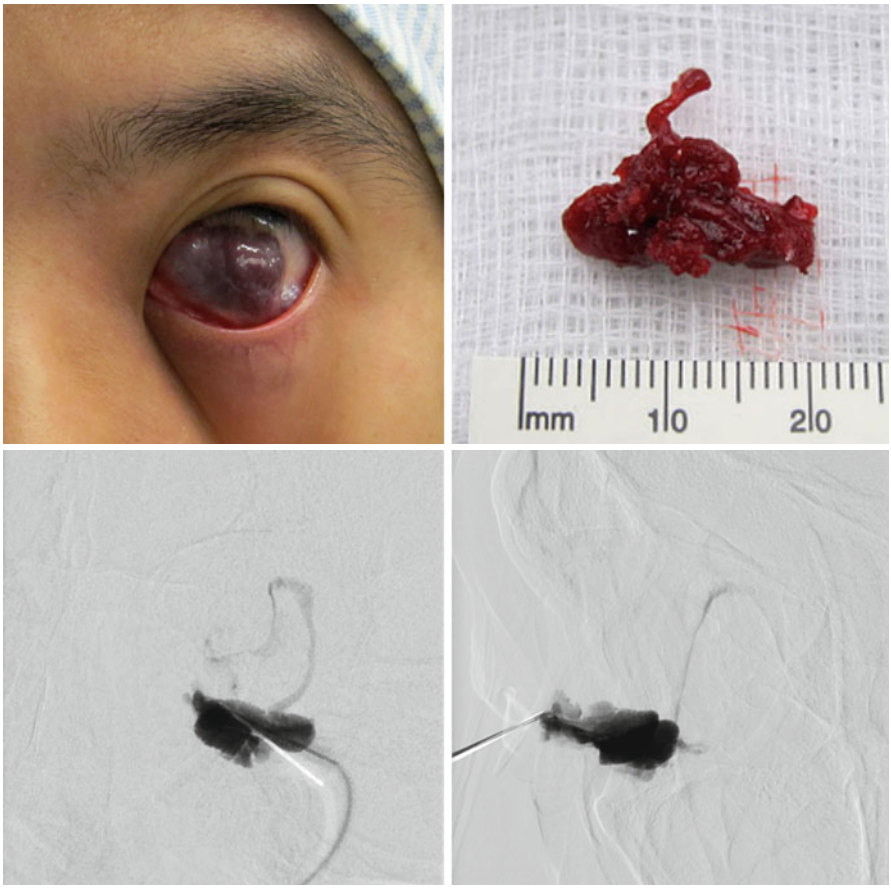

Fig. 6.4 Clinical photos of Case 4. (*Top left*) Clinical appearance of lower lid conjunctival venous malformation. (*Top right*) The venous malformation was excised after glue embolization. The feeder vessel was glued and excised together. (*Bottom left*) Anterior-posterior view during glue-contrast mixture injection over the venography roadmap. Outflow of the venous malformation connected through the inferior ophthalmic vein into the cavernous sinus. (*Bottom right*) The corresponding lateral view under the biplanar angiographic system

showed dilated vascular channels compatible with venous malformation. The patient remained asymptomatic with no recurrence at follow-up 2 years later (Fig. 6.5).

6.3.6 Case 6

An 18-year-old girl was referred for left periorbital mass since childhood, which progressively increased in size over the years and complicated with repeated bleeding from the lesion for 1 year. MRI of the orbit showed diffuse infiltrative lobulated lesions involving subcutaneous, extraconal, and intraconal regions of the left orbit

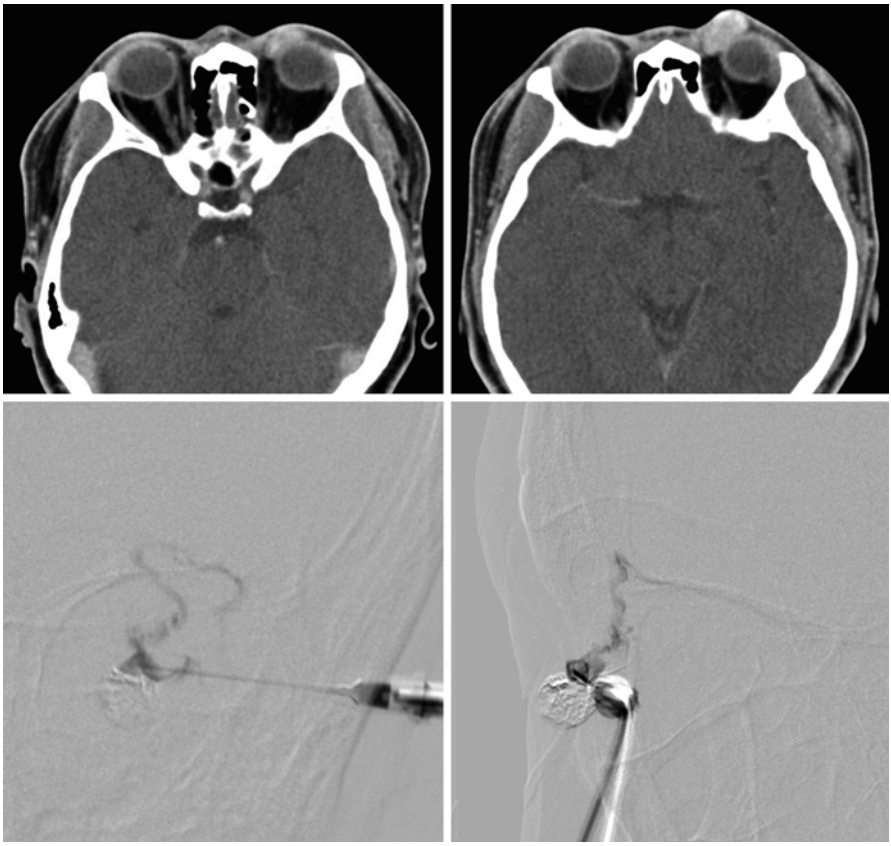

Fig. 6.5 Clinical photos of Case 5. (*Top left*) Dynamic contrast-enhancing computed tomography showing the left upper lid venous malformation before Valsalva maneuver. (*Top right*) Dynamic contrast-enhancing computed tomography showing the distensible nature of the same venous malformation after Valsalva maneuver. (*Bottom left*) Injection of tissue glue and contrast mixture was visualized and localized with the anterior-posterior view under the biplanar digital subtraction angiographic system. (*Bottom right*) The corresponding lateral view under the biplanar angiographic system

with lateral displacement of the lateral rectus and optic nerve encasement suggestive of veno-lymphatic malformation. In the EVOR, transconjunctival inferior orbitotomy by the swinging eyelid approach was performed, followed by deep orbital dissection to expose the lesion. Direct puncture venogram was performed by interventional radiologists to confirm the extent of the lesion. Sclerotherapy with N-BCA injection was done at two sites. The lesion was excised as much as possible, with some residual lesions and glue cast left behind. The medial rectus, lateral rectus, and inferior oblique all remained intact. Further excision of the left upper lid subcutaneous lesion was performed via a transcutaneous approach. Part of the levator muscle was excised as it was infiltrated by the venous malformation, and such levator resection can improve the long-standing ptosis. The levator was then reattached to the tarsal plate after the

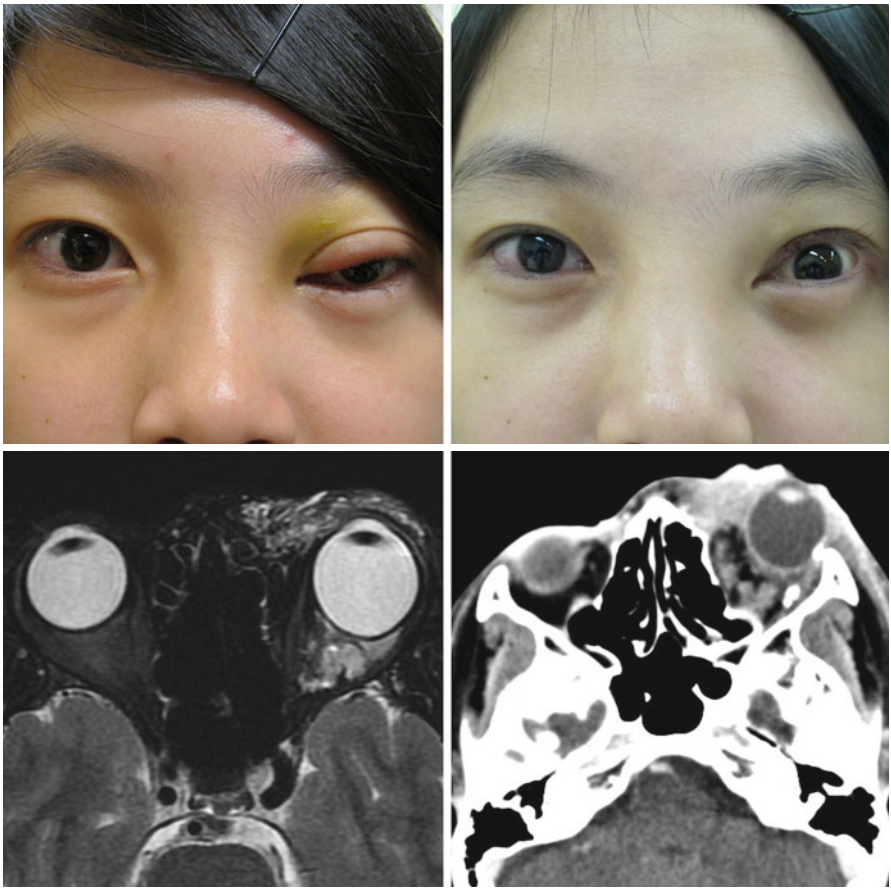

Fig. 6.6 Clinical photos of Case 6. (*Top left*) Preoperative appearance of the patient showing the left upper lid veno-lymphatic malformation causing mechanical ptosis. (*Top right*) Postoperative appearance of the patient with ptosis much improved. (Bottom *left*) Magnetic resonance imaging showing diffuse infiltrative lobulated lesions involving subcutaneous, extraconal, and intraconal regions of the left orbit. (*Bottom right*) Postoperative contrast-enhancing computed tomography showing residual lesion and glue cast in the left orbit

resection. Histopathology confirmed veno-lymphatic malformation. There was no clinical recurrence noted at 1 year despite residual lesions noted at post-op contrast CT. Both cosmesis and ptosis improve after the surgery; there were no visual loss, new-onset diplopia, and recurrent bleeding after the surgery (Fig. 6.6).

6.4 Discussion

Surgical excision of orbital venous malformation is notoriously difficult because of its infiltrative nature, indistinct margins, and collapsible nature. Direct excision can be complicated by profuse intraoperative hemorrhage, which obscures the surgical

field, leading to prolonged operation, inadvertent damage of important structures, and failure of complete excision. Embolization of the lesion prior to surgical excision has been demonstrated to facilitate resection with minimal morbidity. Injection of the embolizing agent or sclerosant can be performed under fluoroscopy guidance preoperatively before the patient is transported to the operating room or carried out intraoperatively with the conventional C-arm system. Couch et al. reported successful surgical resection of orbital varices in four patients using preoperative fluoroscopy-guided embolization with N-BCA [7]. Intraoperative fluoroscopy has been shown to be useful to delineate the full extent of the lesions. Lacey et al. described using intraoperative percutaneous embolization with cyanoacrylate glue guided by fluoroscopy during surgical excision of distensible orbital venous malformation in six patients. Control of outflow via pressure at the superior or inferior orbital fissure was introduced [2]. Using the same technique, Garcia and associates were able to demonstrate complete surgical excision in three patients with anterior orbital venous malformations [12]. Similarly, Tsai and associates described a case of bilateral orbital varices, of which the left one was exposed surgically for intraoperative intralesional injection of cyanoacrylate; complete surgical excision was achieved [4]. While in the earlier studies, mainly conventional fluoroscopy was employed, a biplanar digital subtraction angiographic system capable of obtaining frontal and lateral projections simultaneously during a single injection of contrast was introduced by our group [13]. The advantage of BDSAS is that it allows simultaneous biplane imaging, thus permitting a high-quality three-dimensional assessment of the vascular lesion. Feeder vessels and outflow vessels can be clearly shown. Digital subtraction imaging helps to reduce radiation exposure and interference by bone shadows. Roadmapping of draining pattern is also possible, which allows safer canalization and embolization of the vascular lesion. Risk of accidental intracranial glue injection via the ophthalmic veins can be minimized as the there is real-time control of the glue-dye mixture radiologically. Furthermore, with better image quality, digital recording, and instant review of images in multiple dimensions, delineation of complex or deep-seated lesions is enhanced.

Concerning the choice of embolization agent, various chemicals have been studied. James et al. studied the use of 3 % sodium tetradecyl and 98 % dehydrated alcohol as embolization agent in facial venous malformation, and when compared with controls without preoperative embolization, embolization was associated with shorter operative time and less blood loss. No significant difference is seen between these two agents [8]. Arat et al. proposed the use of Onyx for embolization of high-flow craniofacial vascular malformations in nine patients, four of which followed by surgical excision after embolization. Onyx has a theoretical benefit of reduced risk of catheter adhesion and has used extensively in embolization of cerebral vascular malformations. However, this advantage is less important in direct puncture venogram for superficial orbital venous malformation. Onyx may also cause a bluish discoloration of the overlying skin and may require additional surgical revision for removal of the discolored skin [14]. Cyanoacrylate is a polymer with adhesive properties. N-BCA is approved by the FDA for the embolization of cerebral arteriovenous malformations when presurgical devascularization is desired. A number of studies have demonstrated the safety and efficacy of the use of preoperative

embolization with N-BCA in vascular malformations for intraoperative hemostatic control, enhanced visualization of the surgical field, and better delineation of resection margin [3–8]. Although none of the patients in these studies have embolization-related visual loss, it is important to note that facial and periocular injections of sclerosant have been associated with retinal artery embolization [15, 16]. Hopefully, fluoroscopy or BDSAS-guided injection would help to minimize the risk of this devastating complication.

Apart from the advantage of BDSAS, the setting of EVOR allows one-stop provision of diagnosis, embolization, and surgical excision of vascular malformation. Cil et al. described preoperative embolization with N-BCA followed by delayed surgical resection of the cast 10–15 days after embolization and proposed the benefit of N-BCA-induced soft tissue foreign body reaction would produce a pseudocapsule which allows easier surgical excision. However, prompt surgical resection after embolization may be more appropriate in the case of orbital lesions. Since the orbit is an enclosed space, complete embolization and solidification of the vascular malformation, particularly the large distensible venous malformations, may cause sudden elevation of intraorbital pressure or may even result in compartment syndrome and vascular compromise. In the EVOR, the vascular malformation is resected immediately after the glue injection without the need of patient transfer. The orbital pressure is relieved promptly with orbitotomy, and the duration of elevated orbital pressure is markedly reduced. The setting of EVOR also allows interactive and extended multidisciplinary collaboration. Despite preoperative imaging, there can be incomplete infiltration of N-BCA within the vascular malformation. In the EVOR, supplementary glue injection during surgery is possible for multiloculated or deep-seated lesions. While for deep orbital vascular lesion in which direct puncture is difficult, surgical dissection can be performed for better exposure of lesions for glue injection. This would increase the effectiveness of embolization and reduce unnecessary spillage of sclerosing agent. Furthermore, any complications arising from endovascular procedure like stenosis, occlusion, hemorrhage, and compartment syndrome can be treated timely with immediate surgery, thus improving outcomes of the procedure.

We believe that hybrid operations can enhance surgical outcome on the removal of orbital venous malformation, especially those located in the anterior or mid orbital region. Nevertheless, for those diffusely infiltrative orbital venous malformations, lesions at the orbital apex, and lesions with extensive cutaneous involvement, hybrid operation may enhance the excision, yet complete removal would still be difficult.

6.5 Conclusion

Hybrid procedure with embolization of orbital vascular malformation with N-BCA glue followed by surgical resection has shown promising results in the management of this challenging disease entity, especially in terms of hemostatic

control and more complete surgical resection. The setting of EVOR combining operating theater and angiography suite provides further advantages of real-time imaging surveillance, one-stop operation without the need of patient transfer under anesthesia, and enhanced multidisciplinary collaboration for management of complex lesions and complications. Overall, the procedure is safe with minimal complications, and surgical outcomes are encouraging with great patient satisfaction.

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Chapter 7
Endovascular Approaches to Orbital Vascular Lesions and Carotid Cavernous Sinus Fistulas

Stephen R. Chen

7.1 Introduction

High-flow vascular lesions of the orbit have a long history of open surgical treatment. In more recent times, endovascular approaches have overtaken open surgical approaches for many of these lesions due to decreased complication rates and the minimally invasive nature of catheter-based therapy.

Although many high-flow vascular lesions of the orbit have been reported, their orbit-related symptoms have a common source, arterial and venous channels, which bypass the capillary bed and pass high pressure to the venous structures of the orbit. They can be divided into two broad categories. The first category, arterial venous fistula, has no identifiable nidus between the arterial and venous channels. The second category, arteriovenous malformation, has an identifiable vascular nidus or a dysplastic bundle of vessels forming vascular channels between the arteries and veins.

The most common high-flow vascular lesion of the orbit, the carotid cavernous sinus fistula, resides outside the orbit and has the best outcomes from endovascular treatment. True intraorbital arterial venous fistulas are rare, but also have favorable endovascular treatment options. Periorbital tumors with high-flow intratumoral fistula can also have secondary orbital symptoms. The true intraorbital arteriovenous malformations (AVMs) are extremely rare. They have been treated with endovascular management, but often are surgically managed due to the danger of inadvertent central retinal artery embolization. In rare instances even parenchymal cerebral AVM can also present with orbital manifestations.

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7.2 Clinical Symptoms

The common symptoms of high-flow orbital vascular lesions are secondary to the abnormal elevation of the elevation of pressure in the periorbital and intraorbital veins. The symptoms more specific to carotid cavernous fistula are secondary to effects on the cranial nerves within the cavernous sinus. Clinically identifying the type of vascular lesion can be difficult, often needing MRI, CT, and conventional angiography for full evaluation. Furthermore, the spectrum and progression of symptoms are individual to the degree of shunting within the lesion and the architecture of the venous drainage.

Arterial venous shunting, with anterior drainage into the superior ophthalmic vein, angular and facial veins, can result in damage to the orbit and the cranial nerves in the orbit. In contrast, a shunt with primarily posterior drainage toward the superior and inferior petrosal sinuses can affect cranial nerves within the sinus, but rarely results in ophthalmologic symptoms. Fistulas are also often associated with venous thrombosis. In many cases, it is unclear whether the thrombus is secondary to the fistula or predisposes fistula formation. Regardless, thrombosis of the cavernous sinus and petrosal sinus can result in rapid deterioration, rapidly increasing intraocular pressures. High-pressure shunting, usually seen with traumatic fistulas, presents with the classical Dandy triad of chemosis, exophthalmos, and bruit.

7.2.1 Orbital Pain

Orbital and periorbital pain can present before other signs. These headaches are likely caused by thrombus within the cavernous sinus or superior ophthalmic veins. Thrombus results in an inflammatory response and the associated hemodynamic disturbance also irritate the meninges. Patients with vascular lesions and symptoms of orbital pain have been misdiagnosed as having migraines, cluster headaches, and Tolosa-Hunt syndrome.

7.2.2 Exophthalmos

Elevated orbital venous pressures can result in engorgement of the orbital soft tissues and prolapse of the soft tissues develop. In more mild arterial venous shunts, the degree of prolapse can be overlooked. More massive exophthalmos is seen with high-flow shunting from traumatic fistula or thrombosis of the other posterior outflow pathways of the cavernous sinus. The enlargement and degree of prolapse and swelling seen is often misdiagnosed as an infection. The most common history given for these patients on CT requests is to rule out periorbital abscess.

7.2.3 Conjunctival Engorgement and Chemosis

Shunting and subsequent elevated pressures of the conjunctival veins can be found in 82–100 % of patients with intraorbital symptoms. Corkscrew dilation of the epibulbar veins is seen. The dilation and tortuosity of conjunctival veins is often the cause for a misdiagnosis as inflammatory conjunctivitis. Conjunctival chemosis, edema of the sclera, occurs in 25–90 % of cases. In fact, chemosis may occur before the onset of exophthalmos.

7.2.4 Orbital Bruit

One of the classical symptoms of a high-flow arterial venous shunt is a bruit. The bruit or noise over the temporal bone and orbit can be subjective or objective. A buzzing, roaring, or swishing noise can be heard by the patient and by auscultation. The bruit is the result of turbulent flow within the cavernous sinus which is then transmitted to the inner ear by transmission through the skull. The sound may increase during exercise or with an increase in blood pressure. Although bruit is typically a benign symptom, it may become loud enough to prevent patients from sleeping and causing severe discomfort and distress.

7.2.5 Secondary Glaucoma/Vision Loss

After the onset of orbital symptoms, chronically elevated intraorbital venous pressure may result in blockage of Schlemm's canal. There can be decreased perfusion across the capillary bed of the retina due from loss of a normal arterial venous gradient. The subsequent elevated intraocular pressure and retinal ischemia can result in loss of visual acuity. A loss of visual acuity has been reported in up to 31 % of patients and is bilateral in 11 %.

