Differential Diagnosis of Choroiditis

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Introduction

Choroiditis can be defined as an inflammatory process affecting the choroid. The main cause of inflammation can range from an autoimmune reaction targeting specific ocular antigens to an immune response against an exogenous agent infecting the eye. However, regardless the underlying trigger, the inflammatory status can result in similar clinical pictures in the choroid, making the proper diagnosis a real challenge.

On the other hand, an immunosuppressive therapy, essential to save the eye in case of an autoimmune disease, could be devastating in the presence of a misdiagnosed infectious entity. Thus, to discriminate between infectious and noninfectious conditions is the first step of the diagnostic process while facing these entities. The second goal that must be achieved, especially in case of an infectious disease, is to identify the pathogen which is causing the choroiditis, in order to start the specific treatment.

The aim of this chapter is hence to provide clinicians a schematic algorithm based on simple hints and general rules for the work-up of infectious choroiditis, in order to differentiate them from noninfectious forms and to identify the causative agent.

The Choroid: Primary Target or Accidental Host?

Inflammatory processes involving the choroid can be divided according to their location into choriocapillaritis when the inflammation involves the choriocapillaris and stromal choroiditis when the inflammatory foci are located deep in the Haller and Sattler layers.

When the inflammation is sustained by an autoimmune reaction targeting the choriocapillaris or the retinal pigment epithelium (RPE), we classify the disease as a

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primary inflammatory choriocapillaropathy. On the other hand, the choriocapillaris can show inflammatory signs when contiguous structures such as the retina or the deep choroid are inflamed. These entities can have an infectious etiology and are classified as secondary choriocapillaropathies.

Stromal choroiditis can also be divided into two groups according to the underlying inflammatory process. When the inflammation is sustained by an autoimmune reaction targeting the choroid, the diseases are classified as a primary obligatory choroiditis. On the contrary, when the choroid represents the hosting tissue of a systemic infectious/inflammatory condition accidentally located in the eye, the disease is considered a secondary choroiditis.

A list of the diseases commonly causing choroiditis classified according to the principles above is reported in Table 1.

How to Find Out the Correct Diagnosis?

When we try to reach a diagnosis, we basically compare the clinical history and picture of the patient with several compatible diseases we know. We then select the entities that better fit with the signs and symptoms of the subject we are examining, and we finally perform some tests to isolate the cause of the pathological condition among the others. A schematic representation of this process is reported (Fig. 1).

It is important to notice how the three main consecutive steps, allowing the filtering process that brings us from the global set of diseases we know to the final diagnosis, are linked by two-way arrows. This means that they can influence each other creating a dynamic, self-developing process.

To give an example, a specific sign detected by funduscopic examination (second step) can raise the clinical suspect of precise entities, and consequently bring the clinician back to the medical history (first step), in order to enquire for more focused questions. The same could happen during the interpretation of test results.

The Importance of the Medical History "Who is the Host?"

Most of the time, it is useless and even self-defeating to put the patient through a too detailed, and possibly embarrassing, questionnaire on his/her lifestyle and previous medical history. Nevertheless, we cannot avoid considering details of the patient's history that could make us include rare diseases or unusual clinical pictures.

Despite the quite large number of entities possibly affecting the choroid, we can assess the conditions that could shape our list of diseases by a simple scheme, based on just four main questions (Fig. 2).

The pool of diseases that need to be considered along the diagnostic process will then include specific rare entities in addition to the main conditions commonly causing choroiditis (Table 1).

Table 1 Inflammatory conditions frequently affecting the choroid are divided according to the mainly involved choroidal layer (choriocapillaris or stroma). Diseases directly targeting the eye tissues are listed as "primary," whereas ocular involvement occurring as a manifestation of a systemic disease is classified as "secondary." Serpiginoid tuberculosis is classified in between the two categories since it is caused by an immune reaction against the retinal pigment epithelium (RPE) when the RPE cells present tubercular antigens on their surface after being affected by mycobacteria. Infectious diseases are reported in bold

Choriocapillaropaties	
Primary	**Secondary**
AMPPE	**Toxoplasma Retinocoroiditis**
Serpiginous Choroiditis	**Syphilis**
Multifocal Choroiditis/PIC	
MEWDS	
Other Rare Entities	
Serpiginoid / Serpiginous like / Ampiginous Tuberculosis	
Stromal Choroditis	
Primary	**Secondary**
Vogt Koyanagi Harada Disease	Sarcoidosis
Sympathetic Ophthalmia	**Tuberculosis**
Birdshot Chorioretinopahty	**Syphilis**
	Other more rare infectious entities

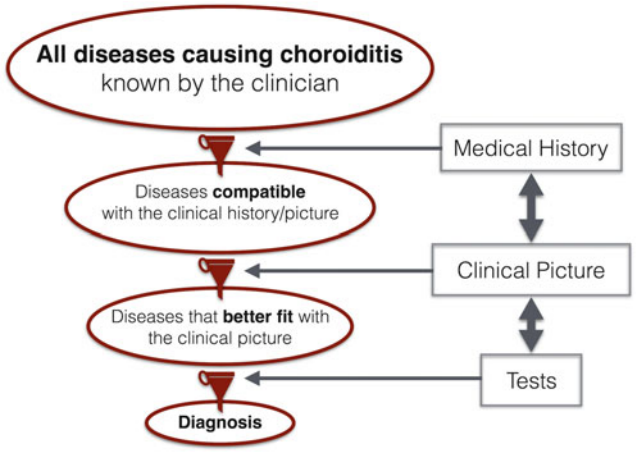

Fig. 1 The diagnostic process (scheme)

The proposed questionnaire is just a basic scheme and should be modified according to clinicians' experience and the geographic/social contexts. Furthermore, as mentioned before, the detection of specific signs during the clinical exam, the imaging examination, or the laboratory tests, could make the clinician suspecting an initially ignored disease and lead back to the medical history collection step in order to ask for targeted questions.

The Main Role Played by the Clinical Picture: "How Does It Look Like?"

