6 Provoking Factors for Aggravation of Congenital Vascular Malformation

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Congenital vascular malformations, which represent developmental abnormalities of vascular or development, may affect capillaries, veins, arteries, lymphatics, or any combination of these vascular channels. Characteristically, these lesions "grow in parallel with the growth of the patient." However, there are certain scenarios in which the vascular malformation can be "aggravated," generating unwanted symptoms and potential complications. Inciting factors include time, trauma, hormonal changes (puberty, the menstrual cycle, pregnancy), infection, thromboses, and surgical intervention. Unwanted associated symptoms include thromboses, bleeding, inflammation, increased size of lesions, functional impairment, tissue hypertrophy, hypertrophic nodules, pathologic fracture, and other morbidities.

Tissue Overgrowth

Capillary malformations generally remain macular for many years; however with time, soft tissue, gingival, and skeletal overgrowth, as well as lesional thickening and nodules, can develop [1–4]. The soft tissue overgrowth occurs in the region of the capillary malformation, predominantly in the V2 distribution, and one study suggests the onset may be delayed with early pulsed dye laser treatment [4]. The exact mechanism of the above progression is not fully understood; however, the provoking factor for capillary malformations to evolve as described is *time*, since the incidence of hypertrophy and lesional changes increases with age. Tark et al. observed histologic findings suggestive of arteriovenous malformations in resected hypertrophic nodules from adults with longstanding capillary malformations [5]. These later-stage lesions are resistant to pulsed dye laser treatment, in contrast to laser in infants, which has been shown to achieve a more favorable response [6].

Hormonal Changes: Puberty, Menstrual Cycle, and Pregnancy

Vascular malformations may remain quiescent for years, and then patients may notice a sense of fullness and intermittent pain, which may progress. Frequently this correlates with peripubertal changes. The onset of puberty is preceded biochemically by hormonal changes, which may affect a vascular malformation, manifesting as pain or discomfort. Recent evidence suggests the onset of pubertal development is occurring earlier [7–9]. The circulating hormones may trigger signs of puberty and accompanying problems in patients with vascular malformations. Kulungowski et al. reviewed hormone receptor expression in vessels of vascular malformations (arteriovenous,

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lymphatic, and venous) and found increased expression of growth hormone receptor, speculating that this may be contributory to puberty-related changes in vascular malformations [10]. Patients may notice increased fullness, pain, and cyclical changes associated with the menstrual cycle. "Growth spurts" during puberty may also magnify limb length discrepancies. The use of estrogen-containing birth control pills may lead to unwanted thromboses, especially in women with a predisposing thrombophilia [11].

Pregnancy poses many challenges to patients with vascular malformations, especially lower extremity malformations. Pregnancy related complications have been studied in women with hereditary hemorrhagic telangiectasia. The rates of miscarriage and congenital anomalies were considered to be comparable to that of the general population. Wain et al. reported the results of a survey of 560 pregnancies in 226 patients with HHT [12], and De Gussem and colleagues reported the results of a retrospective study via telephone interviews of 87 women with HHT (representing 244 pregnancies) [13]. Hemothorax (2.1 %), hemoptysis (1.1 %), transient ischemic attack (possibly from a paradoxical embolus), intracranial hemorrhage, cardiac failure (in patients with hepatic AVMs), increased telangiectasias, and epistaxis were described [12–14].

Pregnancy-related complications such as intrapartum/peripartum hemorrhage and/or thrombosis, increased varicosities (e.g., vulvar), and seizures have been described in women with Klippel-Trenaunay syndrome [15–18]. Successful pregnancies in women with Klippel-Trenaunay syndrome have been reported [19, 20]; however, precautions such as prophylactic anticoagulation and high-risk surveillance are recommended [21, 22]. Anatomic variations such as May-Thurner syndrome place women at increased risk of thrombosis, especially in the setting of pregnancy, immobilization, or exposure to estrogen-containing birth control pills [11, 23, 24]. Prophylactic anticoagulation should therefore be considered in such patients.

Although the risk of intracerebral hemorrhage from intracerebral vascular malformations in pregnancy is rare, it is generally appreciated that pregnancy increases the hemorrhagic risk of AVM. In one case report, a pregnant woman with a developmental venous anomaly experienced a neurologic event, presumably due to dehydration-related thrombosis with secondary hemorrhage [25, 26].

Trauma

Trauma to a vascular malformation may cause infection, bleeding, thrombosis, fracture, or other problems. Some patients report lymphedema following sports trauma. This may be related to damage to fragile subcutaneous lymphatic vessels, e.g., in the shins.