7.2.6 Cranial Nerve Deficits

Cranial nerve deficits and unilateral ophthalmoplegia can be seen in up to 50 % of the patients. These often develop several months after the development of the shunt. Elevated venous pressures result in swelling of the ocular muscles and reduced motility. The dilated vessels and vascular steal can result in both mechanical and ischemic oculomotor nerve damage. With both thrombus formation and elevated pressures in the cavernous sinus, the cranial nerves of the cavernous sinus can be impaired. The sixth cranial nerve is most frequently involved (46–85 %), and the third cranial nerve

is the second most involved (36 %). The fourth cranial nerve is less frequently involved (11 %). The resulting diplopia is often reversible with early intervention, but resolution of symptoms may require up to 12 months. Unfortunately, in cases of long-standing untreated shunts, the cranial nerve damage and diplopia are often permanent.

7.2.7 Other Symptoms

Progression of symptoms can be fatal for high-flow shunts. Intracranial hemorrhage caused by carotid cavernous sinus fistula has been reported to occur from 3 to 8 %. Hemorrhage may be secondary to rupture of intracranial venous varix or hemorrhagic conversion of cerebral infarcts. Fatal epistaxis has been reported from rupture of cavernous sinus varix that bleeds into the sphenoid and adjacent sinuses. Retrograde flow and venous reflux caused by elevated pressure in the sinus can result in venous cerebral infarcts (1 %).

7.3 Carotid Cavernous Fistula

7.3.1 History

Carotid cavernous sinus fistula was originally thought to be a disease of the orbit, described as pulsatile exophthalmos. William Hunter is credited with recognizing the arterial venous communication outside the orbit as the cause in 1762, appreciating the bruit and palpable thrill at the communication between peripheral sites of arterial and venous injury. In 1811, Benjamin Travers, at the Guys Hospital in London, performed the first successful surgical treatment, a left carotid ligation for a left cavernous sinus fistula even before the development of general anesthesia (Fig. 7.1). Gioppi of Padua proposed intermittent compression of the carotid artery in 1856 and is credited for being the first to use it successfully. In 1911 in Berlin, Zeller pioneered a new approach by trapping the fistulous carotid, performing proximal ligation in the neck and distal ligation beyond the origin of the ophthalmic artery to prevent retrograde flow from the Circle of Willis. Although his patient died, other neurosurgeons, Hamby, Gardner, and Dandy, adopted his approach successfully. Later Stern and colleagues reported this technique had a 26 % mortality rate. In 1924, Locke described placing an apparatus with a block on the carotid artery for carotid compression. The first arterial embolization was performed with an open non-angiographic approach. In 1931, Brooks opened the carotid and placed a strip of muscle into the artery. After closing the carotid, it was hypothesized the strip would flow downstream into the fistula. His patient lost vision, but otherwise recovered. In 1963, Parkinson pioneered a direct surgical approach to the cavernous sinus to allow obliteration of the fistula while preserving the carotid artery. The direct approach was performed with hypothermia and cardiac arrest to minimize blood loss while opening the cavernous sinus.

Eventually endovascular angiographic approaches were tried. In 1963, Lang and Bucy performed the first angiographic aided open embolization, successfully treating

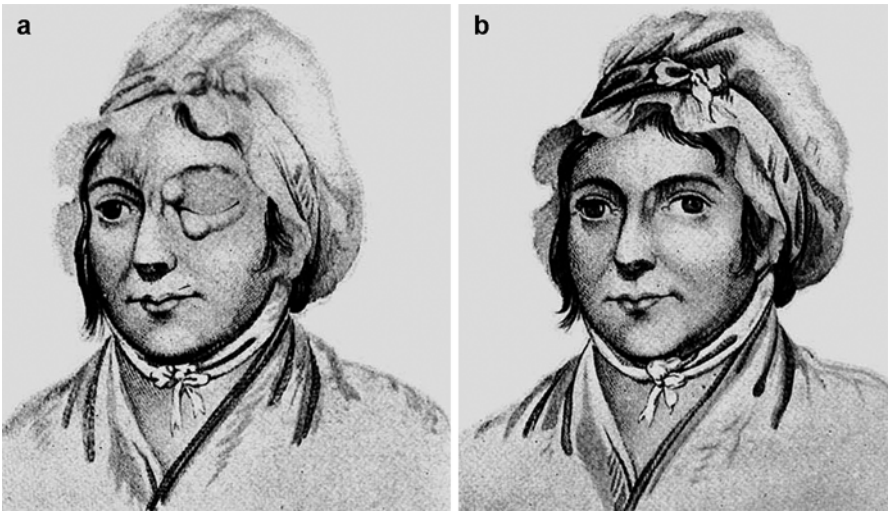

Fig. 7.1 Engravings of Travers' patient before (**a**) and after (**b**) left carotid ligation (*Med Chir Trans* 1813)

a case with free embolization of a strip of muscle marked with a silver clip. The subsequent angiogram confirmed closure of the ipsilateral carotid and fistula and adequate crossfill from the contralateral carotid. In 1968, Arutiunov developed a technique of attaching the muscle embolus to a string to control movement to the fistula site and performed this successfully in 13 patients. In 1969, Peterson and colleagues performed the first retrograde venous passage to the cavernous sinus through the superior ophthalmic vein by placing a copper wire and inducing thrombosis of the fistula and carotid by passing current. Then in 1971, Serbinenko published a pioneering article describing use of detachable balloons for occlusion of cerebral vessels and treatment of fistula. Subsequently, Debrun and colleagues in 1981 reported transvenous balloon embolization of carotid cavernous sinus fistula through the inferior petrosal sinus. These pioneers eventually led to the endovascular era of carotid cavernous sinus fistula management, initially through arterial embolization and then eventually through the more established transvenous approaches in the 1990s.

7.3.2 Anatomy of the Cavernous Sinus

The cavernous sinus is located at the base of the skull, closely associated with the osseous structures of the sphenoid bone and the sella turcica. The foramen rotundum, foramen ovale, and foramen lacerum are immediately adjacent. The cavernous sinus is bordered by two layers of dura mater, with a periosteal layer forming the floor and medial wall and dural layer forming the roof. Cranial nerves III, IV, and V1, and V2 are embedded in the lateral wall of the cavernous sinus. The internal carotid artery passes through the cavernous sinus, both in horizontal and vertical planes. According to the commonly accepted Bouthillier system (1996), the

cavernous carotid is the fourth segment of the internal carotid artery. Within the cavernous segments, meningeal branches include the inferior hypophyseal artery and inferior lateral trunk. These branches may be involved in indirect fistula.

The cavernous sinus is part of the family of dural venous sinuses. They are not classically veins, as they are endothelial tubes, lined with firm connective tissue, and do not contain the valves which are normally seen in veins. The cavernous sinus forms a central collection zone for blood draining from the middle cerebral veins, meningeal veins, the sphenoparietal sinus, and the ophthalmic veins. The sinus is very seldom a single large space. It was Winslow in 1732 that originally termed the sinus as "cavernous" because of the caverns he found formed by multiple fibers and connective tissue septae. In 80 % of patients, an unbroken channel can be found connecting the two sides of the cavernous sinus called the circular sinus.

After receiving blood from the brain and orbits, the cavernous sinus typically drains toward the transverse sinuses and the internal jugular veins. The cavernous sinus connects to the transverse sinus through the superior petrosal sinus and the jugular vein primarily through the inferior petrosal sinus and basilar venous plexus. Another important route for cavernous sinus drainage is via the pterygoid venous plexus which then drains to the maxillary and retromandibular vein into either the external or internal jugular vein (Fig. 7.2).

7.3.3 Craniofacial Veins

The cranial facial veins are of importance as alternative drainage pathways for the cavernous access and alternative methods of transvenous access to the cavernous sinus (Fig. 7.3). The facial vein provides an important route for retrograde transvenous access. The facial vein drains the anterior portion of the scalp and soft tissues of the face, beginning as direct continuation of the angular vein. The facial vein courses obliquely across the face to the body of the body of the mandible where it joins usually with the retromandibular vein to form the common facial vein. In most cases, it then drains into the internal jugular vein but may also drain into the external jugular vein. The facial vein can so connect to the pterygoid venous plus through the deep facial vein. The angular vein is the anastomosis between the facial vein and the superior ophthalmic vein. It forms the confluence between the supraorbital and frontal veins and has a subcutaneous course along the side of the nose adjacent to the angular artery. Both the superficial temporal vein and frontal vein originate in a venous plexus within the forehead. The veins converge to form single right and left pairs of frontal vein trunks which run near the mid forehead and anastomose with the angular vein.

7.3.4 Fistula Classification

Carotid cavernous sinus fistula is an entity with many types based on the source of the fistula and a pathway taken by the arterial source to pressurize the cavernous sinus. Terminology has been very inconsistent in the past, as the anatomy of this fistula can be

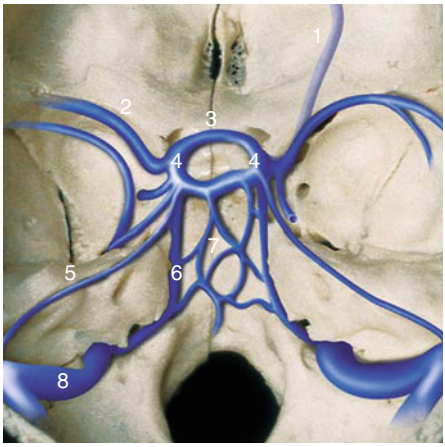

Fig. 7.2 The interconnected nature of the cavernous sinus can be appreciated on this artist rendition of the veins and sinuses viewed from above, superimposed on the skull base. The main structures related to catheterization of the cavernous sinus are labeled. The inferior petrosal sinus is the most common route for embolization of the cavernous sinus with the superior petrosal the second most commonly utilized. *1* Superior Ophthalmic Vein, *2* Sphenoparietal Sinus, *3* Intercavernous Sinus, *4* Cavernous Sinus, *5* Superior Petrosal Sinus, *6* Inferior Petrosal Sinus, *7* Basilar Venous Plexus, *8* Sigmoid Sinus (Bendorf 2010)

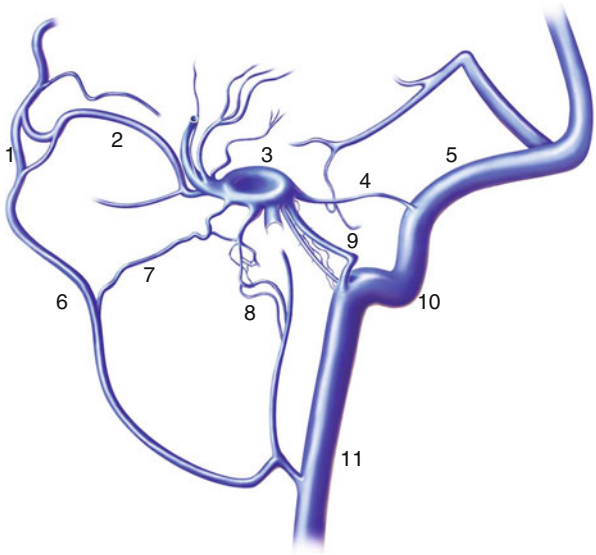

Fig. 7.3 The multiple anastomoses of the facial veins is appreciated on this lateral representation of the facial veins and their connections to the cavernous sinus. Retrograde catheterization of the facial vein as well as percutaneous puncture approaches can be utilized to access the cavernous sinus. The main branches related to fistula embolization are labeled. *1* Angular Vein, *2* Superior Opthalmic Vein, *3* Cavernous Sinus, *4* Superior Petrosal Sinus, *5* Transverse Sinus, *6* Facial Vein, *7* Deep Facial Vein, *8* Pterygoid Venous Plexus, *9* Inferior Petrosal Sinus, *10* Sigmoid Sinus, *11* Internal Jugular Vein (Bendorf 2010)

quite different. Barrow in 1985 named them broadly carotid cavernous sinus fistula. They have even been termed cavernous sinus dural arteriovenous malformations [1], but this terminology is misleading as they do not have a true nidus as seen in other AVMs. Classification of this fistula has been based on many different criteria including etiology and hemodynamics. The well-known Barrow classification system is based solely on the arterial supply to the fistula. Others have subdivided fistula into

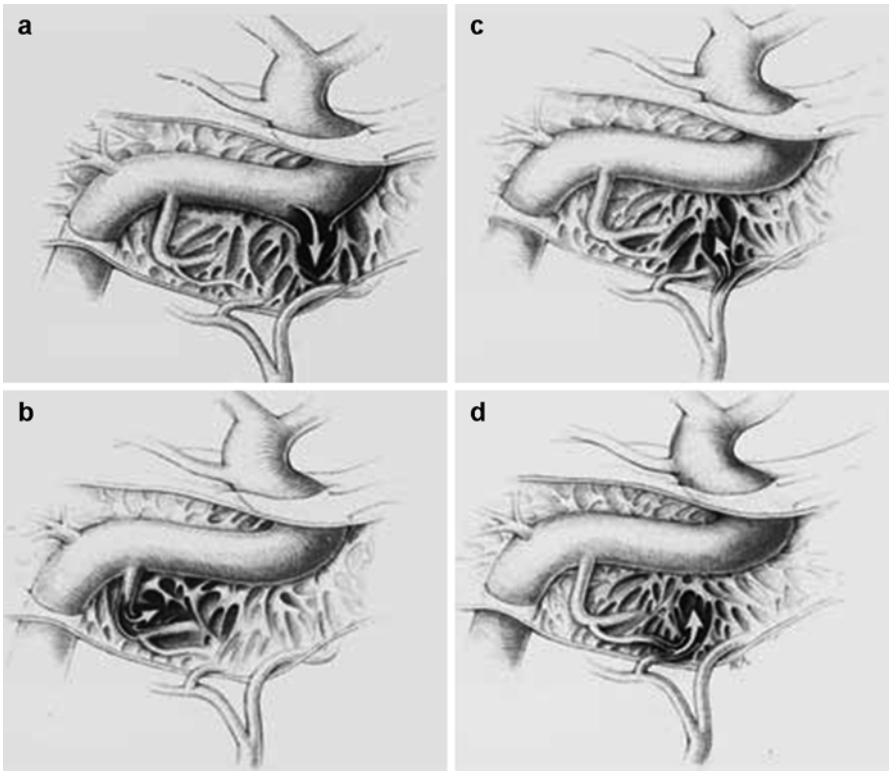

Fig. 7.4 Barrow's classification of spontaneous carotid sinus fistulas, Types (**a–d**) (*J Neurosurg*, 1985)

angiographic patterns of arterial supply combined with venous outflow pathways to more closely correlate classification with clinical symptoms and decision making. The most established classification system is Barrow's cavernous sinus fistula classification system, dividing them into four types A, B, C, and D (Fig. 7.4).

7.3.4.1 Type A Fistula

Type A fistulas are direct rents through the wall of the cavernous carotid or ruptures of a cavernous carotid aneurysm into the venous channels of the cavernous sinus. These fistulas are very high flow with minimal chance of spontaneous resolution and high risk for complication. They can be spontaneous, posttraumatic, and iatrogenic.

Carotid cavernous fistulas frequently are caused by trauma, with motor vehicle accidents being the most common cause. Falls and penetrating injuries are also frequent. With closed head injuries, the internal carotid can be torn at the points of fixed attachment. The carotid is attached to the dura between the foramen lacerum and anterior clinoid process, providing a fixed point. Movement of the carotid can result in a tear, forming a fistula to the surrounding cavernous sinus. Fistula

formation from iatrogenic trauma can occur from transsphenoidal hypophysectomy, trigeminal rhizotomy, and nasopharyngeal biopsy.

In other patients, there can be weakening in the wall of the carotid artery within the cavernous sinus. In patients with a cavernous carotid artery aneurysm, rupture of the aneurysm can result in a fistula. Spontaneous rupture can also occur in patients with connective tissue disorders such as Ehlers-Danlos and pseudoxanthoma elasticum.

7.3.4.2 Type B Fistula

Type B fistulas are due to indirect connections between the dural meningeal branches of cavernous internal carotid artery and the cavernous sinus. These arterial venous fistulas are indirect but still lack the normal tissue and capillary bed between the arteries and veins resulting in a transmission of elevated arterial pressures into the venous system. They can be high or low flow and typically are spontaneous rather than traumatic fistula. Despite some being low flow, many still cause marked elevation of intravenous pressure and severe ophthalmologic symptoms.

7.3.4.3 Type C Fistula

Type C fistulas result from indirect connections between the external carotid and the cavernous sinus through meningeal branches of the external carotid artery. Similar to Type B fistula, lack of a normal capillary bed between arteries and veins results in abnormal transmission of arterial pressure to the venous system. They can also be low or high flow and are more typically spontaneous rather than traumatic in origin.

7.3.4.4 Type D Fistula

Type D fistulas are supplied by both a combination of meningeal external carotid and internal carotid branches with direct transmission of arterial pressures into the cavernous sinus. Of the spontaneous fistula, Type D is the most frequent, occurring in up to 90 % of cases. Originally Type D fistulas were considered the most difficult to treat by transarterial embolization; however, as transvenous approaches are now more common, they are equally easy to treat as the other types.

7.3.5 Etiology for Indirect Fistula

The latter three types of fistula are recognized as a separate entity from Type A, being supplied by the small dural arteries as feeding pedicles. Various factors seem to contribute to their formation. Trauma to the small dural vessels can cause the

development of fistula; however, patients do not always present with a history of trauma. True traumatic indirect fistula may represent a different entity as a single supplying artery would be expected. This would not explain the more common Type D pattern of multiple feeding vessels.

As pregnancy has been found to be associated with 6 % of indirect fistula, hormonal factors may play a role. Furthermore, fistulas are more common in elderly women than men. Thrombosis of the cavernous and dural venous sinuses may play a role and are often observed in patients with fistula. In 1979, Houser suggested that a dural cavernous sinus fistula might develop secondary to thrombus in the cavernous sinus and many authors share this opinion nowadays. Theoretically when thrombosis and phlebitis occurs in the recipient venous system, it undergoes recanalization that triggers opening of latent pre-existing arterial venous communication.

Another theory is that venous hypertension results in fistula formation. Terada in 1994 demonstrated that in animal models, increased venous could cause acquired arterial venous fistula even in the absence of thrombosis. In 1997, Lawton was able to demonstrate a direct causal relationship between venous hypertension and increased angiogenic activity in rabbit cornea assays, supporting this hypothesis.

Some fistulas have been proposed to have a congenital origin. Dural carotid cavernous sinus fistulas are rare in childhood, but many cases in young childhood have been reported. They are not common and may actually represent a separate entity from the indirect fistula seen forming spontaneously in the elderly.

7.3.6 Embolization Agents

Originally treatment of carotid cavernous sinus fistula was primarily through an arterial approach with attempts to occlude the feeding arteries. The first embolic agents were particle embolics, shaved PVA that were handmade in the angiography labs similar to the homemade catheters originally used. These had very poor success rates with complication of cranial nerve dysfunction due to the concomitant embolization of the blood supply of the cranial nerves. Subsequently, treatment methods turned to detachable balloons which were used to both occlude the cavernous sinus as well as for sacrifice of the cavernous carotid artery. Unfortunately, detachable balloons were associated with serious complications, including premature detachment and unpredictable delayed balloon deflation.

Nondetachable pushable coils have also been utilized to occlude fistula. The first coils made of stainless steel are named Gianturco coils after inventor Cesare Gianturco. The coils contain interwoven Dacron fibers to increase thrombogenicity. Some have tried using these coils for transarterial embolization of external carotid feeders; however, this use results only in proximal occlusion and shunt reduction which does not produce permanent results. Due to the inability to reposition pushable coils, nontarget embolization and ischemic strokes may be more common.

More recently, detachable platinum embolization has been used due to improved safety over detachable balloons and pushable coils. The first system was named the Guglielmi detachable coil (GDC) system. As there was a history of using electrical current to occlude carotid cavernous sinus fistula, Guglielmi was performing animal experiments on electrothrombosis in 1979 and accidently discovered the detachment of an electrode from a steel wire through the process of electrolysis. This principle was then utilized in the GDC coil system in 1991. GDC has proven highly effective for the treatment of intracranial aneurysms and was FDA approved in 1995. The ability to precisely position the coils in a distant location, while always having the possibility of retrieving the coil, has been extremely important for safe treatment of not only brain aneurysms but also for occlusion of carotid cavernous sinus fistula. Currently transvenous coil embolization of the cavernous sinus is the most established and likely safest method of treating nearly all types of carotid cavernous sinus fistula.

Historically, liquid embolic agents have had a limited role for embolization outside of treatment of arteriovenous malformation. Recently approved by the FDA in 2005 for brain AVM, a newer liquid embolic agent Onyx, (ev3 Neurovascular Irving, CA) is being used. It can be injected in a slow controlled fashion, and its spread is easily predicted compared to the cyanoacrylate glue agents. Due to the popularity of Onyx for other uses, recent reports of liquid embolic use for CCF have been reported through both transarterial and transvenous approaches. Potentially filling with Onyx can provide immediate and more volumetric filling of the cavernous sinus as opposed to repetitively packing a large sinus with coils. Transarterial dural arterial feeder embolization may also be more expedient when the transvenous route to the cavernous sinus is technically challenging. Some authors have reported a higher incidence of permanent cranial nerve deficits which have been hypothesized to be due to both arterial and venous cranial nerve infarcts or the direct pressure created within the cavernous sinus. Others have recently reported extremely good success with Onyx with complication rates comparable to coil embolization.