The clinical exam is the most important part of the diagnostic process: it can help in understanding the disease appearance and distribution, in perceiving the disease progression

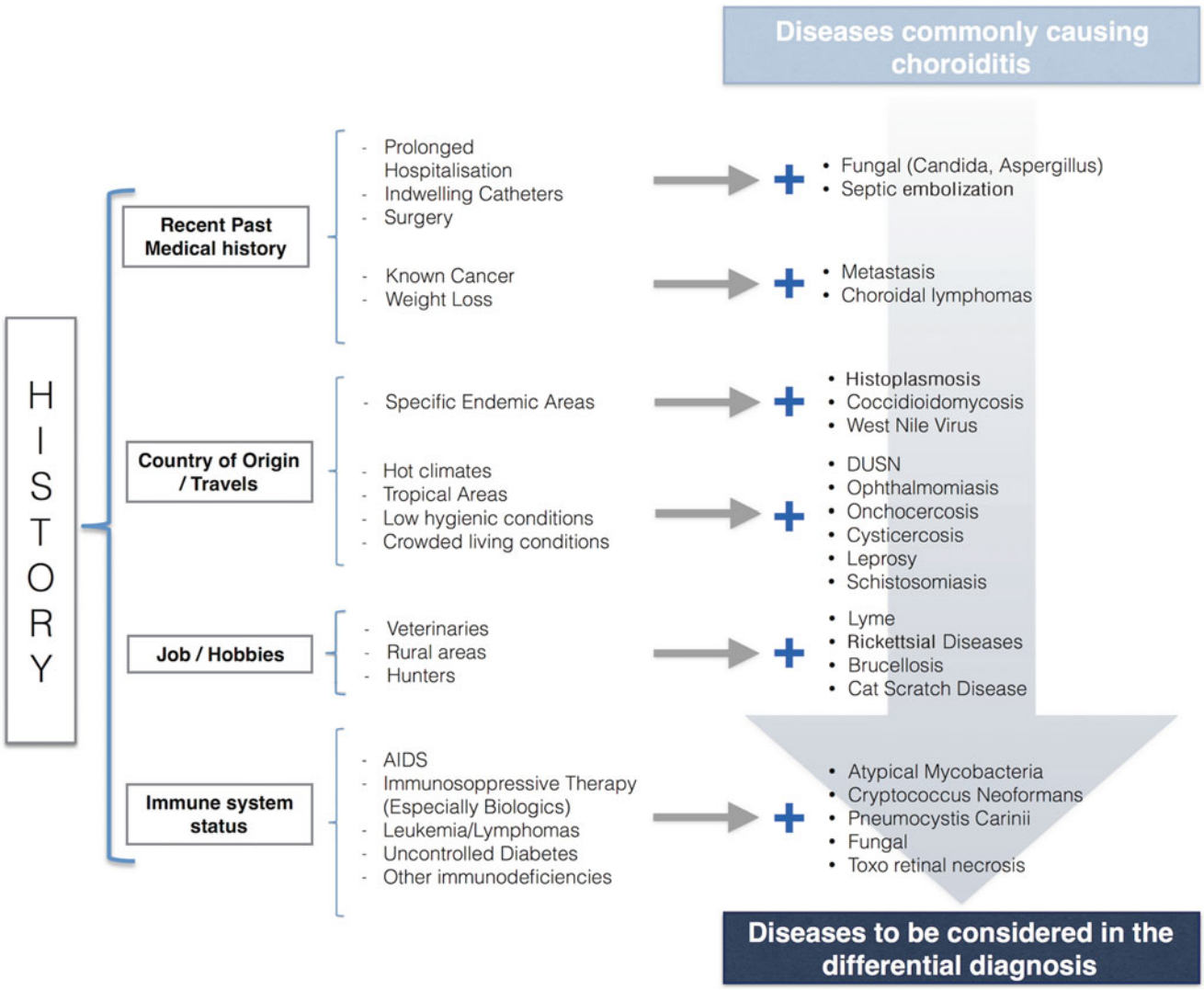

Fig. 2 Simplified scheme for Medical history collection. Testing the reported four main fields of interest allows to include a large number of rare entities that need to be considered in the differential diagnosis when specific risk factors are present

pathway, and in evaluating the surrounding structures involvement.

Choroidal Lesions

In case of a solitary choroidal lesion, the infectious etiology should always be considered as a front-runner. A primary localization of pathogens in the choroid due to hematogenous spread as well as secondary to septic embolization is responsible of such lesions in most of the cases. Nevertheless neoplastic conditions either primitive or metastatic must be ruled out.

On the contrary, multiple choroidal lesions, especially when involving both eyes, could be related both to autoimmune and infectious diseases. For this reason a bilateral involvement always needs for further investigations, including a multi-imaging approach, to be properly studied.

It is almost impossible to differentiate infectious from autoimmune diseases by the sole appearance of choroidal lesions; however, there are some features detectable by the simple funduscopic examination that can address the diagnostic process towards the correct direction:

- Similar size and shape for all the lesions is suggestive of an autoimmune disease.
- Symmetrical and evenly distributed lesions are more likely autoimmune rather than infectious.
- Sign of "penetration" from the choroidal district through the RPE into the subretinal/retinal/vitreous compartment is strongly suggestive of an infectious condition.

Associated Findings: Do the Surrounding Structures Look Involved?

It is always important to carefully examine the whole eyeball searching for inflammatory alterations accompanying choroidal lesions. Being the RPE and the retina contiguous to the choroid, these are the most commonly involved structures secondary to choroidal diseases. In case of infectious pathologies, the RPE and the retina can be either directly targeted by the infective microorganism or indirectly damaged by the inflammatory process occurring within the underlying choroid.

On the contrary, in case of autoimmune choroiditis, an accompanying retinitis is more rare, and the retinal lesions are more often the expression of secondary ischemic or inflammatory damage.

Chorioretinal scars often represent the sign of a previous choroiditis episode. Although non-active, these lesions can be very useful in the differential diagnosis since their shape, distribution, size, and pigmentation differ from a disease to the other. Multiple pigmented scars along the vessels' course are suggestive of TB (Fig. 3a), whereas small round-shaped yellowish atrophic dots in the mid-periphery with a prevalence in the inferior sectors are more frequent in sarcoidosis (Fig. 3b).

A pigmented scar with an active retinochoroiditis along one border strongly supports the diagnosis of reactivate toxoplasmic retinochoroiditis (Fig. 3c). Finally, looking at a serpiginoid scar, pigment clumping at the center of the lesion is suggestive for infectious etiology (Fig. 3d), whereas autoimmune disease usually gets pigmented along the borders.

Intraocular inflammation, regardless of the etiology, is often characterized by a breakdown of the inner blood retinal barrier; however, specific vasculitic alterations can help in developing a diagnostic hypothesis. Although an occlusive vasculitis can be found in several uveitis conditions, including autoimmune diseases such as Behçet disease or systemic lupus erythematosus, in case of choroiditis, an accompanying occlusion of the retinal vessels can be suggestive of infectious etiologies (Fig. 4a). An exudative segmental phlebitis on the contrary, is more likely related to autoimmune conditions such as sarcoidosis (Fig. 4b).

Two exceptions to this general rule are represented by the retinal artery occlusions that can be found along with choroidal infarcts mimicking choroiditis in polyarteritis nodosa (Fig. 5) on one side, and the focal exudative vasculitis that often occurs along retinal vessels crossing a choroidal lesion in TB (Fig. 6).

A careful evaluation of the vitreous involvement can also add useful information. First of all, vitritis is itself a sign of inflammatory reaction and can hence be considered as a direct representation of the immune status of the patient.

