***Original Article***

# Comparison on Clinical Characteristics of Multifocal Choroiditis and Punctate Inner Choroidopathy

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**Abstract**

**Purpose**: To compare the differences in the clinical characteristics of multifocal choroiditis (MFC) and punctate inner choriodopathy (PIC).

**Methods**: A cross-sectional study, consisting of 22 cases (37 eyes) with MFC and 11 cases (18 eyes) with PIC, was carried out. Multiple indexes were measured and analysed to compare the differences in clinical characteristics of the subjects between two groups, including BCVA, avergae age, sex composition, presence of intraocular inflammation, choroidal neovascularization (CNV), and intraocular inflammation complications, such as cataract, cystoid macular edema (CME) and epiretinal membrane (ERM).

**Results**: The avergae age of the MFC and PIC patients were (48.1±13.9) years and (32.1±10.2) years with a significant difference ($P$=0.043). CNV occurred more frequently in patients with PIC (PIC, 55.6%; MFC, 21.6%; $P$=0.016) compared with those with MFC.MFC patients had a higher frequency of intraocular inflammation complications, such as, cataract (27.0%), CME (35.1%), ERM (5.4%). PIC patients presented none of these complications. MFC subjects presented with more visual impairments than PIC patients. Totally 51.4% of MFC patients had visual impairments and 22.2% of PIC patients had BCVA < 0.3 ($P$=0.047).

**Conclusion**: Both MFC and PIC are categorized into the umbrella term of "white spot syndromes". Although sharing similar ocular expressions, they present with different clinical characteristics. Patients with PIC had a higher frequency of CNV but a lower frequency of structural complications caused by intraocular inflammation and lower frequency of visual impairments compared with MFC counterparts. (***Eye Science 2011; 26: 161-165***)

**Keywords**: multifocal choroiditis; punctate inner choriodopathy; choroidal neovascularization; choroiditis; uveitis; clinical characteristics

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Both multifocal choroiditis (MFC) and punctate inner choriodopathy (PIC) are under the umbrella term of "white spot syndromes", which is a category of non-infectious uveitis rarely reported in domestic documents. Although MFC and PIC have different clinical characteristics, they share similar ocular expressions, which commonly cause misdiagnosis in clinical setting.

## Materials and methods

A cross-sectional study involving 22 MFC cases (37 eyes) and 11 PIC cases (18 eyes) was performed. All cases were diagnosed at Ophthalmology Out-patient Department of Ningbo Lihuili Hospital between October 2006 and December 2010. MFC diagnosis was made on the basis of the characteristic retinal morphology of multiple, punched-out, atrophic lesions, with or without pigmentation located in the posterior and midperipheral retina[1], as well as the anterior and/or vitreous inflammation[2]. Fundus examination of PIC subjects revealed multiple (12 to 25), small (approximately 100 to 300 μm in diameter), gray or yellow lesions at the level of RPE and inner choroid, scattered throughout the posterior pole[3,4]. No sign of inflammation was noted in eyes. All patients were absent from systemic diseases associated with choroiditis and were not exposed to Histoplasma-endemic regions across the globe. Eyes with pathologic myopia were excluded from this study.Ophthalmologic examinations included BCVA, intraocular pressure, spherical equivalent refraction, slit-lamp findings, dilated fundus examination, fundus color photographs, fundus fluorescence angiography (FA), and indocyanine green angiography (ICGA). The number of all lesions was counted, and the size of lesion was measured on fundus color photographs (refer to the diameter of optic disc

as 1500 μm). Cystoid macular edema (CME) was defined as the presence of macular thickening with or without cyst formation as shown by clinical examination or by the presence of leakage observed on FA. Epiretinal membrane(ERM) was diagnosed based on typical features by fundus examination, such as wrinkles of fibrotic membrane and sharpening of macular vessel corkscrew. CNV was diagnosed by the presence of typical hyperfluorescence on FA. Cataract was defined as the presence of 1+ nuclear sclerosis, 1+ cortical change or trace posterior subcapsular changes shown by clinical examination. Papilloedema was diagnosed by burring margin of the optic disc. FA showed leakage of dye at late phase. Ocular hypertension was defined as an intraocular pressure ≥22 mmHg without previous history of hypertension and without hypertension in following eye. Chest X-ray, PPD test, serologic testing for syphilis, antibody to toxoplasma and E-B virus were performed to rule out the possibilities of sarcoidosis, syphilis, tuberculosis, toxoplasmosis, which can cause posterior uveitis with chorioretinal lesions.

**Statistical analysis**

All data in this study were statistically analysed by using SPSS13 software.