A number of techniques have been described to close the fistula, with the safest being closure of the cavernous sinus. The various collateral pathways of the brain allow for complete closure of the cavernous sinus without harmful effect as well as provide many interesting vascular pathways to direct catheter-based therapy into the cavernous sinus. The venous drainage pathways of the brain and head and neck are in continuous equilibrium with venous flow centrally into the cavernous sinus and peripherally into the dural venous sinus and then the jugular veins. Likewise, the venous flow from facial structures can drain both toward the cavernous sinus through the ophthalmic vein and pterygoid venous plexus and outwardly toward the facial vein and the jugular vein. The middle and inferior division cortical veins of the hemispheres can both drain toward the middle cerebral vein into the cavernous sinus and bypass the sinus via the basal vein of Rosenthal to the deep venous system or through the middle cerebral vein of Labbe and then the transverse sinus. As a result, complete closure of the cavernous sinus will eliminate transmission of elevated arterial pressure to surrounding venous structures and importantly the veins of the orbit with essentially no complication provided the above collateral pathways exist.

7.4 Treatment Cases

7.4.1 Transvenous Occlusion via Inferior Petrosal Sinus

Transvenous occlusion is the most commonly accepted technique for carotid cavernous sinus fistula treatment due to its ability to potentially treat all fistula types regardless of etiology or source. The most common endovascular route into the cavernous sinus is through the inferior petrosal sinus, the dural venous structure connecting the cavernous sinus to the internal jugular vein. It is the most direct route, for indirect fistula, and is also considered safer than embolization through the carotid for Barrow Type A fistula. Often passage through the inferior petrosal sinus can be difficult due to chronic stenosis or thrombosis of both inferior petrosal sinuses. Stenosis of the inferior petrosal sinus is both theorized to be a secondary response to the chronically elevated venous pressures and a cause of conversion of an asymptomatic fistula into a symptomatic one through preferential shunting of flow to the superior ophthalmic vein.

The case pictured is of an 80-year-old female, with progressive right vision loss and pain. The fistula is an indirect Barrow Type D fistula, filled from both internal carotid and external carotid injections (Fig. 7.5). Prior to the development of the transvenous approaches, it would have been considered very difficult to treat, as each small external carotid feeding would be selected with microcatheters with attempts at particle or coil embolization. The small dural feeders originating from the cavernous carotid would not be treated with embolization due to the danger of reflux resulting in catastrophic strokes. Direct cannulation and contrast injection in the origin of both inferior petrosal sinuses demonstrated severe septations and

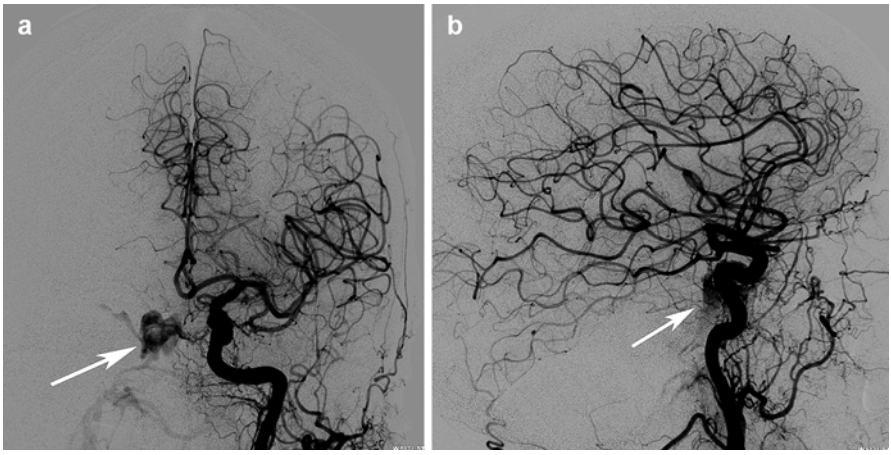

Fig. 7.5 AP (**a**) and lateral (**b**) views from a left cerebral angiogram performed with common carotid injection demonstrate early filling of the right cavernous sinus. Both selective external and internal carotid injections fill the cavernous sinus in an early fashion in this Barrow Type D fistula (*arrows*). Abnormal anterior drainage to the superior ophthalmic vein can be seen, as well as residual drainage into the right inferior petrosal sinus

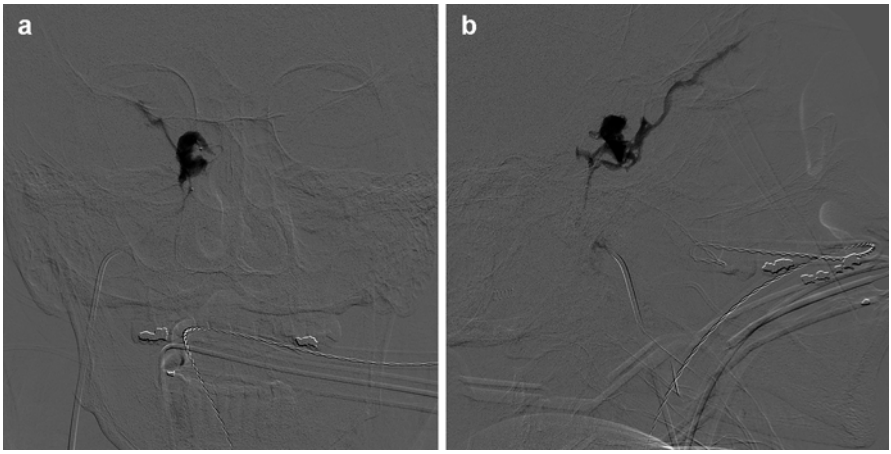

Fig. 7.6 AP (**a**) and lateral (**b**) lateral views demonstrate direct venography of the right cavernous sinus through passage of the microcatheter through the right inferior petrosal sinus. The expected septations and "caverns" within the right cavernous sinus are seen. Abnormal drainage pattern anteriorly and a dilated right superior ophthalmic vein can be seen

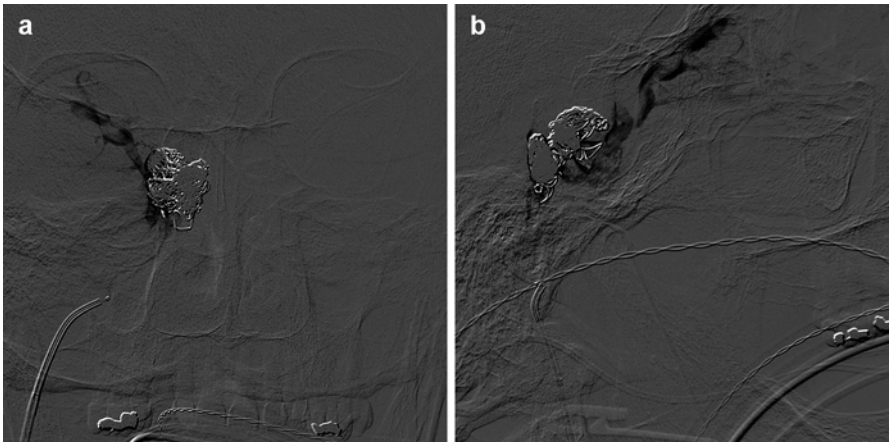

Fig. 7.7 AP (**a**) and lateral (**b**) views demonstrate detachable GDC coils that have been advanced through the microcatheter, forming a coil mass which has molded to the shape of the right cavernous sinus. A tight packing pattern can be seen with minimal free space between the coil loops which is necessary for bare platinum, non-fibered coils to adequately occlude the cavernous sinus

stenosis (Fig. 7.6). With careful wire manipulation, stenosis and even occluded inferior petrosal sinuses can be crossed successfully. Technique which is too aggressive can result in sinus rupture and subarachnoid hemorrhage. The right inferior petrosal sinus was able to be navigated and the right cavernous sinus was occluded with detachable GDC coils (Fig. 7.7). Subsequently repeat right carotid and left carotid angiograms demonstrated complete occlusion of the fistula and the patient's symptoms completely resolved (Fig. 7.8).

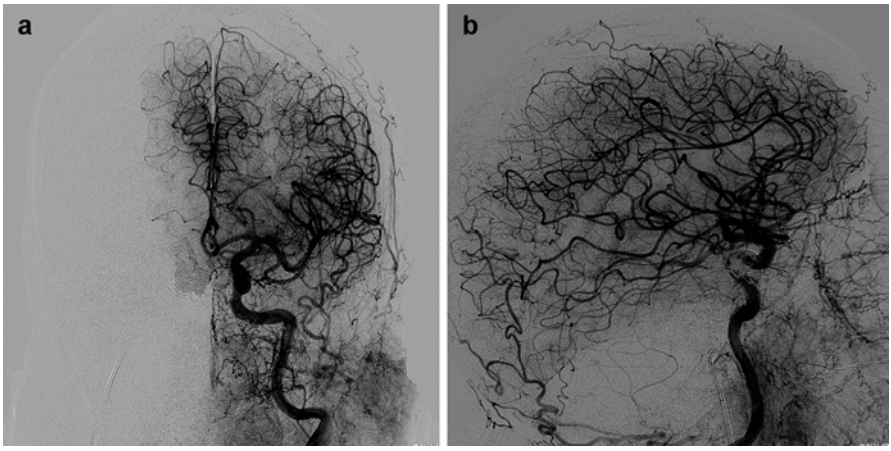

Fig. 7.8 AP (**a**) and lateral (**b**) views from the follow-up left cerebral angiogram confirm that the dural meningeal branches from the opposite carotid also no longer fill the cavernous sinus

7.4.2 Transvenous Occlusion via Superior Petrosal Sinus

The superior petrosal sinus, connecting the transverse sinus to the cavernous sinus, is another possible route for treatment. It is less commonly utilized, as the course of the catheter needs to take a more acute angle from the transverse sinus into the superior petrosal sinus as well as passing beyond the tortuosity of the sigmoid sinus. Thrombosis, stenosis, or occlusion of the inferior petrosal sinus may necessitate this route of entry. Unfortunately for symptomatic carotid cavernous fistulas, this route may also be closed, resulting in the forward shunting of flow into the superior ophthalmic vein.

The following case is of a 21-year-old male who developed persistent right eye swelling following a severe motor vehicle accident, with a right temporal bone fracture. Initially, eye swelling was diagnosed as soft tissue swelling from trauma. After a second motor vehicle accident, a CT scan of the head revealed dilation of the right superior ophthalmic vein (Fig. 7.9). The patient complained of blurry vision through the right eye and severe pain and headache when laying on the right side.

The subsequent diagnostic angiogram demonstrated a Barrow Type A fistula with high-risk features of a cavernous sinus varix and cortical venous shunting (Fig. 7.10). Treatment was attempted first in a transvenous fashion. Due to enlargement of the superior petrosal sinus from high flow, a path through the superior petrosal sinus was chosen to the cavernous sinus. Dual microcatheter placement in the cavernous sinus was performed through the superior petrosal sinus, to allow for placement of larger 020 coils as well as traditional 010 detachable neurovascular coils (Fig. 7.11). A Huber maneuver was performed which demonstrated the precise injury location in the cavernous carotid and allowed for a balloon catheter placement to protect coils from prolapsing into the internal carotid. Over 30 coils were placed into the cavernous sinus which did not completely close the shunt but

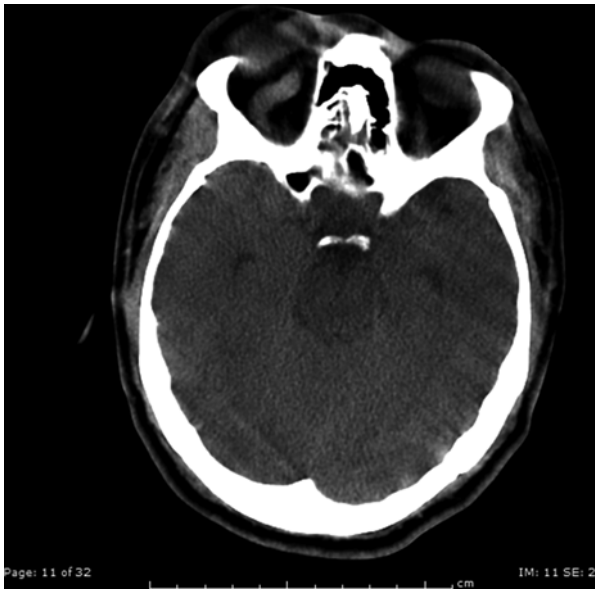

Fig. 7.9 Axial non-contrast image from head CT demonstrates marked dilation of the right superior ophthalmic vein which is very suspicious for the presence of carotid cavernous sinus fistula. Differential diagnosis also includes thrombosis of the superior ophthalmic vein; however, a dense thrombus would be expected

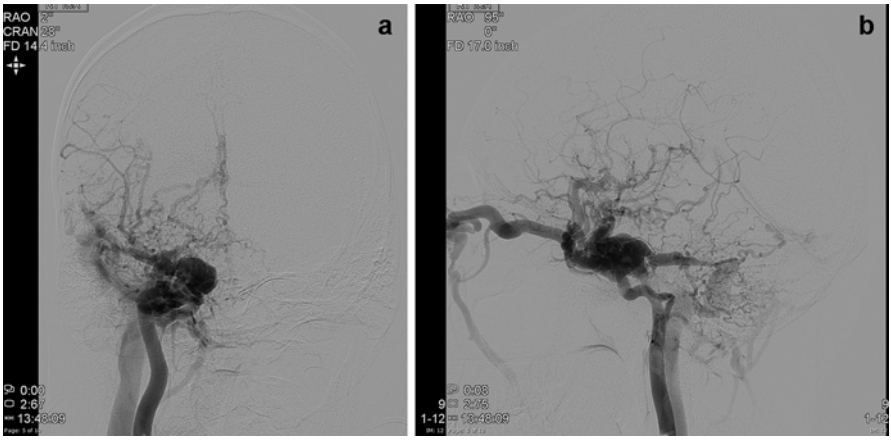

Fig. 7.10 AP (**a**) and lateral (**b**) views from the initial right cerebral angiogram and right internal carotid injection demonstrate essentially no visible intracranial vessels from the severe venous shunting from a Barrow Type A fistula. The cavernous sinus is enlarged from varix formation, and reflux is seen into the cortical and cerebellar veins which is a high-risk feature for hemorrhage and infarct

improved flow beyond the fistula (Fig. 7.12). Patient then returned in 3 weeks for completion coiling. At that time, the coils did not result in thrombosis of the cavernous sinus. Instead sacrifice of the left cavernous carotid was performed after successful balloon test occlusion to cure the fistula. Orbital symptoms and headache completely resolved.

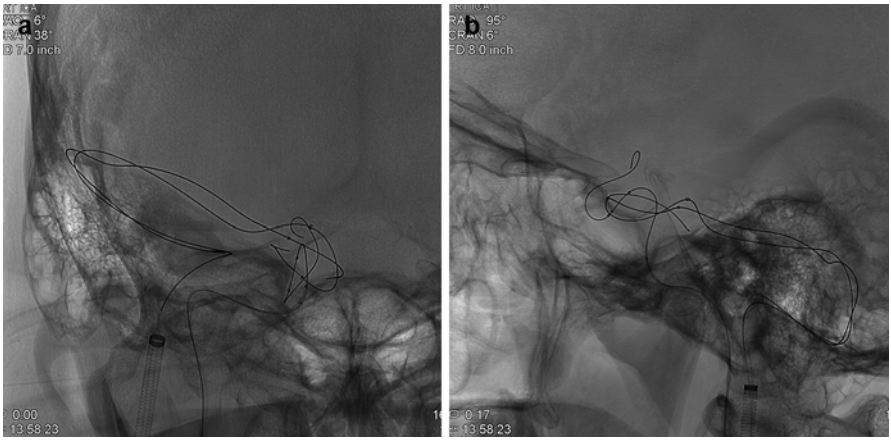

Fig. 7.11 AP (**a**) and lateral (**b**) views demonstrate placement of two microcatheters in the cavernous sinus through the superior petrosal sinus. Balloon catheter is present in the internal carotid from the Huber maneuver and is positioned to protect prolapse of coils from the cavernous sinus into the carotid artery

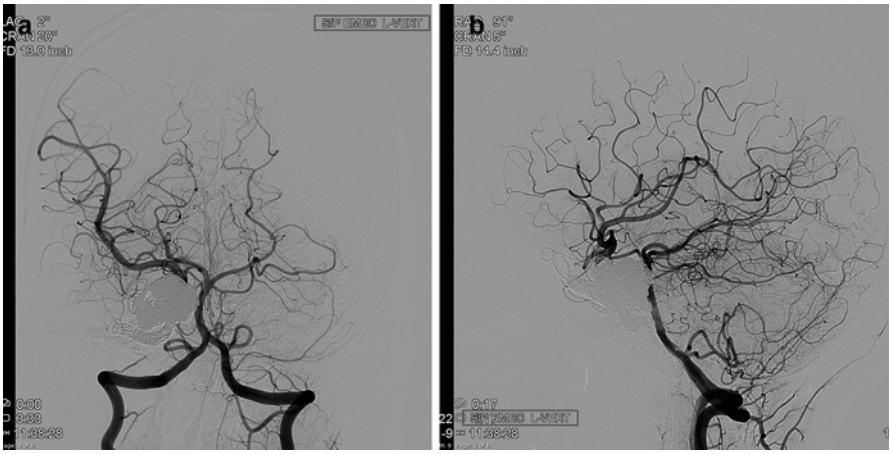

Fig. 7.12 AP (**a**) and lateral (**b**) views after placement of coils into the cavernous sinus

7.4.3 Transvenous Occlusion via Superior Ophthalmic Vein

Accessing the cavernous sinus through the superior ophthalmic vein was one of the first routes taken when treatment by passing a wire and applying a current directly into the cavernous sinus was first described. A distinct advantage to transvenous access to the cavernous sinus through direct superior ophthalmic vein approaches is that the risk of occluding the posterior cavernous sinus without fully occluding the anterior portion is minimized. With the other transvenous approaches, orbital symptoms may fail to improve and actually worsen if the connection between the

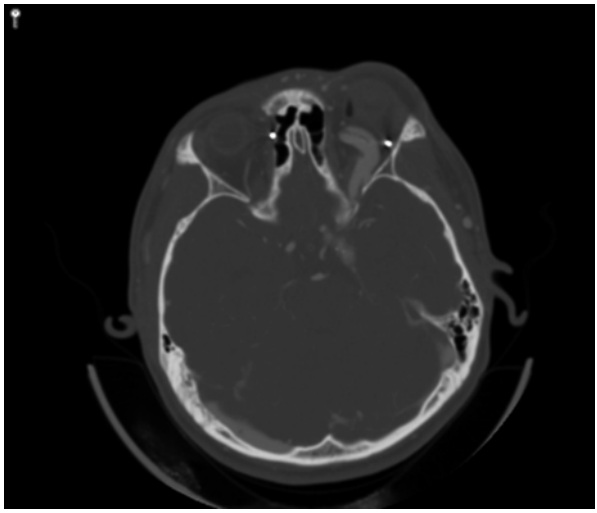

Fig. 7.13 CT scan demonstrating proptosis and a dilated superior ophthalmic vein on the *left side*. Axial contrast enhanced CT scan of the head dilated superior opthalmic vein and cavernous sinus. Two radiopaque shotgun pellets are also seen

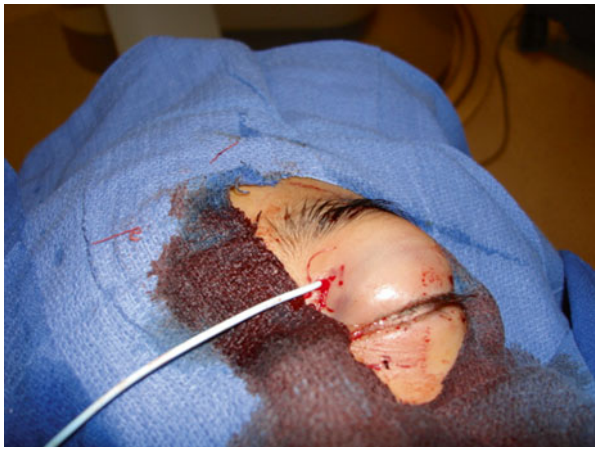

Fig. 7.14 Direct percutaneous puncture of the superior opthalmic vein under ultrasound guidance. Micropuncture system was utilized and exchanged for a larger 5 French Kumpe catheter to access the fistula

superior ophthalmic vein and fistula is not occluded with embolization and instead supplied with increased pressure through embolization of the posterior portion of the cavernous sinus. Unlike approaches through the inferior petrosal or superior petrosal sinus, placing coils as the catheter is withdrawn through the superior ophthalmic vein will directly the occlude routes of abnormal pressurization of the ophthalmic veins.