Thus, the absence of vitreous involvement should always make the clinician doubtful about the diagnosis of a proper choroiditis, and rather consider alternative conditions mimicking choroidal inflammation such as choriocapillaritis or choroidal infarcts. In case the clinical picture is suggestive of an infectious etiology, vitritis should always be present, and its lack should raise the suspect of immunodeficiency, thus inducing the inclusion of unusual pathogens in the differential diagnosis.

Furthermore some specific diseases, typically presenting with choroidal lesions, are associated with particular vitritis features: vitreous aggregates disposed with a "string of pearls" fashion are suggestive of fungal etiology, a dense vitreal reaction overlying a chorioretinal lesion is common in toxoplasmosis, and a dense vitritis organized in parallel sheets is typical of intraocular lymphomas.

Anterior segment is less frequently involved in case of choroiditis being the most far district of the eye from the

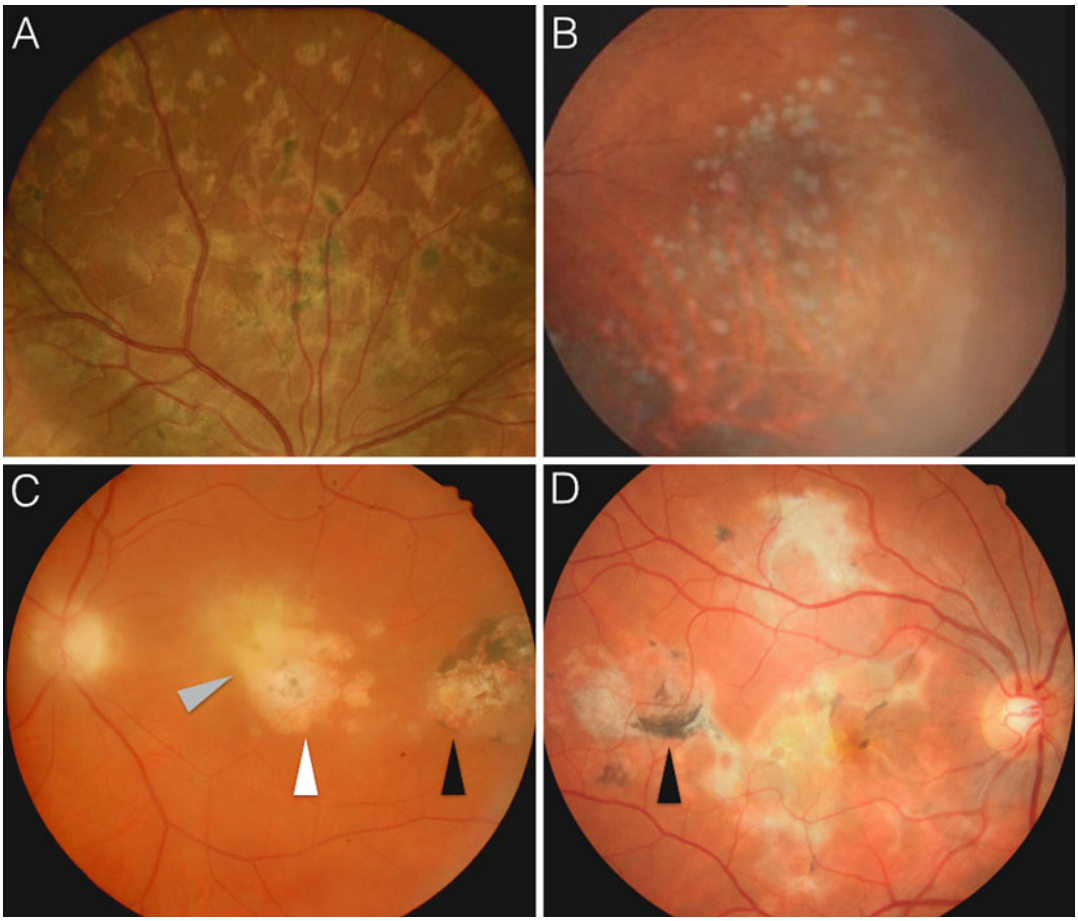

Fig. 3 Chorioretinal scars caused by different diseases. (**a**) Chorioretinal pigmented scars along the vessels' course in a patient affected by tubercular choroiditis. (**b**) Multiple small round-shaped atrophic lesions in the mid-periphery in a patient affected by sarcoidosis. (**c**) An active retinitis focus (*gray arrowhead*) along the border of a chorioretinal scar (*white arrowhead*) and a more pigmented (older) scar (*black arrowhead*) in a patient affected by toxoplasmic retinochoroiditis. (**d**) Serpiginoid choroiditis with pigment clump at the center of the lesion in a patient affected by serpiginoid tuberculosis

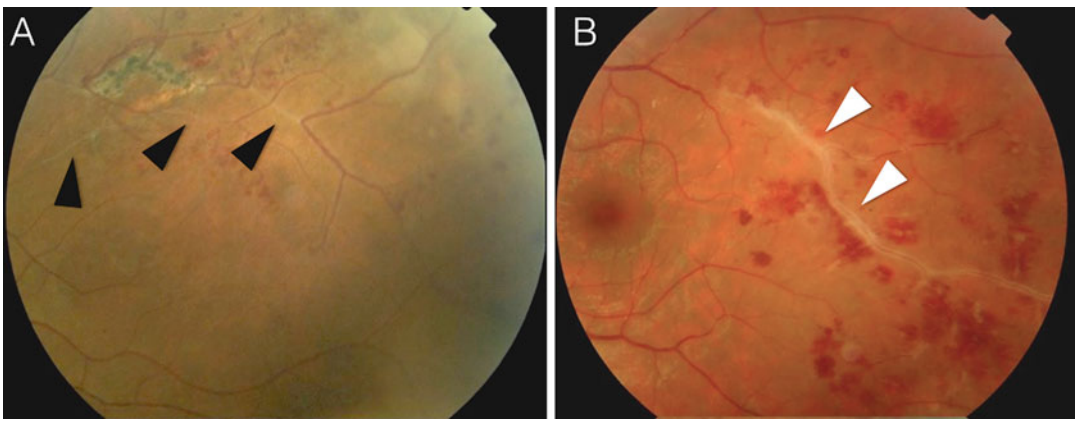

Fig. 4 Retinal vasculitis as an associated finding of choroidal inflammatory conditions. (**a**) Occluded vessels (*black arrowheads*) in a patient affected by intraocular tuberculosis. (**b**) Vascular sheathing (*white arrowheads*) as a sign of exudative vasculitis in a patient affected by sarcoidosis