Iatrogenic Provoking Factors: Surgery and Endovascular Therapy

Boccara et al. investigated if surgical intervention may provoke clinical aggravation of lymphatic malformations (LM) in pediatric patients. This retrospective review of 26 cases revealed that postoperative delayed wound healing, lymphatic oozing, and functional impairment were frequent [27]. Additionally, Trenor and Chaudry warn that rib biopsy can induce chronic pleural effusion in patients with complicated lymphatic anomalies [28]. Patients with vascular anomalies associated with profound thrombocytopenia (e.g., Kasabach-Merritt phenomenon in Kaposiform Hemangioendothelioma) are at risk of bleeding; thus, biopsy of these lesions and surgical intervention overall should be performed with caution.

Careful planning and staged interventional procedures by experienced interventional radiologists can abrogate serious treatment-related complications. In one series of 116 evaluable patients with venous malformations who underwent sclerotherapy with alcohol and/or sodium tetradecyl sulfate, the complications included peripheral nerve injury, deep vein thrombosis, muscle contracture, infection, skin necrosis, and others, most of which ultimately resolved [29]. Pulmonary embolism, hemoglobinuria,

renal complications and coagulopathy, contour deformities, and hyperpigmentation (following bleomycin sclerotherapy) have also been reported as possible sequelae from sclerotherapy [30–34]. Foam sclerotherapy is noted to have a lower complication rate, and alcohol the highest [33, 35, 36].

Delayed wound healing, wound dehiscence, and recurrence were the most common sequelae of surgical intervention for vascular anomalies of the vermilion in a series of 38 patients [37].

In summary, there are many potential "provoking factors" which can aggravate congenital vascular malformations. It is essential to be aware of these issues and to mitigate complications when feasible.

Bibliography

1. Geronemus RG, Ashinoff R. The medical necessity of evaluation and treatment of port-wine stains. J Dermatol Surg Oncol. 1991;17(1):76–9.
2. Greene AK, Taber SF, Ball KL, Padwa BL, Mulliken JB. Sturge-Weber syndrome: soft-tissue and skeletal overgrowth. J Craniofac Surg. 2009;20(Suppl 1): 617–21.
3. van Drooge AM, de Rie M, van der Veen W, Wolkerstorfer A. Port-wine stain progression: is prevention by pulsed dye laser therapy possible? Eur J Dermatol. 2013;23(2):282–3.
4. Lee JW, Chung HY, Cerrati EW, March TM, Waner M. The natural history of soft tissue hypertrophy, bony hypertrophy, and nodule formation in patients with untreated head and neck capillary malformations. Dermatol Surg. 2015;41(11):1241–5.
5. Tark KC, Lew DH, Lee DW. The fate of long-standing port-wine stain and its surgical management. Plast Reconstr Surg. 2011;127(2):784–91.
6. Brightman LA, Geronemus RG, Reddy KK. Laser treatment of port-wine stains. Clin Cosmet Investig Dermatol. 2015;8:27–33.
7. Herman-Giddens ME. Recent data on pubertal milestones in United States children: the secular trend toward earlier development. Int J Androl. 2006;29(1): 241–6. ; discussion 86-90
8. Herman-Giddens ME, Steffes J, Harris D, Slora E, Hussey M, Dowshen SA, et al. Secondary sexual characteristics in boys: data from the Pediatric Research in Office Settings Network. Pediatrics. 2012;130(5):e1058–68.
9. Kaplowitz P. Update on precocious puberty: girls are showing signs of puberty earlier, but most do not require treatment. Adv Pediatr. 2011;58(1):243–58.
10. Kulungowski AM, Hassanein AH, Nose V, Fishman SJ, Mulliken JB, Upton J, et al. Expression of androgen, estrogen, progesterone, and growth hormone receptors in vascular malformations. Plast Reconstr Surg. 2012;129(6):919e–24e.
11. Hughes RL, Collins KA, Sullivan KE. A case of fatal iliac vein rupture associated with May-Thurner syndrome. Am J Forensic Med Pathol. 2013;34(3):222–4.
12. Wain K, Swanson K, Watson W, Jeavons E, Weaver A, Lindor N. Hereditary hemorrhagic telangiectasia and risks for adverse pregnancy outcomes. Am J Med Genet A. 2012;158A(8):2009–14.
13. de Gussem EM, Lausman AY, Beder AJ, Edwards CP, Blanker MH, Terbrugge KG, et al. Outcomes of pregnancy in women with hereditary hemorrhagic telangiectasia. Obstet Gynecol. 2014;123(3):514–20.
14. Berthelot E, Savale L, Guyot A, Rahmoune FC, Bouchachi A, Assayag P. Acute high output heart failure revealing hereditary hemorrhagic telangiectasia in a pregnant woman. Presse Med. 2015;44(3):362–5.
15. Yara N, Masamoto H, Iraha Y, Wakayama A, Chinen Y, Nitta H, et al. Diffuse venous malformation of the uterus in a pregnant woman with Klippel-Trenaunay syndrome diagnosed by DCE-MRI. Case Rep Obstet Gynecol. 2016;2016:4328450.
16. Gonzalez-Mesa E, Blasco M, Anderica J, Herrera J. Klippel-Trenaunay syndrome complicating pregnancy. BMJ Case Rep. 2012;2012
17. Gungor Gundogan T, Jacquemyn Y. Klippel-trenaunay syndrome and pregnancy. Obstet Gynecol Int. 2010; 2010:706850.
18. Koch A, Aissi G, Gaudineau A, Sananes N, Murtada R, Favre R, et al. Klippel-Trenaunay syndrome and pregnancy: difficult choice of delivery from a case and a review of the literature. J Gynecol Obstet Biol Reprod (Paris). 2014;43(7):483–7.
19. Kemfang JD, Dobgima WP, Motzebo RM, Ngassam A, Fokou M, Kasia JM. Successful management of pregnancy in an African woman with Klippel Trenaunay syndrome. Pan Afr Med J. 2013;16:99.
20. Atis A, Ozdemir G, Tuncer G, Cetincelik U, Goker N, Ozsoy S. Management of a Klippel-Trenaunay syndrome in pregnant women with mega-cisterna magna and splenic and vulvar varices at birth: a case report. J Obstet Gynaecol Res. 2012;38(11):1331–4.
21. Martin JR, Pels SG, Paidas M, Seli E. Assisted reproduction in a patient with Klippel-Trenaunay syndrome: management of thrombophilia and consumptive coagulopathy. J Assist Reprod Genet. 2011;28(3):217–9.
22. Rebarber A, Roman AS, Roshan D, Blei F. Obstetric management of Klippel-Trenaunay syndrome. Obstet Gynecol. 2004;104(5 Pt 2):1205–8.
23. DeStephano CC, Werner EF, Holly BP, Lessne ML. Diagnosis and management of iliac vein thrombosis in pregnancy resulting from May-Thurner syndrome. J Perinatol. 2014;34(7):566–8.
24. Wax JR, Pinette MG, Rausch D, Cartin A. May-Thurner syndrome complicating pregnancy: a report of four cases. J Reprod Med. 2014;59(5–6):333–6.
25. Lv X, Li Y. The clinical characteristics and treatment of cerebral AVM in pregnancy. Neuroradiol J. 2015; 28(4):385–8.