This 18-year-old male developed blurry vision, chemosis, and proptosis following a gunshot wound to the face (Fig. 7.13). The initial cerebral angiogram demonstrated the expected Barrow Type A fistula. He was treated initially through coil embolization of the cavernous sinus through a transarterial approach, directly through the carotid artery rather than the more common transvenous approach due to operator preference. As can be seen with traumatic fistula, they are often difficult to completely occlude

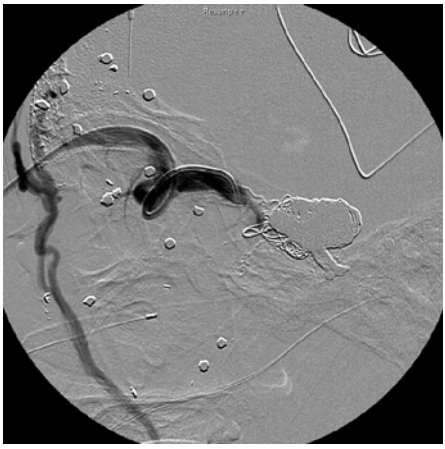

Fig. 7.15 Lateral DSA view performed following percutaneous access of the superior opthalmic vein with embolization of the anterior cavernous sinus with liquid embolic. The previously placed large mass of coils in the cavernous sinus and coils from carotid occlusion is seen posterior to the opacified superior opthalmic vein. Numerous radiopaque shotgun pellets are also seen

and the left carotid was sacrificed with coil embolization in an attempt to occlude the fistula. Unfortunately, his symptoms returned, and a session of liquid embolic embolization with Onyx below the coils was performed as the fistula remained patent. The patient's symptoms did not resolve, and ultrasound of the superior ophthalmic vein was performed which demonstrated an arterial rather than a venous waveform. As the ophthalmic vein was easily visualized on ultrasound, direct ultrasound-guided puncture of the superior ophthalmic vein was utilized (Fig. 7.14). A catheter was directly guided through the superior ophthalmic vein and a liquid embolic agent, Onyx was used to completely occlude the residual anterior cavernous sinus and its connection to the superior ophthalmic vein (Fig. 7.15). The treatment was without complication and symptoms resolved after the final transvenous treatment.

7.4.4 Transarterial Occlusion via Coil Embolization of Ruptured Aneurysm

Cavernous sinus aneurysms can be a cause for Barrow Type A carotid cavernous sinus fistula. Unlike intradural aneurysms, rupture of a cavernous sinus aneurysm does not result in life-threatening subarachnoid hemorrhage. Instead the presentation is typically with signs of a carotid cavernous sinus fistula, making the natural history of cavernous sinus carotid aneurysms much more benign when compared to intradural aneurysms. Typically, treatment is not recommended for cavernous sinus aneurysms until they become symptomatic from either rupture or mass effect on the adjacent cranial nerves. Like ruptured intracranial aneurysms, ruptured cavernous carotid aneurysms can be treated with endovascular coil embolization of the aneurysm sac. Treatment can be more elective in nature.

The following patient is a 41-year-old female who presented with 3 months of progressive left eye pain and swelling, after being seen in multiple emergency

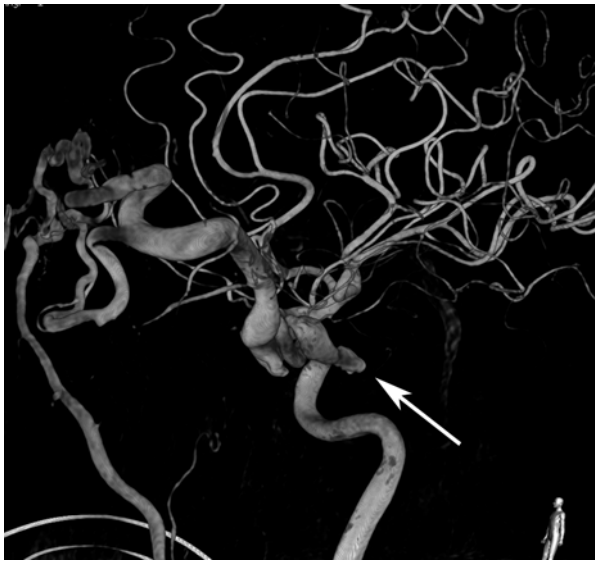

Fig. 7.16 Lateral view of 3D reconstruction from a rotational angiogram demonstrates a ruptured aneurysm of the left cavernous carotid artery (*arrow*). Due to the fistula the adjacent enlarged cavernous sinus is also seen with filling of a dilated superior opthalmic vein draining out the angular and facial vein

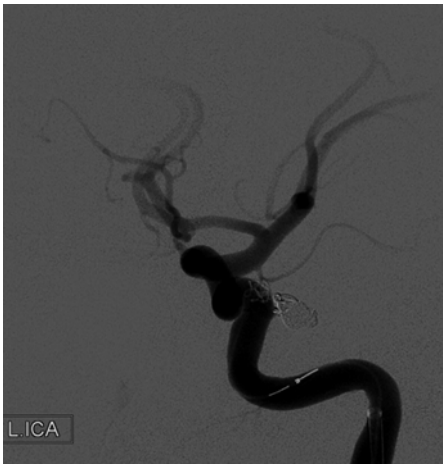

Fig. 7.17 Oblique lateral digital subtraction cerebral angiogram in the same projection as the 3D reconstruction demonstrates placement of detachable coils in the ruptured cavernous carotid aneurysm (*arrow*). No early filling of the cavernous sinus or superior opthalmic vein is seen after coil placement

departments, initially treated with antibiotics. Eventually a CT scan was performed to rule out periorbital abscess, after which the diagnosis of carotid cavernous sinus fistula was made. On physical exam, the patient had chemosis, proptosis, and a periorbital bruit. At the time of treatment, the cerebral angiogram demonstrated a previously undiagnosed ruptured aneurysm in the cavernous segment of the carotid artery (Fig. 7.16). The aneurysm was selectively catheterized and coiled with detachable coils (Fig. 7.17). Following embolization of the ruptured aneurysm, complete angiographic occlusion of the fistula was visualized, and the proptosis was noted to immediately improve.

7.4.5 Transarterial Occlusion with Liquid Embolic

Before the development of transvenous techniques for direct cavernous sinus embolization, the less effective techniques of particle and coil embolization of arterial feeding branches were utilized to treat carotid cavernous sinus fistula. Unfortunately, due to the proximal nature of coil embolization and the ability of particles to continue to move and wash out after embolization, there was a high recurrence rate. The actual point of arterial and venous connection must be obliterated to prevent return of the fistula. Arterial pedicles distal to the point of embolization eventually receive collateral flow from either growth of new vasculature or enlargement of microscopic pre-existing collaterals. Recently, there has been a resurgence in embolization from arterial routes even for indirect fistulas as liquid embolics allow for a more permanent and more distal occlusion at the site of arterial to venous connection. The newer liquid embolic agent Onyx, a polymer of ethylene vinyl alcohol, allows for much more controlled spread and injection compared to the cyanoacrylate agents. In addition, with new balloon microcatheters, difficulty and time taken with Onyx embolization has decreased and the success rate has increased. Initially reports of much higher rates of cranial nerve dysfunction were reported with Onyx embolization, but more recently, some authors have reported comparable complication rates compared to transvenous coil embolization.

This 60-year-old male presented with 2 months of left eye pain and swelling. A CT of the orbit was requested to rule out abscess and cellulitis. The initial read was of a normal study. In retrospect, asymmetric enhancement is seen in the left superior ophthalmic vein (Fig. 7.18). Eventually referred to ophthalmology, elevated pressures were noted in the left eye, and a carotid cavernous sinus fistula was suspected due to blurred vision and chemosis. An MRI and MRA were also performed which was read as normal, and eventually a conventional cerebral angiogram was performed due to the high suspicion and clinical findings. A subtle connection to the cavernous sinus was noted with selective angiography of the left occipital artery that resulted in direct drainage to the superior ophthalmic vein (Fig. 7.19). The location of the fistula is a more common location for a dural arterial venous fistula which typically drains toward the transverse sinuses rather than the cavernous sinus. As the

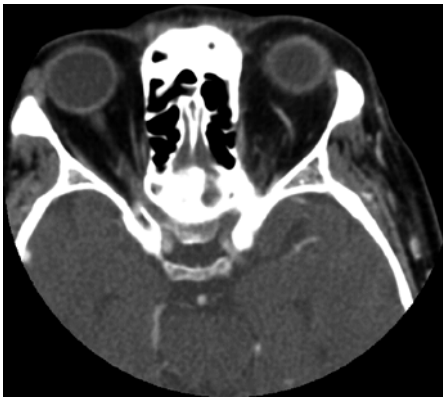

Fig. 7.18 Axial contrast enhanced CT of the head demonstrates very mild enlargement of the left superior opthalmic vein and asymmetric increased contrast opacification in this slow flow but high pressure fistula

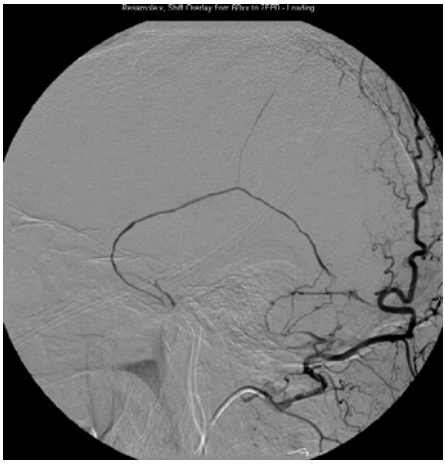

Fig. 7.19 Lateral DSA angiogram of the left occipital artery demonstrates direct fistulous connection through the skull to a temporal dural meningeal vein that slowly filled the cavernous sinus and superior opthalmic vein

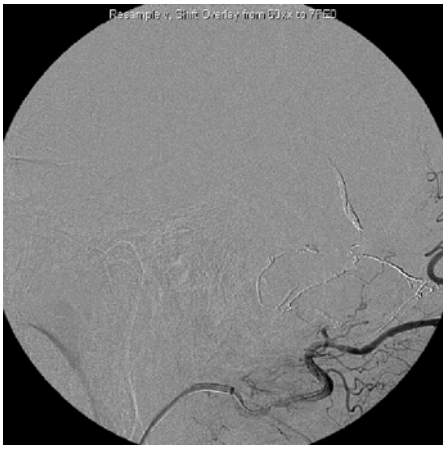

Fig. 7.20 Direct catheterization of the arterial pedicle was obtained and Onyx embolization was performed. This follow up angiogram demonstrates occlusion of the fistula with patency of the occipital artery

anatomy and location was consistent with a dural arterial venous fistula with drainage toward the cavernous sinus and ophthalmic vein, the liquid embolic approach was chosen as this is the commonly utilized approach for dural arterial venous fistula. Direct catheterization of the arterial pedicle through the skull base was obtained with a 0.48 mm microcatheter, and Onyx embolization was performed, occluding the fistula while maintaining patency of the occipital artery (Fig. 7.20).

7.4.6 Treatment Timing

Most patients with carotid cavernous sinus fistula are treated in an elective fashion with long-standing symptoms that develop over months and an underlying asymptomatic fistula that have progressed to symptoms. In certain cases, treatment is considered urgent due to high-risk features. The accepted clinical signs that a patient is

considered high risk include increased intracranial pressure, rapid progression of proptosis, diminished visual acuity, hemorrhage, and transient ischemic attacks. Following a diagnostic angiogram, treatment can also be considered more urgent base on high-risk angiographic features. The high-risk imaging findings include venous pseudoaneurysms, large cavernous sinus varix, outflow vein thrombosis, and retrograde venous drainage into the cortical veins. These features are considered high risk as intracranial hemorrhage is more likely as well as ischemic infarcts from poor venous outflow in the areas of reflux.

7.4.7 Intraorbital Arterial Venous Fistula

As fistulous connections can occur anywhere between an artery and vein, similarly, direct intraorbital arterial venous fistulas have been reported without involvement of the cavernous sinus. Intraorbital AVF are extremely rare with the largest published case series of combined orbital vascular anomalies reporting three intraorbital fistulas and AVM out of 627 patients (Wright 1974).

7.4.8 Intraorbital Arteriovenous Malformation

Intraorbital arteriovenous malformations are another rather high-flow orbital vascular lesion. A vascular nidus or bundle of dysplastic vessels without a capillary bed forms the connection between the ophthalmic artery and vein unlike a fistula. Like the other lesions, they can also present with proptosis, chemosis, and signs of elevated orbital venous pressure. They are believed to be congenital and can enlarge over time. Thrombosis of venous outflow pathways can cause rapid progression of orbital symptoms and there are rare reports of orbital hemorrhage. Unlike arterial venous fistula, endovascular treatment is more difficult as simple venous occlusion would highly risk bleeding from increased pressurization of the AVM nidus. Arterial embolization is difficult and of high risk for vision loss due to the possibility of inadvertent embolization of the central rental artery. To test safety of embolization, some advocate intra-arterial lidocaine test injections prior to intraorbital ophthalmic artery.

7.4.9 Periorbital Tumor AVF

A common feature in highly vascular tumors is the presence of intratumoral arterial venous fistula due to neovascularization. Blood vessels produced from the proangiogenic factors in cancer not normal vessels and can be irregular with decreased distance between blood vessels leading to formation of arterial venous shunts. More commonly periorbital tumors result in direct mass effect on the orbit rather than

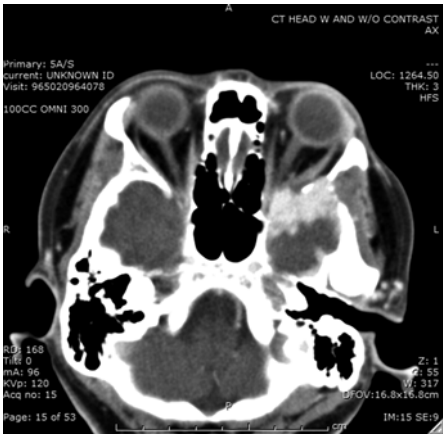

Fig. 7.21 Contrast enhanced CT scan of the head demonstrates left proptosis and an avidly enhancing mass in the left sphenoid wing that directly abuts the optic nerve. Initial concern was for mechanical compression resulting in visual disturbance, and the abnormal the enlargement and early enhancement of the superior opthalmic vein was not initially noted

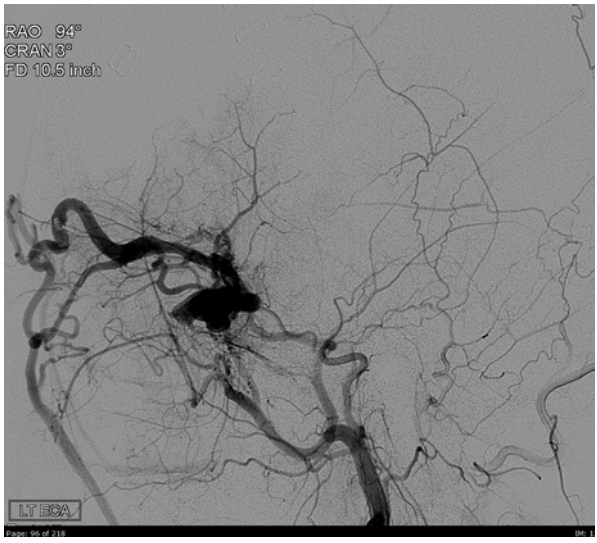

Fig. 7.22 Lateral view from digital subtraction angiography (DSA) of the left external carotid artery demonstrates a hypervascular mass (*arrow*) supplied by middle meningeal and deep temporal arteries with an intratumoral arterial venous fistula draining directly to the superior opthalmic vein and elevating intraoccular pressures

increased venous pressures. However, as with the other causes arterial to venous shunts, they can present with symptoms from increased venous pressures in rare situations.

This 37-year-old female presented initially with left eye pain, left forehead pain, and gradual loss of vision. She originally was prescribed eye drops at a community clinic and then after 30 days of symptoms was seen by an ophthalmologist and was treated with antibiotics. Her symptoms persisted and was seen in the emergency department after 48 days with chemosis, proptosis, and decreased visual acuity. A CT of the orbits ordered for evaluation of periorbital abscess demonstrated a mass in the left sphenoid wing and was describe as compressing the optic nerve without identification of the arterial venous shunting into the enlarged superior ophthalmic vein (Fig. 7.21). She was taken to the operating room by neurosurgery for resection of the

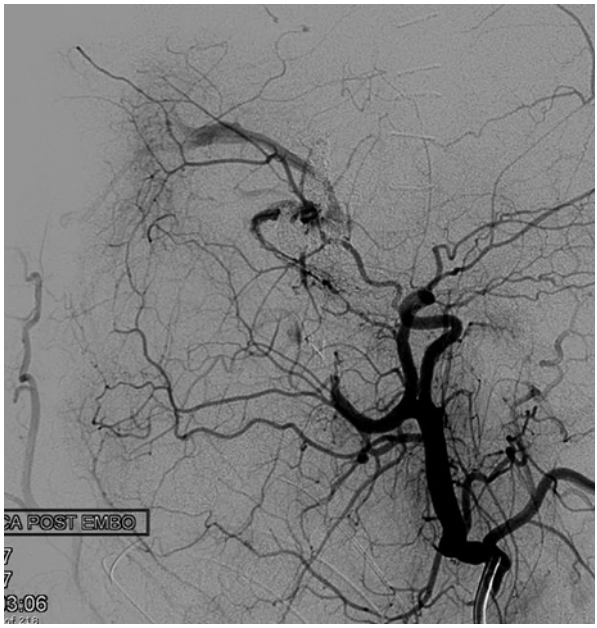

Fig. 7.23 Lateral DSA of the left external carotid artery after Onyx embolization of the middle meningeal and deep temporal arteries demonstrates minimal residual intratumoral shunting to the superior opthalmic vein (*arrow*). No further embolization was performed as tumor resection was anticipated

mass, and due to severe hemorrhage, the surgery was aborted and endovascular consultation for preoperative embolization was requested. The conventional angiogram confirmed the hypervascular mass in the left sphenoid wing with severe arterial to venous shunting from the intratumoral fistula draining directly in the superior ophthalmic vein (Fig. 7.22). Vascular supply to the tumor included anterior division of the middle meningeal artery and deep temporal artery. Through selective catheterization of the segmental middle meningeal artery feeder and deep temporal artery, ethylene vinyl alcohol, Onyx, (ev3 Neurovascular, Irvine, CA) was utilized for liquid embolic embolization (Fig. 7.23). The patient immediately experienced improvement in vision with resolution of chemosis and proptosis. Three days after embolization, surgical biopsy was performed with the resulting rare tissue diagnosis of epithelioid hemangioendothelioma. The patient was offered radiation therapy for treatment of the tumor, which she declined, but remained symptom free 16 months after embolization.

7.5 Cerebral Arteriovenous Malformation

Intracranial parenchymal arteriovenous malformations occur at the rate of 0.04–0.52 % in the general population with peak presentation between 20 and 40 years. Typically, brain AVM present with hemorrhage or seizures. The drainage pattern is classified as superficial or deep with the eventual drainage of flow through the dural venous sinuses to jugular veins. Rare cases have presented with orbital symptoms due to orbital venous drainage pathways of the parenchymal cerebral AVM.

7.6 Summary

High-flow orbital vascular lesions are a family of many different disease processes, unified primarily by their common clinical symptoms which arise from elevated orbital venous pressure. The rarer lesions are more difficult and risky to treat. Fortunately, over 99 % of high-flow orbital vascular lesions are carotid cavernous sinus fistula. Although natural history and etiology of Barrow Type A fistula differ significantly from Type B, C, and D fistulas, now their endovascular treatment approach is nearly identical. Transvenous embolization of the cavernous sinus has proven to be a very safe and effective technique for all four types. Clinical success rate from transvenous embolization is over 90 %. Complications are very low and considerably lower than the older endovascular and open techniques. 11 % transient neurologic symptoms are reported, typically from cranial nerve palsy secondary to over packing of the cavernous sinus. Permanent cranial nerve palsy rates should be less than 2 % and ischemic stroke rates should be no greater than that of diagnostic cerebral angiography. Due to the minimally invasive nature, transvenous embolization can be even performed under conscious sedation or local anesthesia. This evolution of treatment is remarkable, given that once open direct surgical approaches required hypothermia and complete cardiac arrest.

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Chapter 8
Low-Flow Vascular Malformations of the Orbit: Evaluation and Management

Sheena Pimpalwar, Ponraj Chinnadurai, and Douglas P. Marx

8.1 Introduction

Orbital lymphatic and venous malformations are low-flow vascular anomalies that commonly occur in the head and neck region [1, 2]. In most studies, they represent less than 2 % of all orbital and periorbital lesions, occurring most commonly in the first decade of life [1, 2]. A significant number of patients with these malformations present with intralesional bleeding or infection [3, 4]. Without appropriate therapy, approximately 40 % of patients develop reduced vision and 7 % develop blindness [3].

8.2 Clinical Presentation

Periorbital and orbital swelling is the most common clinical presentation of orbital venous and lymphatic malformations [4]. Intralesional bleeding or infection can result in sudden periorbital swelling and proptosis with or without pain (Fig. 8.1a). Lesions that extend anteriorly under the conjunctiva can present with mild to severe chemosis. Orbital involvement may also cause binocular diplopia that is not always appreciated due to associated mechanical ptosis. Another important sequel of mechanical ptosis in early childhood is the development of amblyopia. In addition, exposure keratitis and corneal erosion are other causes of vision loss in these patients [3, 5].