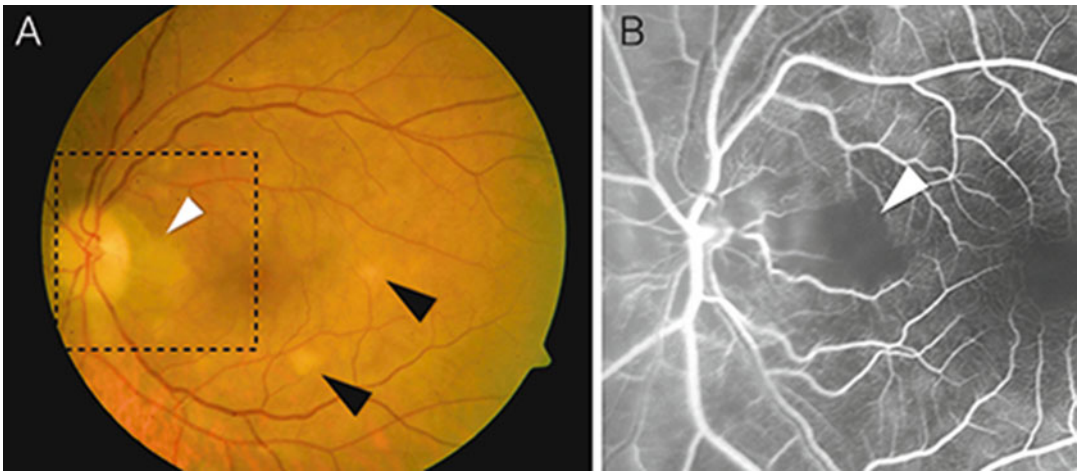

Fig. 5 Funduscopic findings in a patient affected by panarteritis nodosa (*PAN*), a systemic condition causing multiple vascular occlusions that can mimic choroiditis lesions. A whitening of the retina along the papillomacular bundle (*white arrowhead*) is visible at funduscopic examination (**a**) as a sign of retinal ischemia. Multiple yellowish deep lesions (*black arrowheads*) could be misdiagnosed as choroiditis but actually represent choroidal infarcts, a typical finding in PAN. Retinal ischemia is confirmed by fluorescein angiography (**b**)

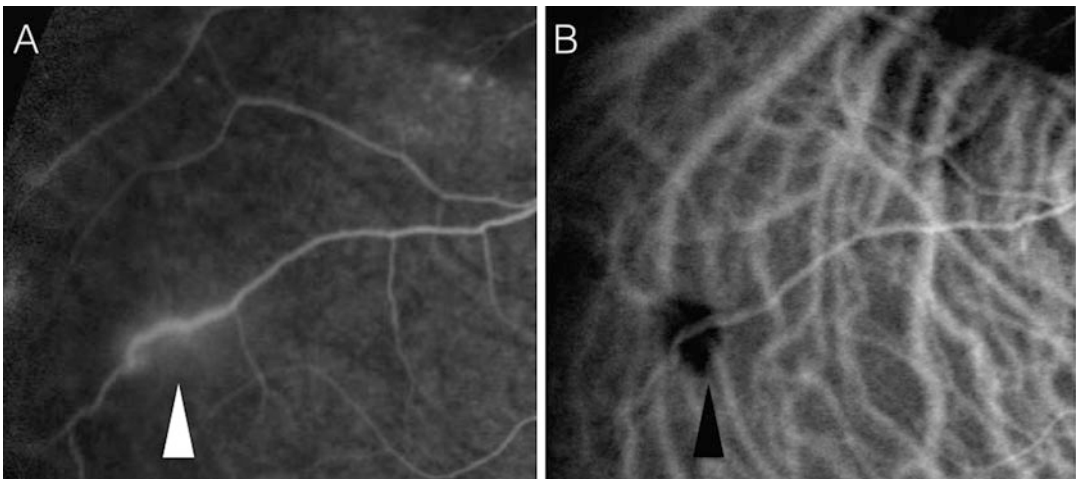

Fig. 6 Segmental exudative vasculitis in a patient affected by intraocular tuberculosis. Tuberculosis usually causes occlusive vasculitis. However focal vascular leakage (*white arrowhead*) can be noted in some patients on fluorescein angiography (**a**) as a sign of exudative vasculitis. Associated indocyanine green angiography (**b**) reveals an underlying choroidal granuloma (*black arrowhead*) likely causing the inflammatory process secondary involving the retinal leaking vessel

choroid. Despite this, observing granulomatous keratic precipitates can be useful in considering granulomatous rather than nongranulomatous uveitis as causative agent.

Multi-Imaging: A Useful Tool to Better Understand the Choroidal Involvement

Being the choroid a deep structure, overlaid by other tissues, different lesions can have a similar appearance at funduscopic examination. A multi-imaging study, on the contrary, can allow a better visualization of the alterations occurring within the choroid, differentiating them according to their location, their perfusion, and the relationships they have with the surrounding structures.

Fundus Autofluorescence (FAF)

FAF images are generated by stimulating the retinal pigment epithelium with a specific wavelength and collecting

the light consequently generated by the fluorophores contained in the RPE cells. Being the choroid located beyond the RPE, in many choroidal lesions FAF looks normal. However, once a deep lesion alters the overlying structures inducing exudative or atrophic changes at the RPE or the retina, FAF can change. As a general rule, an increased autofluorescence can be consequent to atrophic changes of the retina with preserved RPE, whereas a decreased FAF can result either from RPE atrophy or a masking effect secondary to material or fluid accumulated over the RPE.

Specific patterns of FAF are associated with certain pathologic entities such as multiple evanescent white dot syndrome (MEWDS) or serpiginous/serpiginous-like choroiditis and can be useful in the differential diagnosis as well as in the activity assessment of these forms.

Fluorescein Angiography (FA)

FA is commonly used to study the retinal rather than the choroidal perfusion. Nevertheless it can be really useful in collecting additional informations about the retinal involvement and the inflammatory status of the posterior segment in the presence of a choroiditis.

As already mentioned, the identification of a retinal vascular alteration and its characterization as occlusive or exudative can be really helpful in differentiating the etiology of an underlying choroiditis (Fig. 7). In addition, a staining of dye can be visualized by FA in the areas of retina overlying an active choroidal lesion, whereas a window defect is visible in correspondence with retinal scars following the resolution of a preexisting choroiditis. Finally FA represents the gold standard technique to identify retinal or choroidal neovascularization that can complicate some cases of choroiditis.

Indocyanine Green Angiography (ICGA)

Due to their chemical and physical features, the indocyanine green molecules do not get out of the choriocapillaris fenestrations hence allowing a good visualization of the choroidal vasculature. As a consequence, ICGA is the gold standard technique to visualize and study choroidal alterations.

ICGA hyper-fluorescence can have two main causes: the presence of choroidal vessels leaking in the late phases of the angiogram as an a-specific sign of inflammation, or the leakage of dye through RPE disruptions occurring in case of choroidal thickening associated with outer retinal blood barrier alteration such as in Vogt-Koyanagi-Harada disease.

ICGA hypo-fluorescence is frequently associated with choroiditis, and its features throughout the angiogram allow the identification of different choroidal lesions (Fig. 8).

A schematic interpretation of ICGA hypo-fluorescence and its association with possible etiologies is represented in Fig. 9.

