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## Idiopathic Multifocal Choroiditis: A Comment on Present and Past Nomenclature

The term “multifocal choroiditis” (MFC) is generally used to refer to that group of disorders characterized by multifocal choroidal inflammatory lesions occurring predominantly in young myopic females, idiopathic in origin, and not part of a systemic disorder or other recognized ocular syndrome. Any subsequent sequelae, such as choroidal neovascularization or circumscribed areas of chorioretinal atrophy, are regarded as the sequelae of MFC or old MFC (Figure 1). The purpose of this article is to define the disease entity idiopathic MFC and also to clarify the multitude of alternative names that have been given to this idiopathic disease over the years. In some instances, granulomatous or infectious diseases can cause a similar picture to idiopathic MFC, and workup for these diseases may be appropriate before diagnosing idiopathic MFC. Examples of disorders that most closely resemble idiopathic MFC are tuberculosis, brucellosis, coccidiomycosis, candidiasis (and other fungal septicaemias), plus sarcoidosis and other granulomatous diseases (e.g., Blau syndrome). There may be clinical features that differentiate these cases from typical idiopathic MFC—sarcoid, for example, tends to cause inferior lesions—however, the similarities often justify further investigation, particularly in the setting of active disease. These differential diagnoses will not be further discussed here.

In 1970, the term MFC was used to describe eyes with presumed ocular histoplasmosis syndrome (POHS) by Krill and Archer.<sup>2</sup> This usage persisted until at least 1981.<sup>2–4</sup> The disease POHS does not, however, fall within the modern definition of MFC.

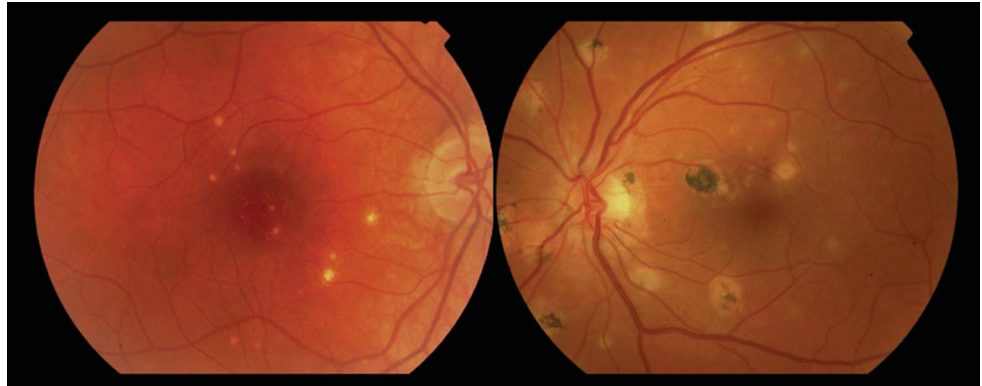
The term multifocal choroiditis (possibly with the prefix “recurrent”) then evolved to describe a distinct entity, separate to and distinct from POHS, predominantly affecting young myopic females and variably associated with vitritis/anterior chamber inflammation and subretinal fibrosis.<sup>5–8</sup> This entity also includes the condition known as punctate inner choroidopathy (PIC). Although it is perfectly reasonable to describe any multifocal inflammatory choroidal disease as MFC, if the disease does not fit this description, it should be made clear that it is distinct from this syndrome.<sup>9</sup>

There are numerous diseases characterized by multifocal choroidal inflammation. Although some are truly distinct disease entities, with recognized pathogenesis, a number of these, listed below, simply refer to the syndrome idiopathic MFC or its sequelae. There is no evidence to support them as separate entities: their clinical course is similar, the treatments are identical, and all are idiopathic. Usage of these terms should therefore be discouraged—these diseases should be included under the single diagnosis idiopathic MFC unless there is evidence to support a distinct disease entity (which at present there is not).

### Diagnostic Terms That Overlap or Duplicate Idiopathic MFC and Should be Reconsidered or Abandoned

1. Punctate inner choroidopathy—as originally described, referred to a group of patients with symptomatic inflammation and choroidal lesions, usually small (but not always), in the absence of other signs of ocular inflammation. These lesions were said to evolve to resemble POHS lesions but serologic tests for *Histoplasma capsulatum* were negative.<sup>10</sup> This description is identical to that of the present day idiopathic MFC. It should be emphasized that the present authors regard PIC and MFC to be the same disorder. For some reason, however, usage of the term PIC has narrowed over the past 25 years to describe predominantly eyes with smaller lesions clustered at the posterior pole.<sup>11</sup> The original broader definition is preferred and supported by a recent United Kingdom–based article, in which the authors were unable to observe any differences between eyes/patients with smaller lesions and those with larger lesions.<sup>1</sup> The terms typical PIC and atypical PIC were used in the article by Essex et al<sup>1</sup> for analysis only, and these terms should not enter the vernacular.
2. Pseudo-POHS—Callanan and Gass<sup>12</sup> used this term to describe the clinical entity that looks like POHS, but in a patient from a non-*Histoplasma*-endemic region. This is MFC as described above.