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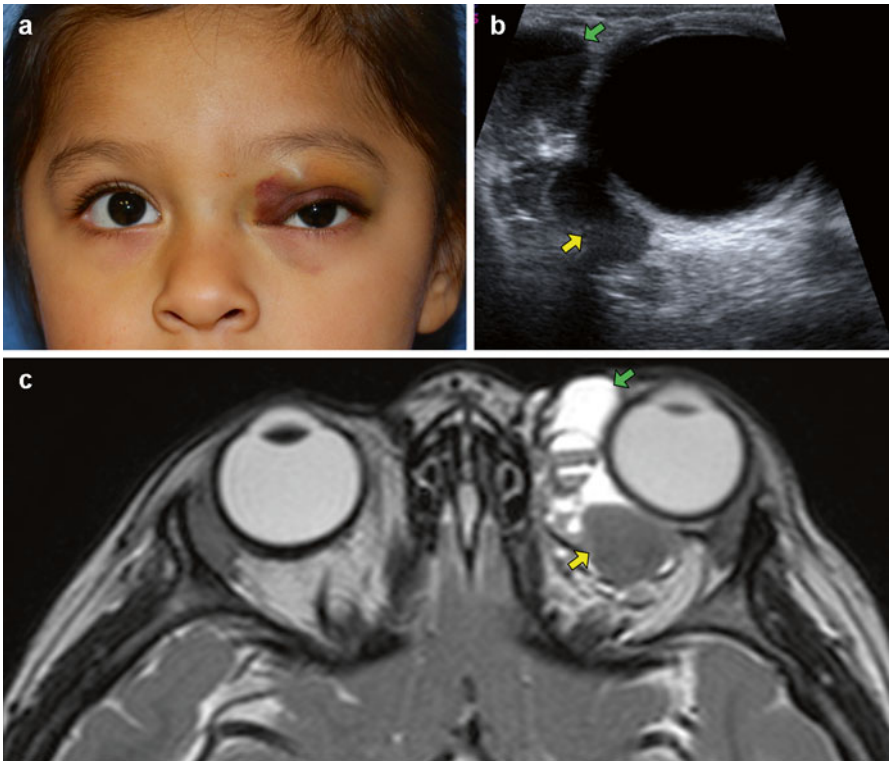

Fig. 8.1 A 3-year-old girl presenting with acute painful proptosis and ecchymosis with normal visual acuity and IOP. (**a**) Clinical photograph showing left eyelid ecchymosis and periorbital swelling. (**b**, **c**) Ultrasound and axial T2W MRI of the left orbit showing intraconal (*yellow arrow*) and pre-septal (*green arrow*) lymphatic microcysts with fluid-fluid levels suggestive of internal hemorrhage

8.3 Evaluation

8.3.1 Clinical

Complete ophthalmic examination including clinical photographs, visual acuity, pupillary response, extra-ocular motility, slit-lamp examination, dilated funduscopic examination, and intraocular pressure (IOP) measurements is performed.

8.3.2 Imaging

The anatomical distribution and characterization of the malformations are evaluated using pre- and post-contrast MRI of the face and orbits, with T2-weighted imaging being most valuable. Ultrasonography is performed by the interventional radiologist for treatment planning (Fig. 8.1).

8.4 Management

Current options for management of low-flow orbital vascular malformations include observation, sclerotherapy, and surgical debulking with partial to total excision. Our institutional protocol for evaluation and management of low-flow orbital vascular malformations is summarized in Fig. 8.2.

Incidentally detected asymptomatic malformations can be managed conservatively, but malformations that present with acute proptosis and compressive optic neuropathy secondary to intralesional bleeding usually require emergent management by image-guided lymphatic cyst aspiration or surgical decompression. Malformations that present with repeated intralesional hemorrhage, infection, chronic proptosis, retro-orbital discomfort, ophthalmoplegia, headaches, or visual impairment may be managed by either surgical excision [5] or sclerotherapy [6–10].

8.4.1 Surgical Therapy

Low-flow orbital malformations are often very infiltrative, and total excision is virtually impossible because of the associated morbidity [11]. However, well-delineated extraconal lesions have been resected with low complication and recurrence rates [12]. In some long-term studies, however, these malformations have a tendency to recur with recurrence rates ranging between 58 % at a mean of 3.4 years [13] and 71 % at a mean of 7.2 years [5]. Therefore, less invasive techniques such as sclerotherapy have emerged as a treatment option.

8.4.2 Sclerotherapy

Sclerotherapy is a well-established management option for low-flow orbital vascular malformations [6–10]. The primary challenge for sclerotherapy is safe access into the retrobulbar space. The secondary challenge is management of orbital compartment syndrome that can occur from the inflammatory response post sclerotherapy [14]. Sclerotherapy requires multidisciplinary management involving ophthalmology, oculoplastic surgery, interventional radiology, and pulmonology services.

8.4.3 Sclerotherapy Agents

A variety of agents used for sclerotherapy including their advantages and disadvantages have been described in the literature [15]. At our institution, we use bleomycin for lymphatic malformations and a sequential injection of 3 % sodium tetradecyl

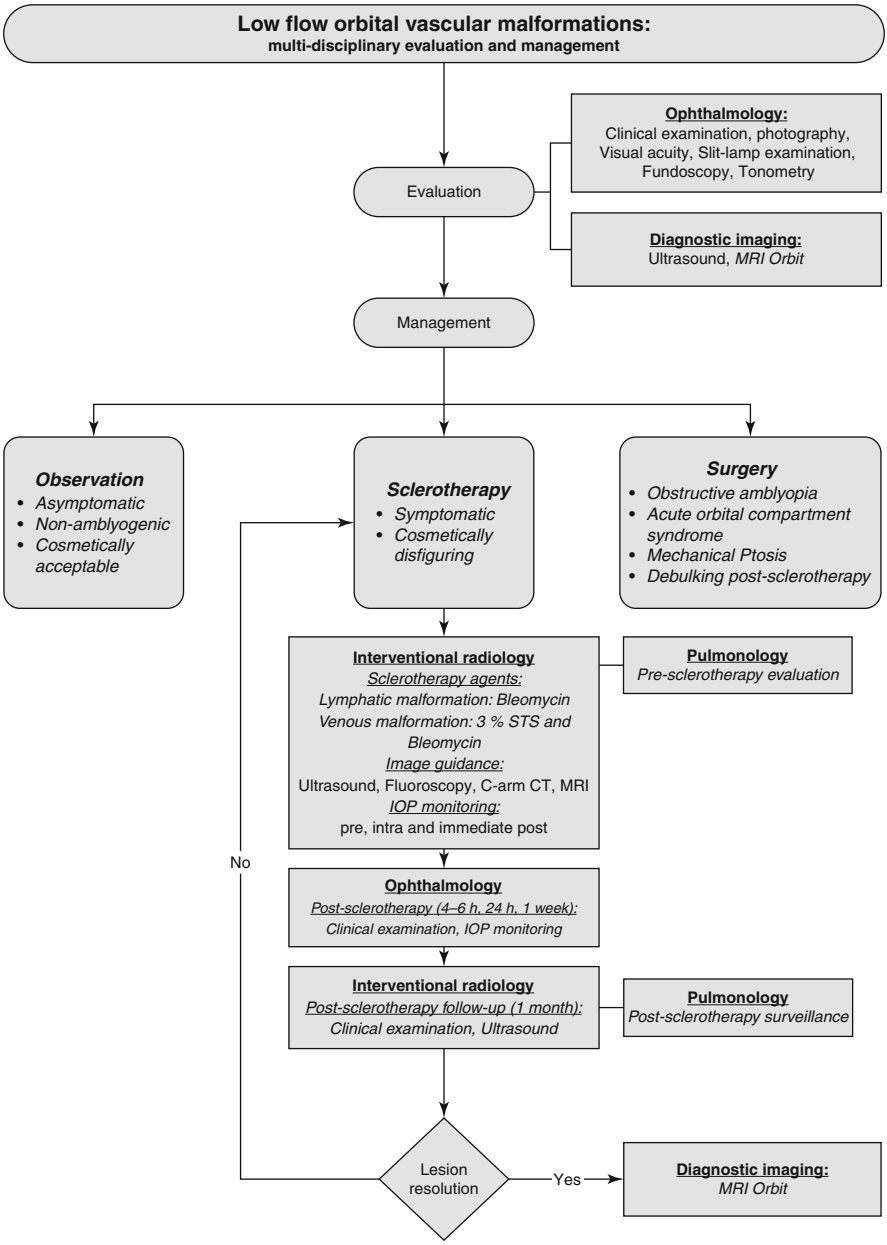

Fig. 8.2 Algorithm for evaluation and management of low-flow orbital vascular malformations

sulfate (STS) and bleomycin for venous malformations. The maximum bleomycin dose per session is 0.5 units/kg for <1-year-old and 15 units for >1-year-old [16].

Cumulative toxicity of systemic bleomycin during treatment of malignancy has been associated with late-onset pulmonary fibrosis [17]. Although no case of pulmonary fibrosis secondary to intralesional injection of bleomycin has been reported thus far, a pulmonary fibrosis surveillance program is followed at our institution. Children older than 7 years undergo exercise tolerance test and pulmonary function tests including spirometry, plethysmography, and diffusion capacity of carbon monoxide. Children younger than 7 years old are screened using exercise tolerance, and chest imaging is performed only if necessary. The clinical and functional pulmonary evaluations are repeated at 6 and 12 months post sclerotherapy and yearly thereafter for 10 years.

Skin pigmentation after intralesional bleomycin has been reported in a few cases [14, 18, 19]. The following precautions are followed to reduce the risk of skin trauma and pigmentation secondary to bleomycin: (i) avoiding tape application to the skin; (ii) using alcohol-free skin barrier film prior to tape application; (iii) securing the endotracheal tube without tape by using a Dale tube holder, a Thomas tube holder, or silk sutures; and (iii) retaining of EKG pads for 48 hours.

8.4.4 Sclerotherapy Technique

The procedure is performed under general anesthesia with oral or nasal intubation. The intraocular pressure (IOP) is measured bilaterally using applanation tonometry, and a corneal protector is placed over the eye.

Lymphatic malformations are accessed under ultrasound guidance using 20G, 21G, and 25G needles for cysts <2 cm and 5 or 7 F pigtail catheters for cysts >2 cm (Figs. 8.3 and 8.4). Whenever ultrasound imaging is limited,

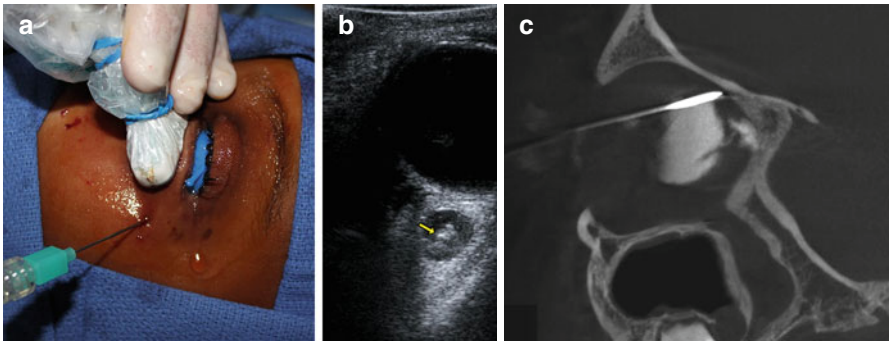

Fig. 8.3 Image-guided access of lymphatic malformation. (**a**, **b**) Ultrasound-guided needle access of retrobulbar lymphatic microcyst (*yellow arrow - needle tip*). (**c**) C-arm cone-beam CT image-guided access of retrobulbar lymphatic macrocyst and visualization of bleomycin-contrast mixture within the cyst

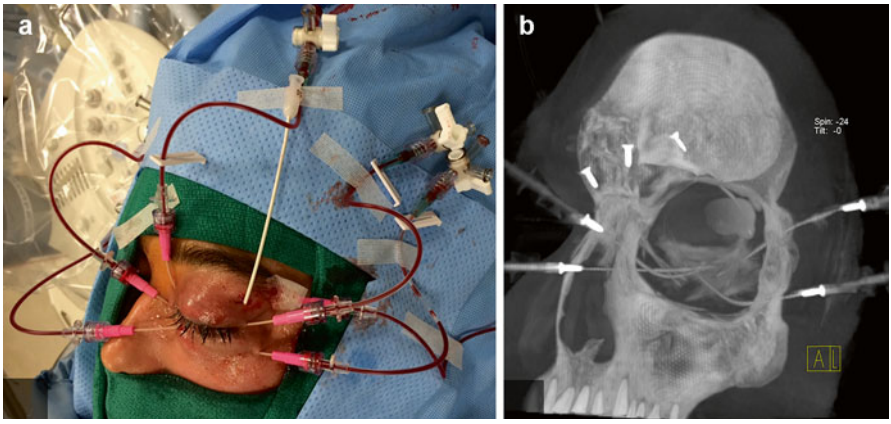

Fig. 8.4 An 18-year-old boy with infiltrative mixed macro-microcystic lymphatic malformation. (**a**) Lesion access using multiple 20G angiocatheters and a pigtail catheter. (**b**) 3D reconstructed C-arm cone-beam CT image showing distribution of bleomycin-contrast mixture within the malformation

particularly in the retrobulbar space, additional intra-procedural C-arm cone-beam CT guidance is utilized to supplement ultrasound. Cysts are aspirated whenever possible prior to injection of bleomycin mixed with 10 % contrast (Omnipaque 300 mg/ml) in a concentration of 1–3 units/ml. The total intra-orbital sclerosant volume is restricted to 5 ml to reduce the risk of rise in IOP post sclerotherapy.

Injection of bleomycin is monitored using visualization of moving microbubbles under ultrasound and 2D fluoroscopy (Fig. 8.5a, b). The detailed anatomical distribution of bleomycin in relationship to critical orbital structures is further evaluated using intra-procedural C-arm cone-beam CT [20] (Fig. 8.5c, d). Image fusion of C-arm cone-beam CT images with pre-procedural T2W MRI is performed to evaluate any untreated areas of the malformation (Fig. 8.5e, f). These areas are accessed and treated in the same or separate session.

Venous malformations are accessed using a similar technique followed by evaluation of their venous drainage using digital subtraction roadmap venography. Then, they are treated with a sequential injection of 3 % sodium tetradecyl sulfate foam followed by bleomycin.

8.4.5 Intraocular Pressure Monitoring

IOP is monitored at the end of the procedure while the patient is still intubated. Ophthalmic examination is performed 4–6 h and 24 h following the procedure. The patients are discharged from the hospital if no concerning findings are identified.

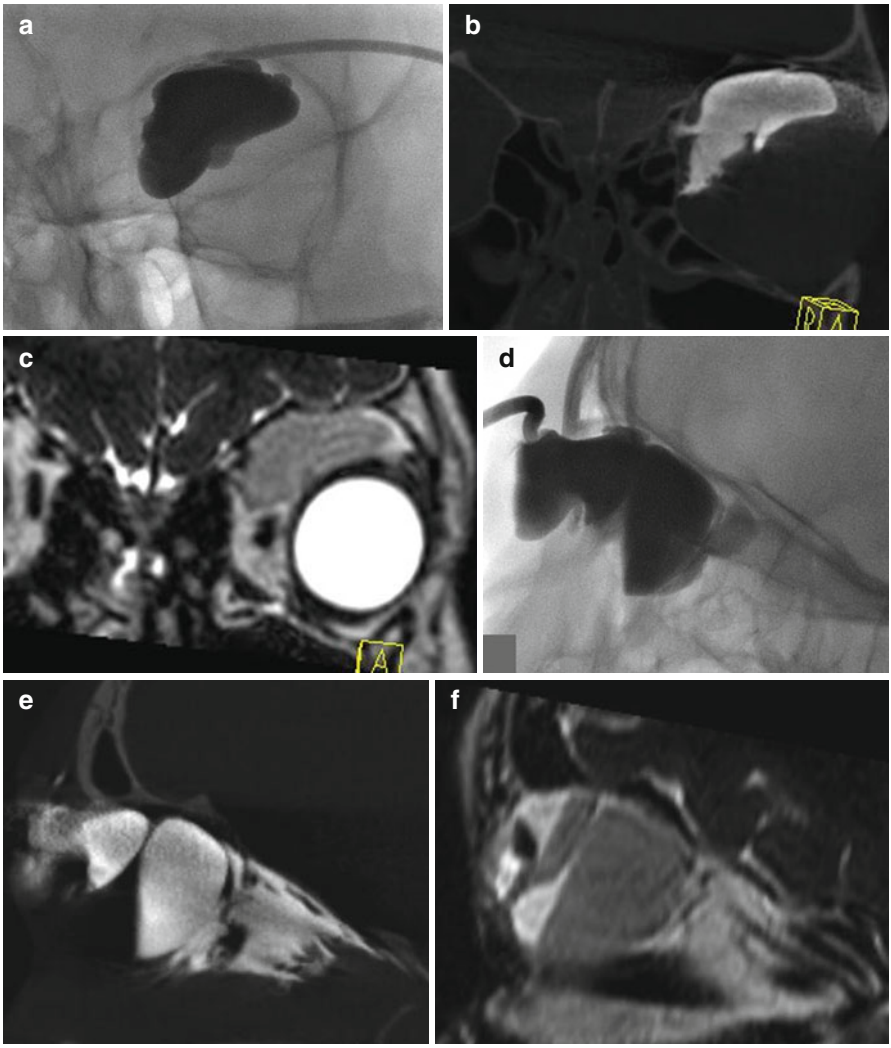

Fig. 8.5 A 13-year-old boy with mixed macro-microcystic lymphatic malformation of the left orbit. (**a**, **b**) Frontal and lateral 2D fluoroscopic images showing distribution of bleomycin-contrast mixture within the malformation. (**c**–**f**) Co-registered images showing good correlation between bleomycin distribution in C-arm CT (**c** coronal, **d** sagittal) and lesion distribution in pre-sclerotherapy MRI (**e** coronal, **f** sagittal)

8.4.6 Management of Post-sclerotherapy Complications

Fever up to 101 F within 24 hours post sclerotherapy and lasting for 24–48 hours is a systemic response to bleomycin and does not require additional investigation or treatment.

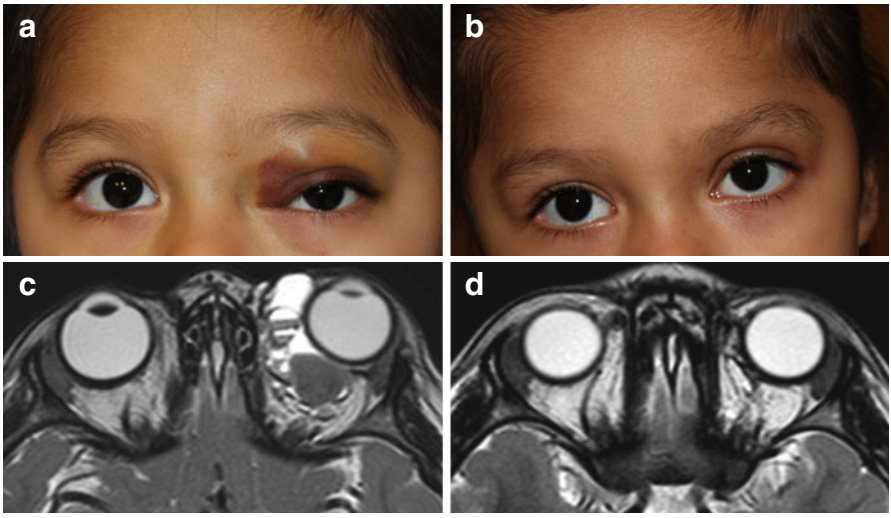

Fig. 8.6 A 3-year-old girl with microcystic lymphatic malformation of the left orbit: comparison of pre- and post-sclerotherapy images. (**a**, **b**) Clinical photographs showing resolution of proptosis and ecchymosis. (**c**, **d**) Axial T2W MRI showing complete resolution of malformation after one sclerotherapy session

One of the most problematic complications of sclerotherapy is elevated IOP resulting in orbital compartment syndrome [14, 18, 21, 22]. Our protocol for management of raised IOP is as follows: A rise in IOP above 35 is managed with topical beta-blockers and alpha-2 agonists. If the IOP rises above 40, systemic steroids are added to reduce swelling secondary to inflammation. In addition, ultrasound or CT imaging is performed to diagnose intralesional bleeding as a cause of raised IOP that can be managed by ultrasound-guided drainage. Surgical decompression is rarely necessary with appropriate monitoring and management of raised IOP.

8.4.7 Follow-Up

Ophthalmic examination is repeated at 1 week post procedure and interventional radiology evaluation including ultrasound examination at 1 month post procedure. If necessary, further sclerotherapy sessions are performed at 6-week intervals. MRI examination is performed at 3 months after the conclusion of sclerotherapy. Post-sclerotherapy MR images are co-registered with pre-sclerotherapy MR images to correlate imaging outcome with clinical resolution (Figs. 8.6 and 8.7).