Spectral Domain Optical Coherence Tomography (SD-OCT)

SD-OCT provides in vivo quasi histological sections of the eye structures. Intraretinal fluid and subretinal fluid can be easily detected as a sign of inflammation associated with choroidal disease. Retinal alterations occurring in the areas of tissue overlying a choroidal lesion, either

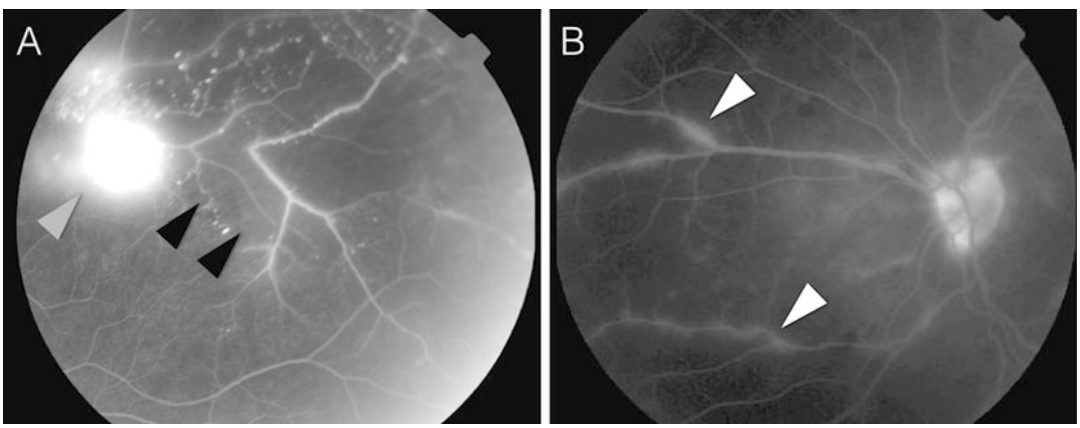

Fig. 7 Fluorescein angiography showing vascular alterations in the retina accompanying choroidal inflammation. (**a**) Retinal ischemic areas (*black arrowheads*) as a consequence of occlusive vasculitis in a patient affected by intraocular tuberculosis. A retinal neovascularization is visible on the left side of the image (*gray arrowhead*). (**b**) Segmental leakage along main vessels (*white arrowheads*) as a sign of exudative vasculitis in a patient affected by sarcoid-related uveitis

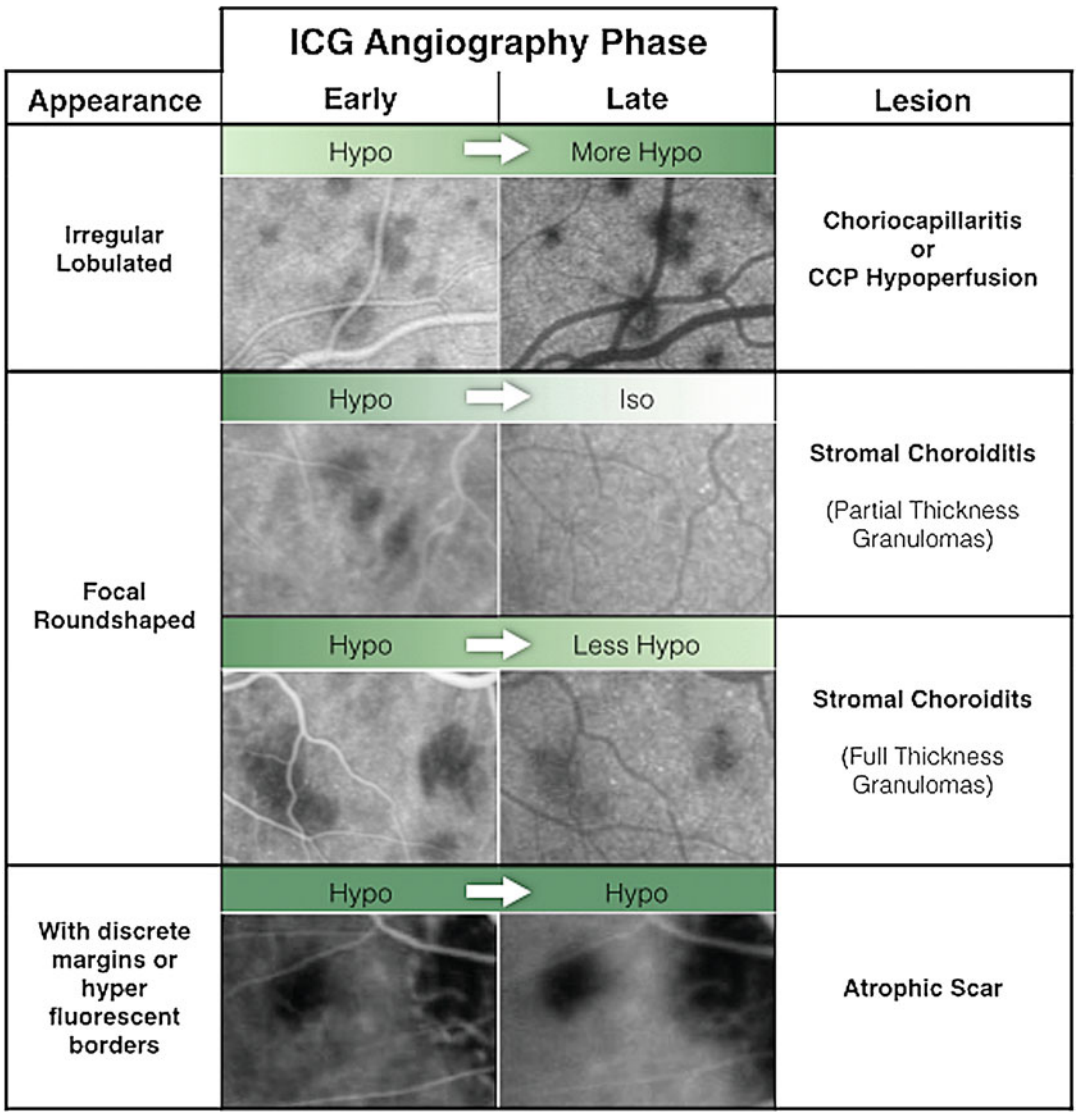

Fig. 8 Schematic interpretation of the hypofluorescent alterations on indocyanine green angiography (*ICGA*) according to their shape and appearance throughout the different phases of the exam. ICGA can visualize more choroidal lesions than any other imaging technique. Furthermore a correct interpretation of hypofluorescent findings allows to identify the exact choroidal layer involved in the inflammatory process (i.e., choriocapillaris, full-thickness choroidal stroma, partial thickness choroidal stroma)

caused by a direct invasion of the retinal cells by the microorganisms such as in retinitis or secondary to an inflammatory or ischemic damage, can also be detected.

SD-OCT features suggestive for specific choroiditis etiologies are reported (Fig. 10).