**Fig. 1.** Examples of the spectrum of fundus lesions in idiopathic MFC (reproduced with permission from Essex et al<sup>1</sup>).



- This term is not in widespread use, and the use of a term that starts with “pseudo-presumed...” is not ideal.
3. Multifocal inner choroiditis<sup>13,14</sup>—This has been used by investigators to describe two different entities. Krill et al<sup>13</sup> used it to describe a group of POHS-like eyes with fundal lesions, choroidal neovascular membrane, and no vitritis. Ninety percent had a positive histoplasmin skin test. This is POHS. Scheider<sup>14</sup> used the term to describe a diverse group of patients: one with vitritis, two with confirmed POHS, and others with fundal lesions consistent with idiopathic MFC. Because of the duplication in nomenclature the term MIC introduces, it is the preference of the authors that this term not be used.
  4. Recurrent multifocal choroiditis—Morgan and Schatz<sup>6</sup> proposed this term be used to describe eyes with PIC, multifocal choroiditis with panuveitis (MFCPU), and MFC with progressive subretinal fibrosis. The term has not been widely adopted. All these disease entities fall under the present definition of idiopathic MFC.
  5. Multifocal choroidopathy<sup>15</sup>—This term is proposed as an umbrella term used to describe MFC/POHS-like eyes regardless of *Histoplasma* exposure. Although there are phenotypic similarities between these disorders, they are generally accepted to be distinct entities. It is not desirable to group them under a single diagnosis.
  6. Multifocal choroiditis with panuveitis—This term is commonly used and originally defined by Dreyer and Gass.<sup>7</sup> Refers to eyes with choroidal lesions, vitreous cells, and often anterior chamber cells. The disease has a tendency to recur. One case with PIC in the original article by Watzke et al<sup>10</sup> had anterior chamber cells and that case could also be classified as MFCPU. Some clinicians prefer to distinguish between idiopathic MFC patients with and without panuveitis. It is, however, the view of the authors that

- this is a spectrum of the same disease—individuals may have inflammation at some times and not others—and we do not subdivide idiopathic MFC by the presence or absence of panuveitis, preferring the single term idiopathic MFC to describe the disease spectrum.<sup>7,16,17</sup> Kedhar et al<sup>18</sup>, however, retrospectively reviewed a group of patients with PIC and MFCPU and found that eyes with previous panuveitis could be differentiated based on ocular phenotype alone. Not included in this series were eyes diagnosed with POHS—it is likely that if such eyes were included, picking eyes with previous panuveitis based on fundal features alone would have been less reliable. Indeed, diagnostic accuracy was lower (although still good) in a similar masked study by Parnell et al<sup>19</sup> comparing POHS with MFCPU. Important to note is the fact that eyes with PIC and MFC were regarded as having the same disease in this series.
7. Disseminated inner choroiditis<sup>20</sup>—This has been referred to POHS-like eyes in a French population with no known *Histoplasma* exposure. One was observed to develop new lesions. Term not in common use. These eyes would today be diagnosed as idiopathic MFC.
  8. Progressive subretinal fibrosis<sup>5,21</sup>—Choroidal lesions variably associated with vitreous or anterior chamber cells and associated with prominent subretinal fibrosis, often bridging between the lesions (as also noted by Doran and Hamilton<sup>22</sup>). Idiopathic MFC is often associated with choroidal neovascularization, which should be regarded as a complication of the disease. It is likely that progressive subretinal fibrosis represents an aggressive form of this process and is not a separate clinical entity.
  9. Hemorrhagic maculopathy (macular choroidopathy) in young adults<sup>23–26</sup>—Describes CNVM in eyes with POHS-like lesions in continental Europe. Term seldom appears in the English language

literature. This disease entity is likely idiopathic MFC complicated by choroidal neovascularization.

The above list is by no means exhaustive, and there are other terms in the literature (e.g., shiny multifocal chorioretinitis, peripheral multifocal chorioretinitis) that may also represent idiopathic MFC.<sup>27,28</sup> It is also likely that idiopathic CNVM is often caused by early or unrecognized idiopathic MFC.<sup>29</sup>

Special mention must be made of POHS. Although phenotypically identical to many cases of PIC/MFC, it appears that the form of multifocal choroidal inflammation in *Histoplasma*-endemic areas of the United States, and labeled POHS, is a distinct entity—it tends to affect men and women equally, is not significantly associated with myopia, presents a little later in life, and seldom (if ever) is associated with recurrent episodes of choroiditis.<sup>30</sup> The term POHS should be reserved for this clinical presentation and not the phenotypically identical form seen in other non-*Histoplasma*-endemic regions of the world.<sup>4,15,23,31–33</sup> It is emphasized that “presumed” should remain in the acronym as the evidence for present or past *Histoplasma* infection of the choroid is scant.<sup>34–36</sup>

In summary, multifocal choroidal lesions can be caused by MFC (with or without panuveitis), POHS, or indeed by other infectious choroiditides or recognized syndromes of idiopathic/autoimmune uveitis. It is hoped that this brief review will help put in their proper place some of these overlapping and at times confusing terms.

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