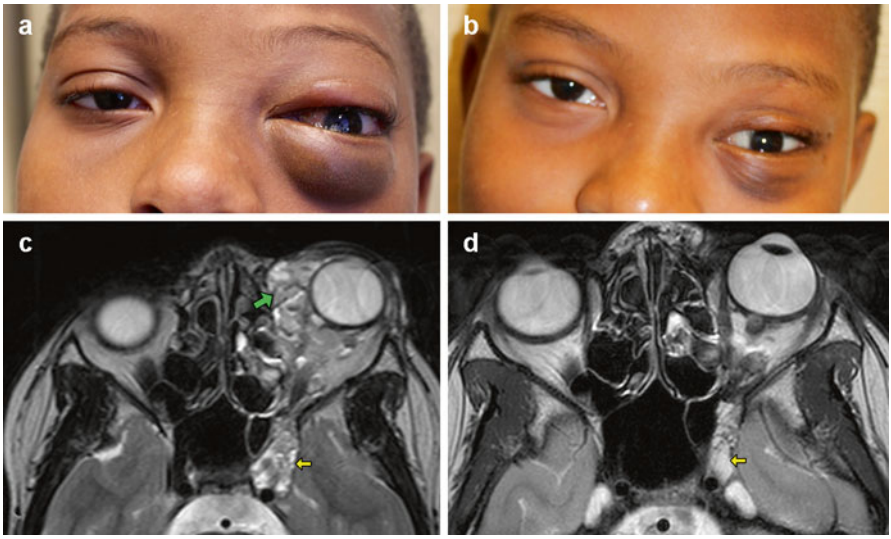

Fig. 8.7 A 9-year-old boy with microcystic lymphatic malformation of left orbit. (**a**, **b**) Clinical photographs showing resolution of proptosis, chemosis, and ecchymosis. Note post-sclerotherapy hyperpigmentation of the lower eyelid secondary to bleomycin. (**c**, **d**) Axial T2W MRI showing complete resolution of intra-orbital malformation (*green arrow*) and partial resolution of malformation within the wall of cavernous sinus (*yellow arrow*) after two sclerotherapy sessions

8.5 Conclusion

Low-flow orbital vascular malformations manifest as cosmetically disfiguring lesions associated with amblyopia, diplopia, ptosis, and even loss of vision. Many of these lesions, particularly those located in the intraconal and extraconal orbital space, are very difficult to treat surgically and often recur. Sclerotherapy has evolved as a minimally invasive treatment option for these malformations with good clinical outcome. The best management of these uncommon, yet vision-threatening lesions is achieved with a multidisciplinary collaborative team effort.

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Chapter 9
Advanced Laser Therapy for Cutaneous Vascular Lesions of the Eyelid and Face

Bryan Hiscox, Wesley Wu, and Ramsey Markus

9.1 Introduction

Laser therapy is the preferred treatment for many cutaneous vascular lesions, including those of the head and neck. Over the past 50 years, medical lasers have evolved from a relatively crude application of high technology to a wide variety of sophisticated, technologically mature devices. With proper technique and safety precautions, modern laser therapy offers safe, noninvasive, and efficacious treatment of vascular lesions that may be otherwise untreatable. This chapter reviews the principles behind laser therapy and applies these principles clinically to the treatment of commonly encountered vascular lesions.

9.1.1 Historical Context

The theoretical basis for lasers was established in the first decades of the twentieth century, as physicists laid out the mathematical framework for quantum mechanics. In 1917, Albert Einstein published a paper describing stimulated emission of radiation. The first true laser was demonstrated in 1960 by Theodore Maiman using a ruby crystal. Almost immediately, physicians began to use it for medical purposes, starting with treatment of retinal detachment [1]. Over the next decades, Leon Goldman pioneered many cutaneous applications of lasers while working at the University of Cincinnati and is widely considered the father of lasers in medicine. Early devices, such as argon and CO_2 lasers, were powerful but difficult to control. For example, efforts to treat port-wine stains initially revolved around

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continuous-wave argon lasers. Although effective at destroying the targeted vasculature, complications such as scarring and dyspigmentation were common and limited the usefulness of this technology [2].

Major progress occurred in the 1980s. In 1983, Rox Anderson and John Parrish published the theory of selective photothermolysis, which rigorously addressed the long-standing observation that different structures within the skin showed different affinities for laser light. Briefly, this theory states that by exposing a target tissue to a preferentially absorbed wavelength of light, a sufficiently brief and powerful laser pulse can selectively destroy that target while sparing the surrounding tissue. Around the same time as this insight into laser-tissue interaction, there were significant advances in laser technology. Most important for vascular lesions was the development of the flashlamp-pumped pulsed dye laser (PDL), also by Anderson and Parrish's group. The PDL produces light in the yellow portion of the spectrum that preferentially targets cutaneous hemoglobin. In addition, these new lasers were capable of producing increasingly short pulses of light. These technical advances, combined with the theoretical insight of selective photothermolysis, led to a revolution in the treatment of vascular lesions.

9.1.2 Laser Fundamentals

Light emitted by lasers is distinctive in a number of important ways [3]. It is monochromatic, meaning that all photons are the same wavelength or color. The emitted light is also coherent, meaning that the photons are in the same phase, both in space and in time. The light is also collimated, which means that the individual photons are traveling in parallel, with no divergence other than that caused by diffraction. Lasers also have the capacity for high intensity or brightness. Although not a strict criterion, medical lasers are also capable of delivering light in short pulses. The most recent generation of "picosecond" lasers can achieve pulse durations on the order of 10^{-10} s. In modern laser devices, every one of these characteristics is precisely controlled and contributes to achieving the desired clinical effect.

In its original form, LASER is an acronym for light amplification by stimulated emission of radiation, which refers to the physical process by which a laser system is able to create light with the preceding characteristics. All laser systems share three basic components: a gain (or lasing) medium, an energy source, and an optically resonant cavity [3]. The gain medium may be a gas, a solid, or a liquid, and the atomic structure of this medium determines the wavelength of the emitted light. Representative examples of common gain media include neodymium-doped yttrium aluminum garnet crystal (Nd:YAG), CO_2 gas, and rhodamine dye in solution (PDL). Although the specifics of the energy source and optical cavity are important in laser design, they are not clinically relevant and are outside the scope of this chapter. To be practical, medical lasers also require a delivery mechanism or handpiece. This component can fine-tune the shape and size of the pulse, direct the pulse to the treatment field in an ergonomic fashion, and may provide additional effects such as epidermal cooling or plume evacuation.

Other light-based technologies may share some features of lasers, such as monochromaticity or high intensity, but are not true lasers. One of these technologies, intense pulsed light (IPL), deserves special attention, as it is useful tool in some vascular conditions. Like a laser, IPL delivers a brief, powerful pulse of energy, but it is neither monochromatic nor coherent. Instead, IPL technology uses a xenon flashlamp to produce a broad-spectrum pulse of light throughout the visible and infrared spectrum, which can then be narrowed by a variety of optical longpass filters to exclude low-wavelength portions of the spectrum (e.g., blue and ultraviolet). IPL technology does not allow the same fine control over the pulse-target interaction as true lasers, and the broad spectrum of the pulse may result in undesired tissue responses; for example, hair removal may be an unintentional side effect in the treatment of poikiloderma. Nevertheless, IPL is a useful tool in some clinical settings [4].

9.1.3 Laser-Target Interaction

One of the fundamental tenets of photochemistry is the Grotthuss-Draper law, which states that radiation must be absorbed by a physical system in order to have an effect on that system [5]. When an incident photon encounters a chromophore (i.e., an absorbing molecule), the photon ceases to exist and its energy is added to the internal energy of the absorbing system. This energy may then be dispersed as heat, re-radiated in the form of one or more photons, or drive a chemical reaction. For the treatment of vascular lesions, lasers are employed as a destructive modality, and the predominant mechanism is the conversion of light into heat.

The concept of absorption spectra is of great importance in photomedicine. All substances are potential chromophores, but their ability to absorb light energy is dependent on the wavelength of the photon to which they are exposed. An absorption spectrum is therefore a mapping of the tendency of a specific chromophore to absorb light at any given wavelength. At the physical level, the absorption spectrum is determined by the chromophore's molecular structure and electronic configuration [6]. In the skin, the three significant chromophores are water, hemoglobin, and melanin, each of which has a distinctive absorption spectrum. Of particular interest for vascular lesions is hemoglobin, which has major absorption peaks at 418, 542, and 577 nm. In an ideal system, all laser light would be absorbed by the targeted chromophore. In reality, some light is lost to reflection away from the skin, scattering into the surrounding tissue, transmission through the target, or absorption by undesired chromophores. All of these factors come into play in selecting a laser's wavelength and settings.

Once a photon has been absorbed by a chromophore, the energy that photon contained can be released as heat into the local environment. Depending on the amount of energy delivered, this effect may range from gentle warming to instantaneous vaporization (i.e. ablation). For most vascular lesions, the desired effect is sufficient heating to cause target damage by denaturing proteins and disrupting cell structures.

Tissue damage can be modeled by the Arrhenius equation, which states that above a certain threshold, thermal denaturation of proteins is an integral function of both time and temperature [7]. Excessive heat leads to undesired thermal injury, such as scarring and dyspigmentation. In particular, temperatures above 60 °C (well short of ablation) can lead to the denaturation of collagen and result in scarring [8].

In addition to the denaturation of proteins through heat, lasers are capable of inducing mechanical, or photoacoustic effects. When a laser pulse is of sufficiently short duration and high fluence, the rapid deposition of thermal energy can vaporize water to steam. The resulting transient cavitation and collapse of steam microbubbles induce pressure waves that propagate beyond the tissue zone targeted by the pulse of light. This effect is of special importance in the treatment of vascular lesions, since the purpuragenic effect of PDL is thought to be at least in part secondary to the rapid thermal expansion and mechanical rupture of vessel walls [9]. As a general rule, photoacoustic effects need to be considered when using lasers with short pulses and high peak power [10].

9.1.4 Selective Photothermolysis

In order to achieve the optimal clinical effect, a balance must be achieved between delivering sufficient energy to destroy the target while sparing surrounding tissue. Selective photothermolysis is a simple yet elegant theoretical framework for understanding how to achieve this balance clinically. This framework states that target selectivity can be achieved by choosing a light wavelength that is selectively absorbed by the target, instead of aiming the laser with microscopic precision [8]. The absolute requirement for this concept is that the target chromophore be more selective than the surrounding tissue for the wavelength of light being used. When this criterion is met, an entire treatment area can be irradiated while restricting damage to structures containing the targeted chromophore. The selection of laser wavelength is therefore based on identifying the target chromophore and its corresponding absorption spectrum, as well as being aware of competing chromophores.

Even if the principles of selective photothermolysis are employed to confine thermal effects to a specific target, excessively long exposure to radiation will eventually heat the entire treatment area. This is due both to nonzero absorption of radiation by nontargeted chromophores and by thermal dissipation from the selectively heated target to the surrounding tissue. This phenomenon is known as bulk heating and can lead to adverse treatment effects. In order to avoid bulk heating, the ideal pulse duration should be no longer than the thermal relaxation time (TRT) of the target. TRT is a parameter defined as the time required for the tissue target to dissipate one half of the absorbed heat [11, 12]. When the target is heated to a sufficient temperature in a time period less than the TRT, the target can be destroyed quickly, before collateral damage is caused by dissipated energy. The TRT varies based on the geometry of structure being targeted, but a useful rule of thumb is that the TRT in seconds is approximated by the square of the target's diameter in millimeters. For

vascular targets, the TRT may range from 1 ms for fine capillaries up to as long as a second for leg veins. Selection of the pulse duration is therefore one of the critical treatment parameters. Even with careful choice of pulse length, the application of repeated pulses to a treatment area in rapid succession (known as pulse stacking) can overcome thermal dissipation and lead to bulk heating.

In addition to wavelength and pulse width, the third critical treatment parameter is the amount of energy delivered to the target tissue. In laser therapeutics, this is referred to as fluence, or the amount of energy delivered per unit area (joules/cm^2). Fluence is a convenient unit, since it standardizes the energy delivered by accounting for the dimensions of the handpiece crystal or beam diameter. Once an appropriate pulse width is chosen based on the TRT of the target chromophore, a sufficient fluence must be selected to ensure destruction of the target. Fluence is perhaps the most challenging laser parameter, since there can be a narrow therapeutic window in which sufficient heating is achieved to reach the desired clinical endpoint, but the complications associated with excess heating are avoided.

9.1.5 Epidermal Cooling

Despite optimal selection of a laser wavelength and treatment parameters, absorption of light by unintended chromophores remains a significant factor. In the treatment of vascular lesions, melanin is a special concern, as excessive absorption can lead to overheating of the epidermis and cause burns, scarring, and dyspigmentation. It logically follows that the risk of epidermal damage is greater in patients with darker skin. Direct cooling of the skin is an important adjunct for mitigating epidermal damage, and a variety of strategies have been developed for this purpose. As an additional benefit, cooling provides a degree of analgesia and improves treatment tolerance.

Cooling can take place before (precooling), during (parallel cooling), or after (postcooling) the treatment. Both pre- and parallel cooling work by lowering the temperature of the epidermis, which in turn creates a larger thermal buffer for heating to occur before crossing the threshold temperature for damage [13]. Precooling is often achieved with a cryogen gas which is sprayed on the treatment area immediately before the pulse or with chilled air blowers. Parallel cooling is often accomplished by directly contacting the skin with a chilled, transparent, sapphire crystal through which the laser passes directly into the target area. Both cryogen spray and chilled plate cooling methods remove heat predominately by conduction and are spatially selective [14]. By contrast, postcooling is typically bulk cooling of the entire treatment area and is usually delivered with ice packs or chilled air blowers. In addition to analgesia, postcooling provides two further benefits: it reduces epidermal damage from retrograde heating (dissipation of heat from the target into the surrounding tissue), and it helps decrease the inflammatory response to tissue injury [15].

Although epidermal cooling is generally straightforward, there are a few caveats. Although it is clear that darker skin types require more aggressive epidermal

protection, studies of heat shock protein expression in animal models have shown that there is a point of maximum benefit, beyond which additional cooling does not lead to additional benefit [16]. Deep cooling can lead to vasoconstriction and decreased treatment efficacy for vascular lesions. Although rare, cold injury can occur with overzealous cooling, leading to dyspigmentation and even frostbite [17]. Excessive pressure applied by the operator with a chilled handpiece can also blanch vessels, reducing the target chromophore and leading to treatment failure.

9.1.6 Patient Selection

Although there are no absolute contraindications to laser therapy, it is not appropriate for all patients. While there is no compelling physiologic reason that laser therapy be absolutely contraindicated in pregnancy, lasers are not generally approved by device manufacturers for use on pregnant women. Due to changes in healing, increased risk of bruising, and increased medicolegal risk, most practitioners will avoid treating pregnant women. Patients with medical reasons for poor wound healing, such as diabetes or therapy with isotretinoin, should be approached cautiously, as should patients with a history of keloid or hypertrophic scar formation. Of note, photosensitizing drugs have not been documented to cause complications during laser treatment since the action spectra of most such drugs are in the ultraviolet range [18].

Extra caution also needs to be taken when treating non-Caucasian skin. As a general rule, darker skin types are more likely to experience complications from laser treatment [19, 20]. Lighter skin-type patients who are tanned or sunburned are similarly affected. Complications of treatment in such individuals range from acute, such as posttreatment vesiculation, to longer term, such as dyspigmentation. In order to treat darker-skinned patients, close attention must be paid to clinical endpoints, aggressive epidermal cooling must be practiced, and a more protracted treatment course should be anticipated. While treatment in darker-skinned patients is possible, it is fortunate that vascular lesions are usually less visually evident and many vascular lesions are less prevalent in this population.

9.1.7 Laser Safety

Laser surgery is a powerful tool, and with the proper precautions, it is a safe and effective treatment modality. Like all powerful tools, though, lasers carry risks. The potential for significant harm exists for the operator, the patient, and bystanders when lasers are mishandled. Underlying all of the following recommendations is the need for appropriate training before the use of any light-based device.

The hazards associated with laser surgery can be divided into those related to the beam itself and those that are not. Beam-related hazards are unique to lasers. In

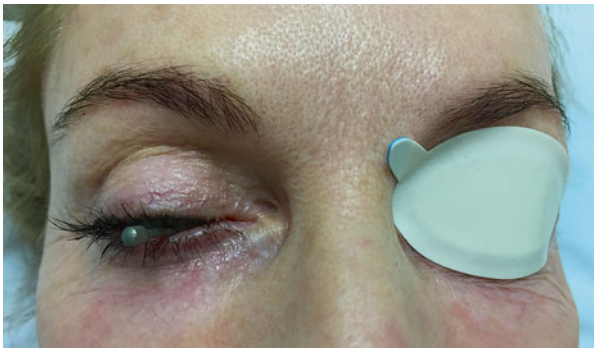

Fig. 9.1 Comparison of metal and adhesive eyeshields. The adhesive eyeshield is convenient for treatments on the face, but is not appropriate for treatment close to the orbit

addition to cutaneous burns caused by inappropriate setting selection or device misfire, the single most important consideration is protection of the eye. Ocular structures that can be affected by various laser wavelengths include the cornea, the iris, the lens, and the retina [21, 22]. The retina is richly vascular and contains abundant melanin in the retinal pigment epithelium; therefore, it is particularly susceptible to wavelengths in the 400–1400 nm range – the same portion of the spectrum used in the treatment of vascular lesions. Only a small, reflected fraction of a laser pulse is sufficient to cause permanent damage or blindness.

Laser safety begins with the design of the laser workspace. In an outpatient setting, the layout of a laser treatment room should be such that light pulses cannot leak out outside the treatment area, and reflective surfaces should be minimized. Access to lasers should be restricted to authorized personnel who have been trained in laser safety. All laser rooms are legally required to have warning signs posted in areas of laser use. Ideally, such areas should also be equipped with signage indicating when the laser is in use. Doors to treatment areas should not be opened except by the operator, after ensuring that the laser is off or in standby mode. Smoke evacuators specifically designed to handle the plume of a laser device should be available, given the risk of aerosolizing cellular material and viruses.

During treatment, both the laser operator and the patient should wear laser protective eyewear that is rated specifically for the wavelength of the laser in use. An optical density of 4 or greater is necessary to ensure adequate protection. Eyewear should fit closely and comfortably and should wrap around to include protection of the peripheral vision. If the face is being treated, protection of the patient's eyes with opaque, adhesive eyeshields or with metallic eyeshields is preferred; metallic shields should be considered mandatory for treatments near the orbit (Fig. 9.1). Specialized corneal protectors that can be placed under the eyelid in direct contact with the globe are required for safe treatment of the eyelid or skin within the orbital rim (Fig. 9.2).

Although uncommon, fire is a potentially serious hazard associated with laser use. The necessary elements for fire to occur are the simultaneous presence of fuel, an oxidizer (usually oxygen), and an ignition source. When these elements coincide,

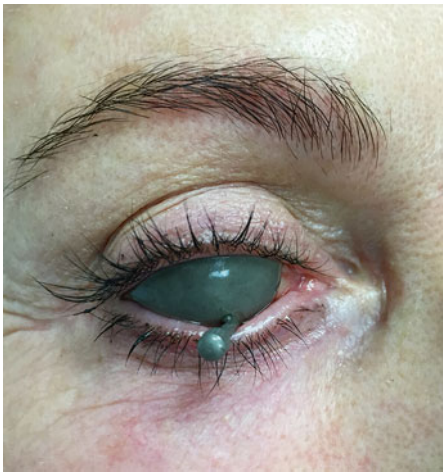

Fig. 9.2 Metallic contact eyeshield used for eyelid and periorbital laser and IPL treatments

the exothermic chain reaction called combustion takes place. Likewise, by removing one of these elements, fire can be prevented or extinguished.

The intensity of a laser pulse can cause peak temperatures sufficient for ignition. Although the highest risk for ignition comes from ablative lasers such as CO_2 and erbium:YAG, vascular lasers such as the PDL have also started fires [23]. Inadvertent activation of the laser can lead to the device firing onto unintended targets, such as drapes, which serve as fuel sources. Familiarity with the laser device, reduction of clutter near the device's control pedals, and keeping the device in standby mode until conditions are ready for use are all important ways to avoid misfires. Flammable disinfectants and skin-defatting agents, such as alcohols and acetone, should be allowed to dry completely before treatment. Readily flammable materials should be kept clear of the treatment field; hair, gauze, and drapes that cannot be removed may be covered with dampened towels. As the most common accelerant, oxygen should be kept away from the treatment field. For procedures which occur within an operating room, close collaboration with the anesthesiologist is recommended in order to avoid flammable anesthetics, reduce oxygen use to the lowest safe levels, and select airway hardware and draping techniques that avoid oxygen pooling. An appropriately maintained fire extinguisher should be readily available. In the event of fire on the body of the patient, saline should be used to extinguish the flames and appropriate first aid delivered.