Enhanced Depth Imaging Optical Coherence Tomography (EDI-OCT)

EDI-OCT is an advanced OCT technique that allows the visualization of structures deeper than the RPE, hardly reached by the standard SD-OCT. The possibility to image the choroid and to measure its thickness has increased the importance of EDI-OCT in the management of posterior uveitis, especially choroiditis. Changes in choroidal thickness reflecting disease activity have been reported in several inflammatory entities and are nowadays used for monitoring the inflammatory status and the response to therapy.

In contrast to the proved usefulness of EDI-OCT in monitoring choroiditis activity, its use as a diagnostic tool is still poorly explored. Few papers have reported the possibility to visualize choroidal lesions (e.g., granulomas) by the use of EDI-OCT. However a differential diagnosis among the causative agents based on EDI-OCT characteristics of the

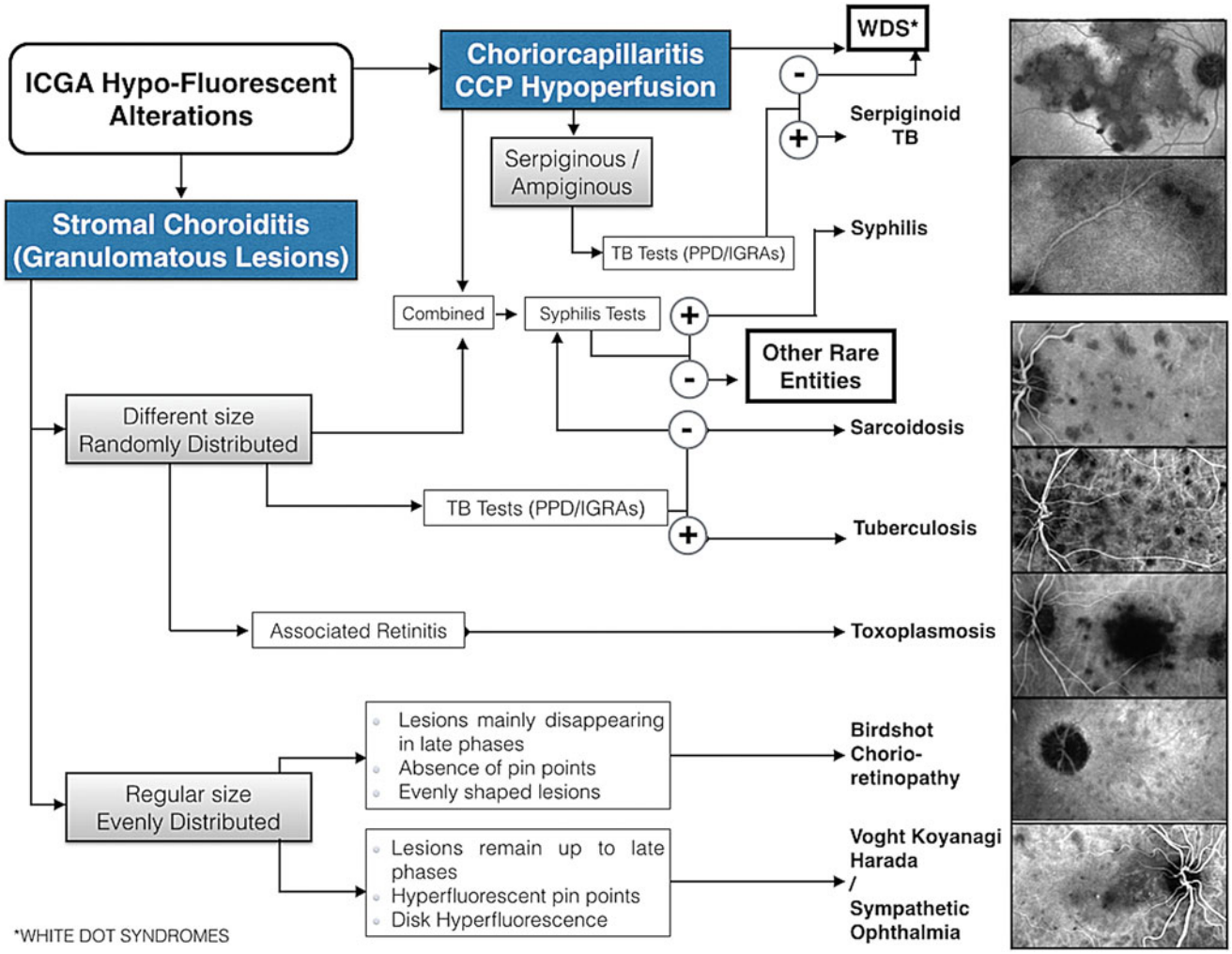

Fig. 9 Indocyanine green angiography (*ICGA*) hypofluorescent alterations and their association with choroidal inflammatory diseases. After the first differentiation between choriocapillaris inflammation/hypoperfusion and stromal choroiditis, a further classification of the ICGA hypofluorescent alterations according to their localization, shape, and associated findings can help in identifying the underlying disease. A schematic algorithm to correlate the ICGA findings with the presumed causative agent is reported. It has to be underlined that ICGA can support an etiological hypothesis or guide the diagnostic process, but the definitive diagnosis cannot be made just on these technique's findings

choroidal granulomas is still impossible although certain features show a higher prevalence in TB-related lesions (Fig. 11).

EDI-based structural analysis of the choroidal sublayers has also showed Sattler's layer enlargement in sarcoidosis, not detectable in TB-related uveitis.

Finally, EDI-OCT features of several entities other than uveitis have been described, making this technique really useful in differentiating these entities from choroiditis. Several neoplastic entitles such as intraocular lymphoma, for example, show specific EDI-OCT signs that can help in confirming or excluding this masquerading syndrome from the possible differential diagnosis.

Systemic Investigations: Is It Just in the Eye?

Being infectious choroiditis the expression of a systemic disease in most cases, clinicians dealing with such entities cannot avoid extending their investigations beyond the eye.

Nevertheless, it is almost impossible to list all the tests that could be performed to investigate a patient affected by a choroidal infectious disease, considering the prominent number of possible etiologies.