26. Seki M, Shibata M, Itoh Y, Suzuki N. Intracerebral hemorrhage due to venous thrombosis of developmental venous anomaly during pregnancy. J Stroke Cerebrovasc Dis. 2015;24(7):e185–7.
27. Boccara O, Chrétien-Marquet B, Pannier S, Guéro S, Khen-Dunlop N, Hadj-Rabia S, et al. Is surgery a triggering factor for clinical worsening of lymphatic malformations? 21st Workshop, International Society for the Study of Vascular Anomalies (ISSVA); April 26–29, 2016. Argentina: Buenos Aires; 2016.
28. Trenor 3rd CC, Chaudry G. Complex lymphatic anomalies. Semin Pediatr Surg. 2014;23(4):186–90.
29. Ali S, Weiss CR, Sinha A, Eng J, Mitchell SE. The treatment of venous malformations with percutaneous sclerotherapy at a single academic medical center. Phlebology. 2016;31(9):603–9.
30. Burrows PE. Endovascular treatment of slow-flow vascular malformations. Tech Vasc Interv Radiol. 2013;16(1):12–21.
31. Qiu Y, Chen H, Lin X, Hu X, Jin Y, Ma G. Outcomes and complications of sclerotherapy for venous malformations. Vasc Endovascular Surg. 2013;47(6):454–61.
32. van der Vleuten CJ, Kater A, Wijnen MH, Schultze Kool LJ, Rovers MM. Effectiveness of sclerotherapy, surgery, and laser therapy in patients with venous malformations: a systematic review. Cardiovasc Intervent Radiol. 2014;37(4):977–89.
33. Aronniemi J, Castrén E, Lappalainen K, Vuola P, Salminen P, Pitkäranta A, Pekkola J. Sclerotherapy complications of peripheral venous malformations. Phlebology. 2015. [Epub ahead of print]
34. Mohan AT, Adams S, Adams K, Hudson DA. Intralesional bleomycin injection in management of low flow vascular malformations in children. J Plast Surg Hand Surg. 2015;49(2):116–20.
35. Rabe E, Pannier F. Sclerotherapy in venous malformation. Phlebology. 2013;28(Suppl 1):188–91.
36. Horbach SE, Lokhorst MM, Saeed P, de Gouyon Matignon de Pontouraude CM, Rothova A, van der Horst CM. Sclerotherapy for low-flow vascular malformations of the head and neck: a systematic review of sclerosing agents. J Plast Reconstr Aesthet Surg. 2016;69(3):295–304.
37. Park SM, Bae YC, Lee JW, Kim HS, Lee IS. Outcomes of surgical treatment of vascular anomalies on the vermilion. Arch Plast Surg. 2016;43(1):19–25.