9.2 Clinical Applications

For a brief overview of the lasers described in this chapter, see Table 9.1. The successful use of laser or light-based technologies is best achieved by a practitioner who has appropriate equipment along with a deep knowledge of the basic science of laser technology combined with a medical understanding of the vascular lesions to

Table 9.1 Selected lasers used for vascular conditions

Laser	Wavelength	Color	Melanin absorptivity	Vascular targets
Potassium titanyl phosphate (KTP)	532 nm	Green	+++++	Small vessel lesions
Pulsed dye laser (PDL)	585, 595 nm	Yellow	++	Small vessel lesions
Intense pulsed light (IPL)	512[a]–1200 nm	Polychromatic	+++	Diffuse erythema, small to moderate vessel lesions
Alexandrite	755 nm	Red	++	Large vessels and blebs
Diode	800 nm	Infrared	++	Large vessels and blebs
Neodymium:yttrium aluminum garnet (Nd:YAG)	1064 nm	Infrared	+	Large vessels and blebs
Carbon dioxide (CO_2)	10,600 nm	Infrared	–	Ablation; no vascular specificity

[a]Lower bound determined by filter selection

be treated. It is important to mention that there are many competing technologies available to a practitioner, and laser parameters that are ideal on one machine may not be suitable for a similar type of device produced by a different manufacturer. As a result, for the most part, we will not give comprehensive laser parameters but instead focus on the key concepts and decisions for best treatment practices. For specific settings, we refer the reader to the recommended start settings detailed in each laser machine manual or in medical journal publications specific to the device in question. The settings listed therein tend to be very conservative, and with experience and an understanding of the problem to be treated, the practitioner will adjust the parameters for optimal treatment results.

9.2.1 Cherry Angiomas

Cherry angiomas, less flatteringly known as senile angiomas, are the most common acquired vascular proliferation. They manifest clinically as well-circumscribed, bright red papules most often on the trunk, although they may appear anywhere on the body. While generally asymptomatic, these lesions can bleed if traumatized and are a common cosmetic complaint. Cherry angiomas are highly amenable to laser treatment. This is largely due to very superficial nature of the lesion, since its hemoglobin chromophore is readily available to the laser pulse.

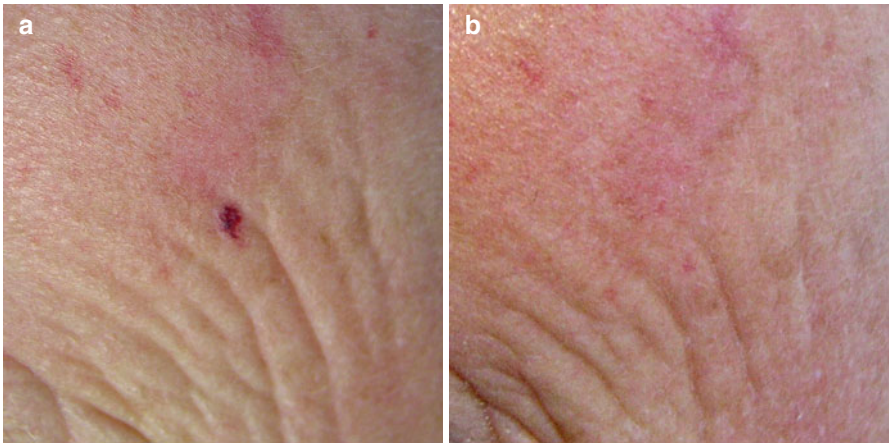

Fig. 9.3 (**a**) Cherry angioma on the cheek. (**b**) Same cherry angioma after a single treatment session with PDL

Pulsed Dye Laser (PDL) PDL is one of the most commonly used technologies in dermatology offices for vascular treatment. Depending on the device, the wavelength is between 585 and 595 nm, which promotes more hemoglobin targeting versus melanin due to the differences in light absorption of the two chromophores at those wavelengths. Although highly effective, initial devices caused significant purpura. The most recent versions allow for selection of pulse duration as well as pulse stacking (repeatedly firing a laser pulse at the same point quickly in succession) at subpurpuric fluence; these features are critical for achieving treatment benefit while avoiding purpura [24]. Cherry angiomas respond very well to PDL technology (Fig. 9.3a, b). The round beam pattern typical of PDL devices conveniently matches silhouette of a typical angioma, and a choice of spot sizes allows the beam diameter to be matched to the lesion so as to minimize the unnecessary treatment of surrounding tissue. All of these considerations make PDL the current best choice of technology. Another shallow penetrating vascular laser, the potassium titanyl phosphate (KTP), is also a reasonable consideration for cherry angiomas; however, it has been compared directly to PDL in a blinded trial and found to have no better efficacy, but was associated with greater pain and worse textural change [25].

Most patients desiring treatment are Caucasian, which minimizes the risk of light absorption of melanin and subsequent epidermal injury. An additional layer of protection can be obtained with aggressive epidermal cooling. As a result, moderately aggressive settings can be used for the most beneficial results. While using the PDL, the authors regularly use pulse stacking with two to three consecutive pulses for all but the smallest of lesions without significant complications.

With moderately aggressive settings and pulse stacking, nearly all of the treated angiomas fade away after a single treatment. The exceptions are occasional larger

lesions that are exophytic, purple, and 5 mm or larger. For recalcitrant lesions such as those, the authors may use a higher energy level and pulse stack even further (up to 4 pulses stacked). It is also important to note the risk of failure, the potential need for multiple sessions, or use of a different technology such as electrodesiccation alone or in combination with laser. For very large, polypoid lesions, shave removal may be preferable.

Intense Pulsed Light An alternative to the PDL, IPL can also be successfully used for the treatment of cherry angiomas. Though the beam shape and broad-spectrum pulse are not as well suited as the PDL, it is still usually effective. The authors advise careful patient selection as the IPL technology is more likely to produce unintended epidermal injury. In a common scenario, tanned patients are asked to wait until the winter to minimize competition by melanin for the light energy meant to target the hemoglobin in the angioma. Recommendations for best use include using aggressive filters (515 or 560 nm), relatively high fluence, small spot sizes if available, and a triple pulse with short individual pulse durations. Although research on IPL for cherry angiomas is sparse, IPL has been compared directly to Nd:YAG in the treatment of cherry angioma, with greater patient satisfaction after IPL [26].

9.2.2 Diffuse Erythema and Flushing

Much like telangiectasia, redness and flushing is a relatively common issue seen mostly in patients with rosacea, sun damage, or both. In practice, it may be difficult to differentiate these entities, but there are some helpful clues. In general, patients with sun damage will have fair skin and extensive history of sun exposure resulting in lentigines (brown spots), skin cancer, and wrinkling. The erythema, texture changes, and telangiectasia are frequently referred to collectively as poikiloderma of Civatte. A younger patient is more likely to have rosacea than the extensive amount of cumulative sun damage needed to cause redness. Although flushing, burning, and irritation are known to occur in sun damage, they are more common in rosacea [27]. Despite these clues, in some patients, it is difficult to determine a single etiology, and many likely have both sun damage and rosacea. As treatment selection is often the same, making a diagnosis is not absolutely necessary; however, the authors believe that rosacea may need more frequent periodic treatments over time.

Rosacea is a complex skin disorder usually seen in middle-aged Caucasian patient and typically affects only the face [28]. Several features are often noted including telangiectases, diffuse erythema, flushing, and acne-like inflammatory papules. Pharmacologic treatment of the erythema and telangiectasia is either absent or unsatisfactory [29]. Telangiectases in rosacea are treated similarly to any others, and the reader is referred to the section devoted to telangiectases for further information; treatment of erythema is considered below. Of note, in addition to improving redness, the laser treatments often help the inflammatory component leading to benefit the papular component as well.

Many years of sun exposure will often cause a delayed appearance of diffuse redness of the skin. This is usually seen on the face, neck, and chest from exposure 10–15 years or more in the past, so patients may not be aware of the connection. The term redneck, a derogatory term used to connote a country bumpkin attested to as early as 1830, is a prototypical example of sun damage leading to diffuse redness. In that case, the term likely originated from the intense redness seen in rural farmers who spend much of their lives outdoors, thereby chronically exposing the neck to the sun.

The best technologies for diffuse redness tend to have relatively short pulse durations and short wavelengths in order to best treat the very small blood vessels that cause the appearance of redness. The most widely used devices tend to be IPL- and PDL-based technologies. Although there is a general lack of high-quality trials, a Cochrane review for rosacea found PDL and IPL to be roughly equivalent in terms of outcomes [30]. Although less commonly used, 532 nm KTP and similar wavelength technologies can also be helpful. Longer pulse durations and longer wavelengths tend to be relatively ineffective as they lack the ability to confine the laser energy to the quickly cooled small vessels in zones of redness.

Intense Pulsed Light IPL is the authors' preferred technology for diffuse redness provided the machine employed is capable of relatively short pulse durations of 3.5 ms or less. Advantages of this device include a larger rectangular area treated with each pulse, which allows for even, efficient treatment over large areas (Fig. 9.4a, b). Since coupling gel is used on the skin surface, lifting the handpiece after each pulse leaves a rippled area of gel, indicating the already treated area also helping in the delivery of uniform treatment. The light pulse can be tailored to skin type by selecting from the variety of filters that come with the device. Because IPL targets both melanin and hemoglobin, it also has the ability to even out dyspigmentation; for patients with solar lentigines this effect is an added cosmetic benefit [31]. Typically, one to three sessions are needed for patient satisfaction. Unlike treatment of discrete vessels, there is no set clinical endpoint for treating facial erythema, so experience and proper parameter selection are important.

The most significant negative attribute of the technology is the potential for blistering and discoloration in patients with darker skin, highlighting the importance of patient selection. With careful selection of treatment parameters, side effects such as dyspigmentation and scarring can be largely avoided.

Pulsed Dye Laser PDL has been used extensively for diffuse redness due to its preferential targeting of hemoglobin over melanin at its typical wavelength between 585 and 595 nm. It can also be useful when IPL fails, due to its ability to employ very short pulse durations (0.45 ms) which may better target very tiny vessels. One blinded series found nonpurpuragenic PDL and IPL to be equivalent in terms of outcomes [32]. Nevertheless, PDL should not be considered the first-line treatment for diffuse erythema. One major drawback is the smaller round spot size compared to the large rectangular shape of the IPL technologies. This smaller size leads to longer treatment times and greater demand on the operator. An even more problematic issue is the

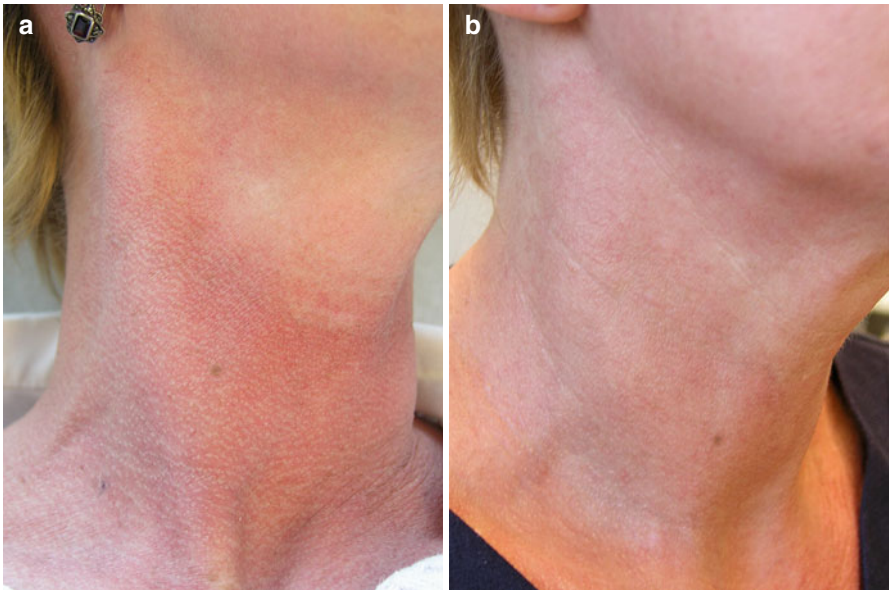

Fig. 9.4 (**a**) Sun damage-related erythema of the face. (**b**) Same patient after two treatment sessions with IPL

difficulty in evenly treating zones with the round shape of the laser pulses. This may lead to uneven clearance causing a lacy or polka-dotted pattern that can be challenging to fix. The neck and chest are particularly susceptible to such pigmentary changes and should be approached with caution [33]. Like IPL, there is no discrete identifiable endpoint when treating erythema with subpurpuragenic settings.

Potassium Titanyl Phosphate Historically favored over purpuragenic treatment with PDL, the KTP can be effective in the treatment of diffuse redness. As mentioned previously, it is important to have a device capable of generating sufficiently short pulse duration, in order to treat the small target vessels that create the appearance of red skin. At 532 nm, there is significant melanin absorption making it critical that the physician only treats patients with relatively light skin. While KTP lasers may play a role for treatment-resistant erythema, IPL and nonpurpuragenic PDL are now preferred technologies.

9.2.3 Infantile Hemangiomas

Infantile hemangiomas (IHs) are the most common soft tissue tumor in children, with an estimated incidence of 1–2 % [34]. IHs are true vascular tumors and represent proliferating vasculature. Although IH affects all races, it is substantially more

common in Caucasian infants, where incidence is estimated at 10 %. Additional (albeit confounding) risk factors include female sex, low birth weight, prematurity, and multiple gestations. Although IH may appear anywhere on the body, the most common locations are the head and neck [35]. IH may be located deep to the skin, superficially within the skin, or both. Superficial IH corresponds to bright red papules and plaques, while deeper components may be ill-defined tumors with a bluish hue and telangiectasia (Fig. 9.5).

IH follows a predictable pattern of rapid growth within the first year of life (proliferation phase), followed by a period of stability (plateau phase) and then gradual resolution (involution phase). Involution is generally complete by the age of 10, and failure to follow the general course should call the diagnosis of IH into question. For more in-depth discussion of IH of the orbit and eyelid, please refer to Chap. 4.

One of the key questions in the management of IH is whether to treat at all. In most children, IH is a benign and self-limited process without complication. Therefore, treatment is generally reserved for lesions that are either disfiguring, functionally compromising, or are complicated by ulceration. Criteria for a disfiguring lesion depend in part on the patient's family and the risk of social stigmatization, but certainly large facial lesions and lesions over cartilage (which may cause permanent distortion in the underlying structure) would be included. Location that obstructs vision, the auditory canals, and the airway or prevents feeding is an indication for active treatment rather than watchful waiting. Ulceration is the most frequent complication of IH. Although mild ulceration can be managed supportively, active intervention is indicated for ulcerations that are recurrent, painful, or characterized by clinically significant bleeding. Of note, lesions on the lower lip and on the neck are at high risk for ulceration [36].

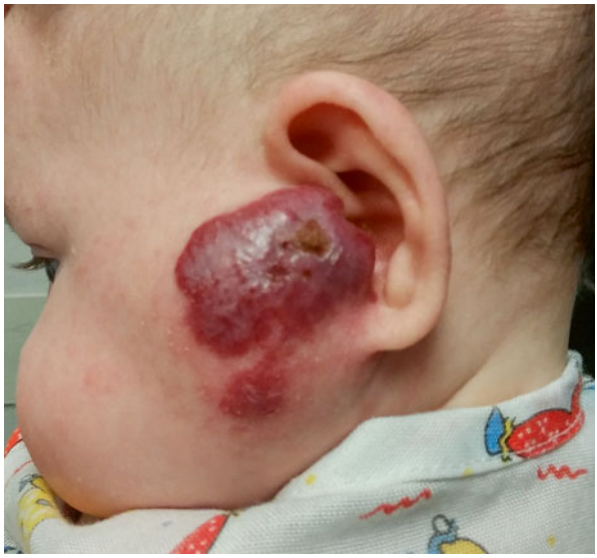

Fig. 9.5 A preauricular infantile hemangioma with a large superficial component and mild crusting. Although subtle, the deep component is evident at the inferior edge (Photograph courtesy of Dr. Audrey Chan)

There are a variety of systemic therapies that can be used for IH that need active intervention, including β-blockers, corticosteroids, interferon, and vincristine. β-blockers, which were serendipitously found to be therapeutic in 2008, are of particular importance given their efficacy and low side effect profile [37]. Both oral propranolol and topical timolol are being increasingly used as first-line agents, reducing the need for both traditional systemic therapy and lasers.

Pulsed Dye Laser When laser therapy is undertaken for the treatment of IH, PDL is widely considered to be the device of choice. Laser treatment of proliferating IH, however, remains controversial, in part because of lack of high-quality evidence [38]. While some controlled trials have suggested that early treatment with PDL is capable of curtailing the proliferative phase [39, 40], other studies have failed to support this conclusion [41]. A recent prospective, randomized trial of 22 children found significant improvements in color, but not in-depth or surface area of treated IH when compared to nonintervention [42]. What is clear, however, is that systemic therapy such as β-blockers are highly effective. Propranolol alone has also been compared directly to PDL and was found to induce significantly earlier involution and reduce erythema [43]. In the authors' opinion, PDL as monotherapy does not provide a significant benefit over its alternatives for curtailing IH proliferation. More intriguing, however, are pilot studies suggesting that there a synergistic benefit to the combined therapy with both laser and β-blocker [44–46]. While these studies have yet to be rigorously validated, preliminary results have suggested more rapid clearance compared with propranolol alone and decreased total propranolol doses. If laser treatment is pursued for proliferating IH, the goal is endothelial damage without vessel rupture, so purpura is not a desirable clinical endpoint [47, 48].

The role of PDL is better established for treatment of IH that is in the involuting stage. During this stage, the lesion has already achieved its maximum size and is no longer actively proliferating, so coagulation of the small-caliber vasculature can hasten resolution. Results with PDL are best in thin, superficial lesions. With modern PDL devices, blanching is a reasonable clinical endpoint rather than purpura. Deep or mixed IH is less responsive, since penetration of PDL is limited to 1–2 mm [49]. For the subcutaneous portions of IH, addition of deeper penetrating Nd:YAG and direct insertion of a laser probe intralesionally have both been used [50, 51]. The residua of completely involuted IH are frequently fibrofatty papules or plaques overlying vascular ectasia. Treatment of these telangiectases is similar to the treatment of other telangiectasia, and the reader is referred to relevant section of this chapter. Ablative lasers such as CO2 may be used to improving any accompanying changes to the texture of the skin.

The other notable use of PDL in IH is in the treatment of ulcerated hemangiomas. For ulcerated IH, PDL hastens reepithelialization and decreases associated pain [52, 53]. When treating ulcerated IH, PDL should always be used in combination with appropriate wound care and often with concomitant systemic therapy. In general, PDL should not be considered until patients have failed conservative therapy.

The most common complications of treating IH with PDL are those typical of the device and include scarring, dyspigmentation, and textural change. These results can be minimized with adequate epidermal cooling and judicious choice of both initial settings and treatment endpoint. In some cases, however, patients have worsened, including several cases in which ulceration was felt to be precipitated by the laser [52, 54].

9.2.4 Port-Wine Stains

Port-wine stains (PWSs), also known as capillary malformations, are the most common congenital vascular malformation, affecting 0.3–0.5 % of newborns [55]. They are located predominantly on the head and neck. Unlike IH, they are not proliferative tumors. PWSs represent cutaneous collections of slow-flowing ectatic capillaries and venules of the superficial vascular plexus [56]. Initially, these vessels range from 10 to 500 μm in diameter, but they may increase in size with age. Clinically, this may manifest in up to two thirds of patients as thickening and darkening of the lesion, with development of hypertrophic nodules and friable blebs. Without treatment, PWSs are persistent.

Selective photothermolysis via laser is the gold standard for PWS. Although complete clearance is difficult to achieve, treatment is recommended to improve vascular color, hypertrophy, and blebbing and to reduce psychosocial distress. Ideally, treatment should be initiated early. Chapas et al. demonstrated an average clearance of 88.6 % in patients aged less than 6 months using PDL [57]. Young skin is thinner, which minimizes scatter and improves vessel targeting. Younger patients also heal more readily. Generally, treatment is repeated every 4–6 weeks, and optimal results may be seen after eight to ten treatments. However, clinical improvement usually plateaus after five treatments. Pulse stacking, overlapping, double passes, and repetitive treatments have been shown to offer variable results with potentially greater adverse effects.

The most common side effects are purpura, erythema, and swelling. Purpura naturally fades in 1–2 weeks on the head and neck. NSAIDS should be avoided as platelet function is necessary for photothermolysis and may lead to more severe bruising. Blistering, crusting, and ulceration may also occur and can be managed with petrolatum jelly under a moist, occlusive dressing. Follicular damage and permanent alopecia have been reported, and thus, avoidance of eyelashes is important.

Anesthesia can be helpful with discomfort. If local anesthesia is used, it is important to demarcate the PWS prior to treatment since perilesional erythema may obscure the true borders of the PWS. Conversely, blanching of the PWS with epinephrine-containing lidocaine injection due to vasoconstriction may reduce lesion visualization and reduce available chromophore.