Among the most common choroiditis entities, two infectious diseases should always be considered as possible causative agents until otherwise proven: syphilis and

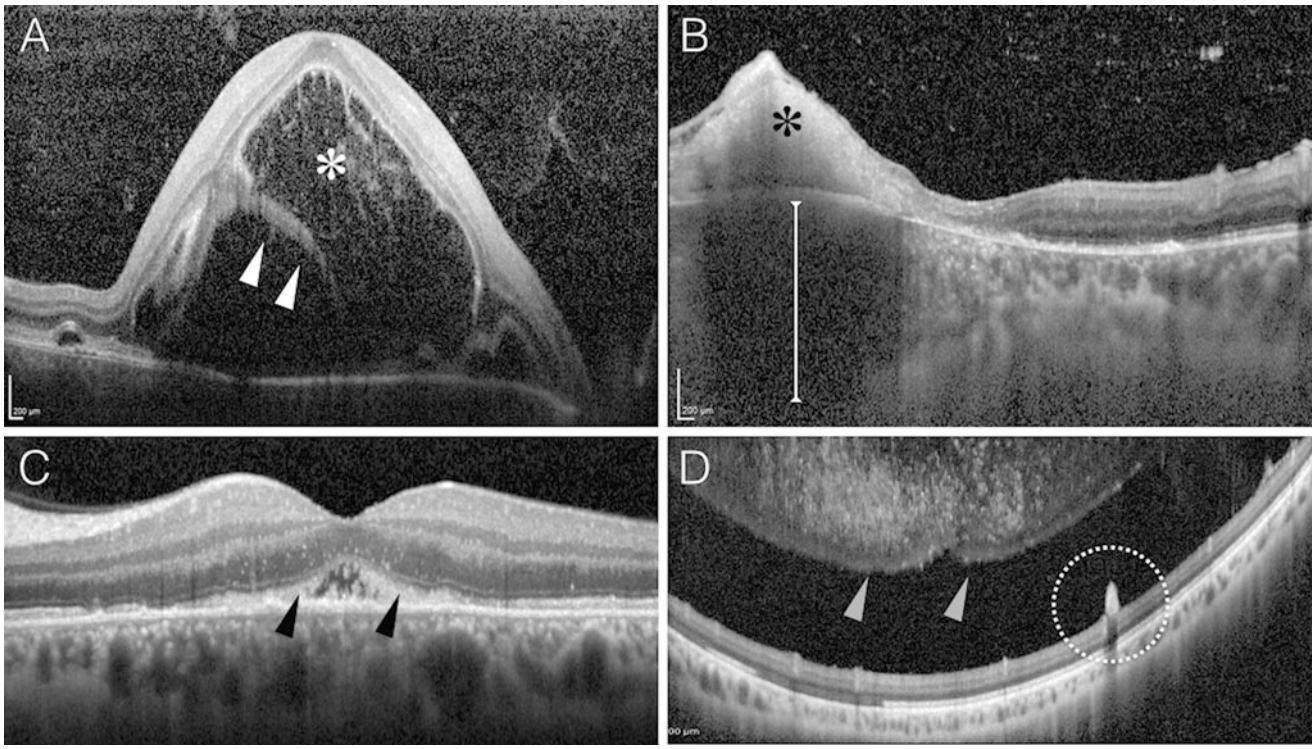

Fig. 10 Spectral domain optical coherence tomography (*SD-OCT*) findings suggestive for specific uveitis entities associated with choroidal inflammation. (**a**) Subretinal fluid pockets (*white asterisk*) with multiple septa (*white arrowheads*) in a patient affected by Vogt-Koyanagi-Harada disease (Ishihara et al. 2009). (**b**) Retinal thickening and hyperreflectivity as a sign of active retinitis (*black asterisk*) in a patient affected by toxoplasmic retinochoroiditis. The inflammatory involvement of the underlying choroid is visible as a huge thickening (*white segment*) (Goldenberg et al. 2013). (**c**) Photoreceptor outer segment and outer retinal layer alterations (*black arrowheads*) in a patient affected by syphilitic placoid chorioretinitis (Pichi et al. 2014). (**d**) A pre-retinal hyperreflective deposit (*dotted circle*) in a case of toxoplasmic retinochoroiditis. This sign has been reported in about 30% of cases and strongly supports toxoplasmic etiology. Accompanying vitritis (*grey arrowheads*) is also visible (Goldenberg et al. 2013)

tuberculosis. For both of them, the systemic involvement can be assessed by several tests with different levels of sensitivity and specificity. In the suspect of intraocular TB, it has been demonstrated that a combination of Mantoux intradermal reaction (PPD) and an IGRA test (e.g., QuantiFERON TB Gold) offers a higher specificity and sensitivity as compared to each of the two tests alone. In regard to syphilis, the presence of specific antibodies offers the strongest evidence of disease presence. When such assay is not available, a combination of treponemic and non-treponemic tests should be performed.

In order to avoid time and resource wasting, other tests should only be performed under the strong suspect, based on the medical history and the clinical picture, for a specific entity.

Regardless the systemic investigation we ask for, a careful interpretation of the results is mandatory. In fact, a systemic 'positivity' means that the subject is affected or has been affected by the tested disease, but does not prove that infectious agent to be responsible for the ongoing choroiditis. On the other hand, false negatives are frequent in case of immunocompromised hosts.

Only the experience of the clinician and the combined evaluation of the medical history and the clinical picture allow a proper interpretation of the tests results.

Intraocular Specimens Analysis: The Final Proof

Although a correct diagnosis can be reached in most of the cases without collecting any intraocular sample, this is the only way to really prove the intraocular localization of a specific infectious agent.

In fact, blood test positivity can only demonstrate a subject has been infected by a certain pathogen, but the connection with the choroidal involvement can only be supposed.

As a consequence, when the clinical picture remains unclear or there is need for a stronger evidence of intraocular involvement, the collection and the analysis of intraocular samples are mandatory.

The choroid is hard to be reached; thus, a choroidal biopsy, although used for the management of certain

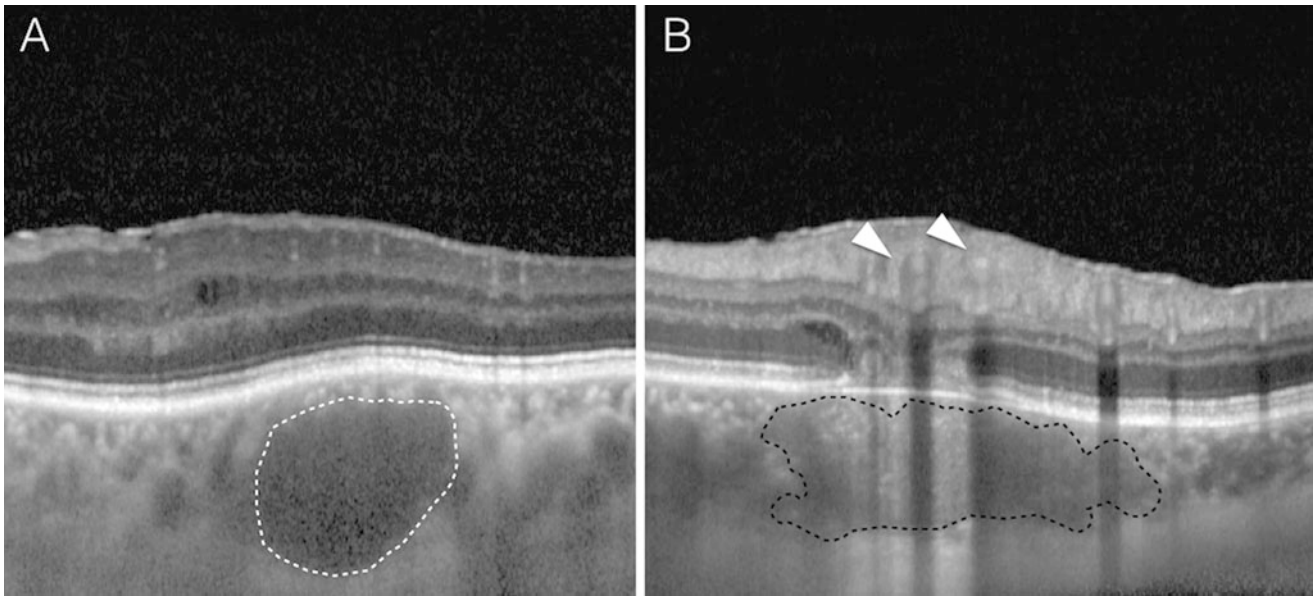

Fig. 11 Enhanced depth imaging optical coherence tomography (*EDI-OCT*) of choroidal granulomas. (**a**) A sarcoid-related choroidal granuloma (*white dotted line*) appearing as a hyporeflective round-shaped lesion with distinct margins and a homogeneous intralesional pattern. (**b**) A tubercular granulomatous lesion (*black dotted line*) appearing lobulated in shape and isoreflective as compared to the surrounding choroid. Margins are difficult to be determined, and the intralesional pattern is dishomogeneous. The choroidal lesion as frequently happens in TB is located beneath retinal vessels (*white arrowheads*). Contrary to reflectivity and internal pattern that does not show prevalence variations in different diseases, undefined margins and lobulated shape are more frequently observed and consequently suggestive for tubercular etiology (Invernizzi et al. 2015)

intraocular tumors, is not routinely adopted in choroiditis diagnosis due to the related surgical difficulties and complications. On the contrary, vitreous specimens are easily collected, and most of the times, their examination allow to perform several lab tests including polymerase chain reaction (PCR), cultures, and slice analysis in order to identify the infecting pathogen and exclude neoplastic entities mimicking uveitis (e.g., intraocular lymphoma).

Vitrectomy is also useful to allow the visualization of posterior structures (i.e., retina and choroid) in case of dense vitritis obscuring the fundus. On the contrary, when the disease is confined to the choroidal space only, with no sign of retinal or vitreal involvement, vitreous specimens can result negative since the pathogens have not yet reached the vitreal compartment. In such cases an invasive approach should be carefully evaluated.

Conclusions

Despite the improvements in diagnostic techniques and the increased scientific knowledge we reached in the last decades, uveitis are still a difficult conditions to be managed, with choroidal involvement representing the hardest challenge.

In most of the cases, a prompt therapy is mandatory to avoid sight-treating complications, but the proper treatment strictly depends on a correct diagnosis.

With this purpose clinicians should focus on two main targets: (1) to differentiate autoimmune from infectious diseases first and (2) to identify the causative agent in case of infection.

Following a schematic algorithm such as the one purposed in this chapter can help in searching for the correct diagnosis, avoiding time and resource wasting. However, a book will never be able to describe the complexity of the clinic, and only a passionate clinical practice and a trained experience will allow clinicians to properly interpret the whole data and to reach the correct diagnosis.

Key Points

- The differential diagnosis of choroiditis is challenging.
- Differentiating autoimmune from infectious etiology is mandatory in order to start a specific treatment.
- The medical history and the clinical picture are the main elements to select the possible differential diagnosis.
- A multi-imaging study with ICGA as a leading technique is helpful.
- Only the experience allows clinicians to properly interpret the whole picture and to reach the correct diagnosis.

Ocular Toxoplasmosis: The Choroidal Involvement

Ocular toxoplasmosis traditionally manifests as an active retinitis, and this sign is such characteristic to allow the disease diagnosis in most of cases. Nevertheless, the retinal pigment epithelium (RPE) and the choroid can be involved in the inflammatory process as well (Atmaca et al. 2006).

A focal choroidal thickening, visible beneath the areas of retinitis, is the expression of the inflammatory response against the parasite, actively duplicating into the overlying retinal lesion. However, choroidal involvement in toxoplasmosis can extend far more from what is clinically visible. Indocyanine green angiography (ICGA) in fact, reveals multiple satellite hypofluorescent dots in most of the patients, invisible at funduscopic examination due to the absence of an associated alteration in the overlying retina. The nature of these lesions is still unclear since they could represent choroidal granulomas containing the parasites as well as the expression of focal inflammatory reaction. Regardless of their pathophysiology, these lesions are the proof of diffuse choroidal involvement justifying the classification of ocular toxoplasmosis as a chorioretinitis, and supporting the use of ICGA in the management of this condition (Auer et al. 1999).

Serpiginous Choroiditis Versus Infectious Multifocal Serpiginoid Choroiditis (Nazari Khanamiri and Rao 2013)

One of the most impressive similarities between an autoimmune and an infectious choroiditis is represented by the serpiginous choroiditis and the infectious multifocal serpiginoid choroiditis.

Serpiginous choroiditis is a posterior uveitis manifesting with ameboid inflammatory lesions spreading from the peripapillary region throughout the fundus with a primary involvement of the choroid and the overlying retinal pigment epithelium (RPE). The pathogenesis is still unclear, but a favorable response to immunosuppressive therapy along with the absence of a proven infectious etiology supports the hypothesis of an autoimmune disease.

On the contrary, a similar clinical picture named as "serpiginous-like" or "multifocal serpiginoid" choroiditis has been associated with several infectious conditions with tuberculosis as a front-runner.

In both the conditions, infectious and autoimmune, the inflammatory process is mainly focused at the level of the RPE and the choriocapillaris with typical hypoperfusion signs on indocyanine green angiography. The RPE is supposed to be the target of the immune reaction: against RPE self-antigens in the serpiginous form or against exogenous antigens expressed on the infected RPE cells in the serpiginoid form.

Patient history, clinical feature, and systemic tests can help in differentiating between serpiginous choroiditis and tubercular multifocal serpiginoid choroiditis as reported below. However, only intraocular specimen analysis can definitively prove or exclude the infectious etiology.

Serpiginous choroiditis (likely autoimmune)	Tubercular multifocal serpiginoid choroiditis
Born/raised in non-endemic areas	Lived in endemic areas
Non-multifocal	Multifocal
Bilateral	Unilateral/bilateral
Absence of vitreous/anterior chamber inflammatory reaction	Vitreous/anterior chamber inflammatory reaction
Lesions starting from the peripapillary area	Lesions starting from the posterior pole without primary involvement
No response to anti-TB treatment	Improved with anti-TB treatment
Pigment clumping at the border of healed lesions	Pigment clumping usually at the center of lesions
TB systemic tests negative	TB systemic tests positive
Chest X-ray normal	Chest X-ray usually negative

(*continued*)

Suggested Reading

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