Pulsed Dye Laser Historically, PDL was by far the most popular technology used for PWS and the most well-studied treatment modality. Its wavelength of 595 nm is

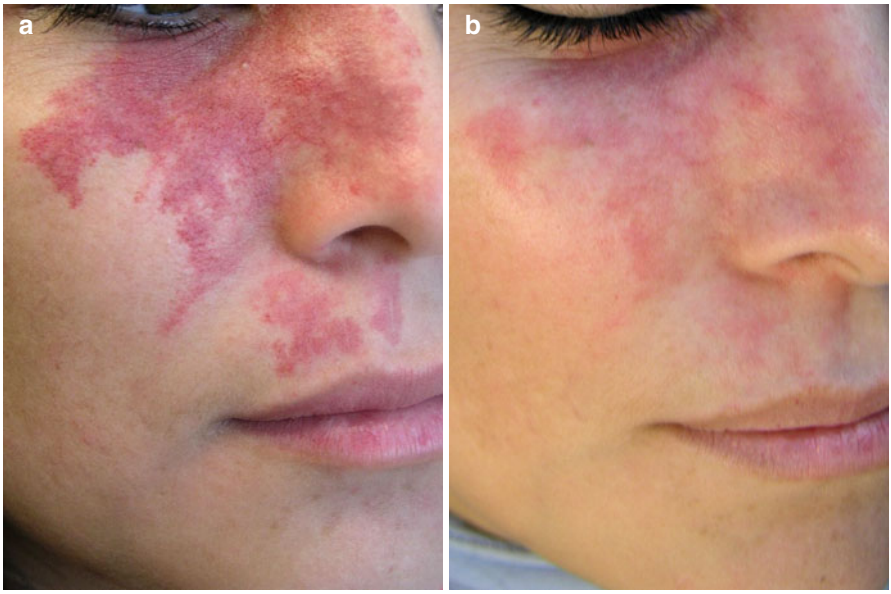

Fig. 9.6 (**a**) Centrofacial port-wine stain before treatment. (**b**) Same lesion after eight treatment sessions of with PDL. Although improved, the persistent erythema demonstrates the often refractory nature of this lesion

effective for the optimal absorption spectrum of hemoglobin, with comparatively low melanin absorption. When using PDL for PWS, purpura is a treatment endpoint; however, if a non-transient confluent gray color is seen, then the fluence should be reduced (Fig. 9.6a, b). For ethnic skin, we recommend decreasing the fluence, increasing the pulse duration, and optimizing epidermal cooling to minimize the risk of blistering.

Alexandrite The alexandrite laser is a near-infrared laser which operates at 755 nm. It has been primarily used for PWS that are refractory to other lasers and for darker lesions [58]. Theoretically, the alexandrite laser selectively targets deoxyhemoglobin over oxyhemoglobin and has a greater degree of dermal penetration. However, melanin is also more likely to absorb the laser, and increased scarring and dyschromia have been reported in more pigmented skin types. Treatment endpoints are purpura and grayish color.

Diode The diode laser (800 nm) has been very effective in the authors' experience in the treatment of blebs and, to a lesser degree, the hypertrophic purple plaques of PWS (Fig. 9.7a, b). The wavelength has sufficient hemoglobin absorption to be effective, and its decreased water absorption reduces bulk heating. For blebs, higher fluences that are required for the pulse stacks of two to three pulses may be useful. A slight gray appearance to blebs and flattening are useful clinical endpoints during treatment.

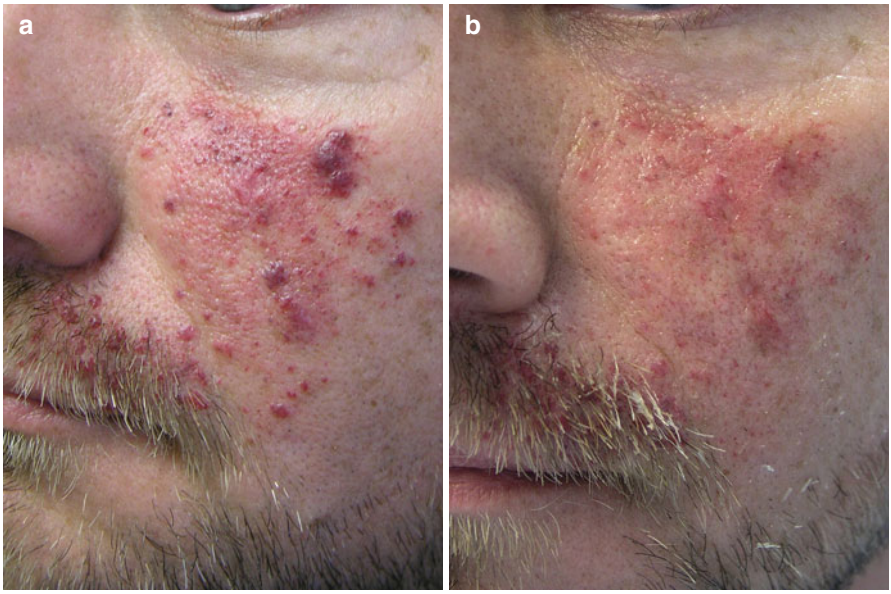

Fig. 9.7 (**a**) Larger blebs within a port-wine stain. (**b**) Same blebs after a single treatment session with a diode laser. With improvement of these blebs, treatment can be continued with an IPL or PDL device

Long-Pulsed Nd:YAG The Nd:YAG laser is safer in darker skin types and may also be considered for deep PWS. Given its longer wavelength (1064 nm), it can penetrate 5–6 mm in the dermis compared to the PDL (2 mm deep) and has demonstrated clinical improvement with PWS hypertrophy and blebs. However, ulceration is a serious side effect due to bulk heating as there is some water absorption at the 1064 nm wavelength. For this reason, it is recommended that caution should be exercised when using the Nd:YAG laser in the treatment of PWS, and diligent epidermal cooling is mandatory. Combination therapy with PDL initially, followed by Nd:YAG lasers, has demonstrated potential for improved efficacy, even at subpurpuragenic treatment settings.

Intense Pulsed Light IPL's variability in wavelengths, pulse duration, and fluence allows for treatment of PWS with different vessel colors, depths, and diameters. With its large, rectangular spot size and low risk of purpura, IPL can be an attractive treatment option, especially for treating extensive lesions. In patients with significant amounts of melanin, however, its side effect profile is unfavorable. As there is wide variety in IPL devices, the exact parameters must be optimized for each machine. Generally, a double-pulse pattern is used, while the filter should be selected based on skin type.

Treatment of Resistant PWS Various mechanisms of treatment resistance have been reported [59]. Refractory lesions tend to be thicker, larger, and lie in the central

face. Deep vessels, even when small, are also relatively resistant to treatment. Because of heterogeneity of vessel size and depth, it is common that several different lasers using a variety of settings will be needed for optimal results. In this situation, it may be best to treat the largest vessels with the first laser treatment then progress to the target smaller vessels with later treatments. If a patient has blebs, the authors usually start with the diode laser, then perhaps IPL, and eventually PDL in later treatment sessions.

Topical antiangiogenic agents such as rapamycin and imiquimod have been shown to prevent vessel repair and may augment effectiveness [60, 61]. In the authors' experience, imiquimod was not felt to be very helpful and is not typically used due to its cost and side effect profile. Rapamycin has been more recently studied and is a promising future adjuvant therapy, but is still not in common usage.

9.2.5 Pyogenic Granulomas

Pyogenic granuloma (PG), also known as lobular capillary hemangioma, is a common, benign vascular proliferation that may occur on both the skin and the mucous membranes. The nomenclature is misleading, as it is neither granulomatous nor pyogenic. Although the specific etiology is unknown, PGs are thought to arise from an aberrant angiogenic stimulus. PGs are especially common in children and have also been associated with pregnancy, a variety of medications, chronic irritation, and minor trauma. It is interesting to note that there have been several reports of pyogenic granulomas arising as a consequence of PDL treatment for capillary malformations and for cherry angiomas [62]. Clinically PGs appear as friable, red nodules which can be either sessile or pedunculated. The typical history is one of rapid growth and bothersome bleeding. Although spontaneous involution may occur, PGs are usually persistent without treatment [63].

Traditional therapy involves surgical excision, sclerotherapy, chemical cautery, and cryotherapy. Compared with these techniques, laser treatment offers low rates of recurrence and reduced scar formation. When selecting a laser, it is important to ensure that the laser is capable of destroying any large-caliber afferent vessels in order to prevent recurrence. Treatment of PGs has been attempted with a wide variety of laser devices. Of these, PDL, Nd:YAG, and CO_2 have been the most extensively studied and offer favorable results in the properly selected patient.

Pulsed Dye Laser The basis of PDL treatment of PG is selective targeting of proliferating vasculature within the lesion. PDL is ideal for the treatment of small, sessile PGs (Fig. 9.8a, b). The two major advantages to PDL are low risk of scarring and low associated discomfort [64]. The greatest drawback of PDL is that it is really only suitable for the treatment of relatively small lesions. For moderately sized lesions, multiple treatments are necessary, and for large, thick lesions, recurrence is common even if initial clearance can be achieved. For larger lesions,

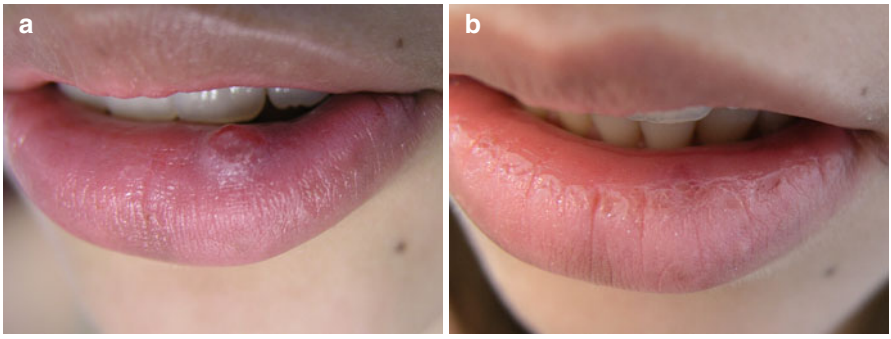

Fig. 9.8 (**a**) A labial pyogenic granuloma. (**b**) Same pyogenic granuloma after a single treatment session with PDL

combination therapy may be useful. One case series reported good results with a treatment algorithm in which lesions less than 5 mm in diameter were treated with PDL alone, while larger lesions were debulked by shaving, then immediately followed by PDL [65].

Long-Pulsed Nd:YAG The Nd:YAG laser can be used in long-pulsed mode for the treatment of PGs that are too large to be effectively treated with PDL. The advantage of the Nd:YAG laser is deeper penetration into larger, thicker lesions and a more sustained pulse that is capable of coagulating larger-caliber vessels. Because of the deep penetration of 1064 nm light, pulse stacking should be avoided to prevent bulk heating. Fluence should be gradually increased in a stepwise fashion and epidermal cooling used to purge excess thermal energy between pulses in order to avoid scarring. Like PDL, the need for more than one treatment session is common [66]. Tolerance of treatment with Nd:YAG is somewhere between PDL and CO_2, with local anesthesia occasionally required but not mandatory.

Carbon Dioxide Laser The CO_2 laser is not extensively discussed elsewhere in this chapter, as it is an ablative laser operating at 10,600 nm. Light from CO_2 lasers uses water as their chromophore. Given the ubiquity of water in skin, it is not a selective laser, and its effect is not confined to the vascular proliferation. Most literature on the use of CO_2 lasers for PG has reported on a combination of continuous wave and pulsed technology.

The CO_2 laser can be an effective tool for the treatment of PG. Unlike the PDL, the CO2 laser can be used as monotherapy on larger lesions, without the need to debulk the lesion first. The coagulative effect of the laser also provides a hemostasis, which may be of significant practical importance for highly vascular, bleeding lesions. Because of its aggressive ablative effect, anesthesia is required with the use of this device. Using a CO_2 laser, the vast majority of PGs can be treated with a single session and low risk of recurrence [64]. These benefits must be weighed against the increased risk of scarring and the need for anesthesia.

9.2.6 Telangiectasia

Telangiectases are small-caliber, dilated blood vessels that may appear anywhere on the body. Typical diameters on the face range from 0.1 to 1 mm [67]. Clinically, telangiectases appear as fine, blanching vessels that may be linear, punctate, and ramifying or may extend radially from a central point. Color ranges from dull purple to bright crimson. The pathophysiology of facial telangiectases is heterogeneous, but there are many known associations. The most common causes are photodamage, rosacea, and normal aging; other causes include hyperestrogenemia (as in pregnancy and liver disease), connective tissue disease, corticosteroid atrophy, and post-radiation change. Telangiectases are also associated with genetic syndromes, such as hereditary hemorrhagic telangiectasia and ataxia telangiectasia. Telangiectases on the legs have been attributed to venous reflux and arteriovenous shunting; the treatment approach for these is not the same as for facial telangiectasia [68].

A variety of treatment modalities has been used for facial telangiectasia. Sclerotherapy, dermabrasion, and electrosurgery have all been used with varying degrees of success [24]. Although sclerotherapy remains a useful technique for larger, reticular veins on the legs, its use on the face is limited by the difficulty of cannulating all but the largest facial vessels and its side effect profile (including skin necrosis and arterial embolization leading to blindness). Electrodessication is still used commonly due to the very low associated cost, but results are highly operator dependent. In general, light-based modalities, such as lasers and IPL, have eclipsed all other modalities given their efficacy and favorable side effect profile when used with proper technique.

Many types of visible light technology have been used effectively in the treatment of telangiectasia. In the authors' experience, matching the best wavelength, fluence, and pulse duration to the individual lesion is key for successful treatment. The most common side effect is bruising, which happens most commonly with short pulse durations. Careful observation during treatment and avoidance of anticoagulants are helpful in prevention of excess bruising. As with all light-based modalities, proper patient selection is key as patients with darker skin are at a higher risk of blistering, discoloration, and scarring. The following is an overview of modern light-based treatment options for telangiectases:

Pulsed Dye Laser PDL is highly effective for the treatment of telangiectases. For most patients, complete resolution of treated lesions can be achieved in one to two treatment sessions (Fig. 9.9a, b). Although purpura was a common side effect with older devices, modern devices have made this less common. The clinical endpoint during treatment is blanching or visible thrombosis of the vessel. With proper selection of treatment parameters, side effects other than purpura are relatively uncommon.

Intense Pulsed Light IPL is an excellent modality for facial telangiectasia, since its broad-spectrum light can treat facial vessels of varying calibers. Blinded, split face studies have shown equivalent efficacy to PDL [69]. Modern devices allow

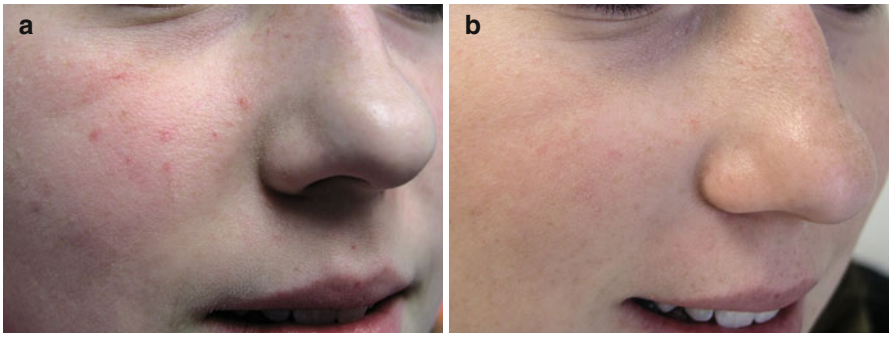

Fig. 9.9 (**a**) Multiple small-caliber facial telangiectases. (**b**) Same area after a single treatment session with PDL

extensive customization of treatment parameters. In general, filters are used to allow wavelengths of light greater than 515, 560, or 590. The lower wavelengths are most effective for vascular targeting but also more likely to cause superficial epidermal blistering in patients of color. Typical best treatment strategies to avoid blistering and maximize benefit involve the use of epidermal cooling along with a double- or triple-pulse pattern.

Potassium Titanyl Phosphate This technology has been in use for facial vessels for many years and can be highly effective. KTP's 532 nm light has relatively lower penetration; thus, it is best suited for superficial telangiectasia. One study suggested that KTP is most effective for lesions that are less than 0.6 mm in diameter [70]. One advantage compared with PDL is that KTP lasers are not associated with significant purpura; however, this advantage is offset by higher rates of erythema, edema, and postprocedural crusting [71, 72]. Due to the extremely high absorption of laser energy by melanin at the 532 wavelength, this device should be used mostly in patients with relatively light skin.

Diode Like the 1064 nm Nd:YAG, this technology, long pulse durations, and the 800 nm wavelength make this machine better suited for the larger, blue vessels [73]. Mostly used for laser hair removal, this technology often does not employ smaller spot sizes that restrict the treatment field and concentrate laser energy in order to deliver stronger treatment. The fixed larger spot sizes restrict the usage of this device to some of the largest vessels. One possible side effect is the removal of dark facial hair, a consideration most important when treating men.

Long-Pulsed Nd:YAG At 1064 nm, this device is one of the best at the avoidance of epidermal blistering due to the low absorption coefficient of melanin along with typically longer pulse durations. Laser energy emitted tends to penetrate more deeply than other machines allowing for excellent treatment of larger and deeper veins [74]. Many current devices also allow for the adjustment of spot size, which

allows the user to fine-tune the area and depth of treatment. It is important to avoid overtreatment by pulse stacking due to the targeting of the water chromophore leading to bulk heating. Bulk heating is particularly problematic when confronted by a denser collection of vasculature (such as a PWS) but can be an issue when treating solitary telangiectases as well. The result of bulk heating is nonspecific tissue destruction that can leave permanent scarring. In the authors' experience, this machine works best for the more prominent blue veins as opposed to the finer, redder variety of telangiectasia.

9.2.7 Venous Lakes

Venous lakes are very common purple papules that represent single or interconnected ectatic vascular spaces in the upper dermis [56]. Usually solitary, venous lakes are often found on the lower lip of the elderly, although they can also be found on the ears and face starting in middle age. Venous lakes are thought to occur as a consequence of accumulated actinic damage [75]. They can be easily diagnosed by the use of diascopy, a technique using a glass slide to compress the lesion, thereby removing the blood causing the purple appearance. The lesions are asymptomatic but are a cosmetic nuisance as patients report other people frequently telling them that they have food on their lip.

Multiple treatment modalities have been described, including excision, cryotherapy, thermal coagulation, and sclerotherapy. Although effective, these treatments are all highly operator dependent, with a comparatively high risk of patient discomfort, recurrence, or scarring. Laser treatment represents a useful noninvasive therapeutic option. In the author's experience, venous lakes are often unsuccessfully treated by surgery or by laser technology with too short of a pulse duration or fluence. Low-wavelength lasers such as PDL and KTP are generally not useful. The authors have had great success with higher energy and long pulse duration technologies with both the long-pulsed Nd:YAG and diode laser.

Long-Pulsed Nd:YAG The Nd:YAG laser is an effective treatment for venous lakes and is commonly regarded as the first-line laser treatment. Two features of this device are thought to underlie its efficacy: (1) the relatively deep penetration of 1064 nm light compared to visible light is preferred given the thickness of venous lakes, and (2) pulse widths in the 10s of ms allow for effective treatment of slow-flow vascular malformations. Several series have confirmed the use of Nd:YAG for safe and effective clearance of venous lakes with minimal side effects [76, 77].

Diode Laser The diode laser is also an effective treatment for venous lakes (Fig. 9.10a, b). Although less well studied, two small series have shown excellent outcomes [78, 79]. Although the Nd:YAG is often considered the laser of choice for venous lakes, the authors prefer diode lasers for several reasons. First, the large size of the typical venous lake meshes nicely with the fixed larger spot size of most diode

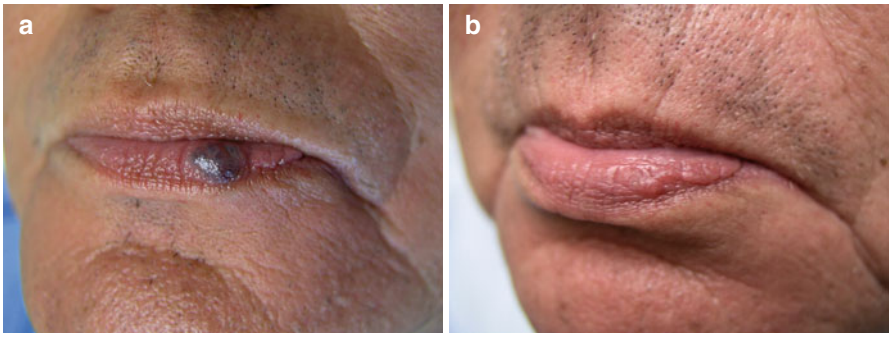

Fig. 9.10 (**a**) A labial venous lake. (**b**) Same labial venous lake after two treatment sessions of a diode laser

lasers. Furthermore, there is better hemoglobin absorption of light at 800 vs. 1064 nm leading to more efficient treatment. The relative lack of water targeting at that wavelength reduces the risk of bulk heating, thereby improving the safety profile compared to the long-pulsed Nd:YAG and allowing for pulse stacking increasing treatment efficacy. Lastly, the most common area of treatment is the lower lip, an area with very little pigmentation, so the greater targeting of melanin by this device is not an issue in most patients. This combination of factors has led to a very high satisfaction rate in our practice, with most patients needing only one to two sessions for clearance.

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