## Results

The average age of MFC patients was 41.8±13.9 years (ranged from 14 to 70 years), 16 females (72.7%) were affected and 15 cases (68.2%) were bilaterally affected in MFC subjects. Average age of PIC patients was (32.1±10.2) years (ranged from 18 to 53 years), 8 females (72.7%) were affected and 7 cases (63.6%) had bilateral diseasse in PIC group. PIC team was younger than MFC in average age of patients($P$<0.05). Both MFC and PIC tend to affect young healthy women, most of patients had bilateral diseases. Most patients in two groups were myopia, the average was (−5.98±2.00)D in MFC group (ranged from-1.25D to -12.0D), compared with (−3.32±2.40) D in PIC group (ranged from +1.00D to -8.00D) ($P$ <0.001). MFC lesions measured 300-1000 μm in diameter, while PIC mainly ranged between 50 to 280 μm in diameter. Two types of lesions were intermingled and were enlarged as disease progressed. Either MFC or PIC lesions developed into chorioretinal scars with sharp margins in acute phase, with or without pigmentation (Figures 1a, 2a, 2b). Twenty cases (23 eyes) in MFC group involved anterior and/or vitreous inflammation. Among the MFC patients who were absent of active intraocular inflammation, 6 cases (6 eyes) had a history of intraocular inflammation. However, no patients with PIC had active intraocular inflammation ($P$<0.001). Ten eyes(27.0%) with MFC had cataract, 13 eyes (35.1%) were affected by CME, 2 eyes (5.4%) showed ERM, 2 eyes (5.4%) had papilloedema. No PIC patients had cataract, CME, ERM or papilloedema. Patients with PIC were more likely to have CNV than those with MFC. Eight eyes (21.6%) with MFC had CNV while 10 eyes (55.6%) with PIC had CNV ($P$ =0.016). Three eyes with MFC presented with ocular hypertension. All PIC subjects showed normal IOP. MFC patients had more severe decline in visual acuity than PIC counterparts. In MFC group, BCVA≤0.3 in 16 cases (72.7%), 19 eyes (51.4%) and 6 cases(27.3%) 6 eyes(16.2%) with BCVA≤0.1, and 3 cases(13.6%) with bilateral BCVA≤0.3, and no patients with bilateral BCVA ≤0.1. In PIC group, 4 cases (36.4%)4 eyes (22.2%) with BCVA ≤0.3, 1 case (9.09%) 1 eye (5.56%) with BCVA ≤0.1, and no one with bilateral BCVA ≤0.3.Among those eyes with BCVA ≤0.3, all had CNV in PIC group, while 8 eyes(42.1%)had CNV in MFC group, while cataract (4 eyes), CME (5 eyes), ERM(1 eye) and papilloedema (2 eyes), 12 eyes with anterior and/or vitreous inflammation (Tables 1, 2). Thus, it can be concluded that CNV is the major factor resulting in poor visual acuity in PIC patients. However, most complications secondary to the intraocular inflammation negatively affect the visual acuity of MFC patients.

PIC and MFC shared similar results in FA and ICGA. The leakage of dye was observed in active inflammatory foci during fluorescein angiography, caused by damages to the blood-retina barrier. Scarred foci appearred as sharply margined hyperfluorescent areas without leakage of dye (Figures 1b, 2c).CNV was found by evident leakage from the vascular membrane (Figures 1d,2d). ICG angiography was able to explicitly display the areas of poor blood flow in the choriocapillaris (Figures 1c,2f),

**Table 1** Patient-specific characteristics in MFC and PIC

| Characteristics | MFC($n$=22) | PIC($n$=11) | $P$ |
|---|---|---|---|
| Average ages, year (range) | 41.8±13.39 | 32.1±10.2 | 0.043 |
| Sex, % | | | |
| Female | 72.7 | 72.7 | 1.000 |
| Male | 27.3 | 27.3 | |
| Cylinder power | −5.98±2.00D | −3.32±2.40D | <0.001 |
| BCVA, %, | | | |
| One eye ≤0.1 | 16.2 | 5.5 | 0.406 |
| One eye ≤0.3 | 51.4 | 22.2 | 0.047 |
| Bilateral eyes≤0.3 | 13.6 | 0 | 0.53 |

**Table 2** Eye-specific characteristics at presentation in MFC and PIC

| Characteristics | MFC($n$=37) | PIC($n$=18) | $P$ |
|---|---|---|---|
| Active inflammation, % | 62.2 | 0 | <0.001 |
| Cataract, % | 27.0 | 0 | 0.021 |
| CME, % | 35.1 | 0 | 0.005 |
| ERM, % | 5.4 | 0 | 1.000 |
| Papilloedema, % | 5.4 | 0 | 1.000 |
| Ocular hypertension, % | 8.1 | 0 | 0.543 |
| CNV, % | 21.6 | 55.6 | 0.016 |

whereas the localized hyperfluorescence indicated the vasculitis and leakage of dye from choriocapillaris (Figure1e). Most MFC patients had intraocular inflammation, therefore, inflammatory signs, including dye leakage from optic disc and retinal vessels (Figure 2e), dye-staining of ERM and macular multiple cysts that filled with dye, were observed in FA.

## Discussion

Nozia and Dorsch[5] first reported an unprecedent chorioretinopathy associated with anterior uveitis in 1973.-Until 1984, Dreyer and Gass[6] named this disease as "multifocal choroiditis with panuveitis (MCP)". In the same year, Watzke et al[7] reported a syndrome in young women characterized as small, yellow-gray chorioretinal scars without signs of uveitis, and nominated the syndrome as "punctate inner choriodopathy (PIC)"

Our study summarized the similarities between MFC and PIC as below: (1) both MFC and PIC are non-infectious uveitis with unknown etiology, and mainly affect healthy young women with myopia and manifested by a high frequency of bilateral involvement[8,9]. (2) MFC and PIC show similar retinal morphology, and both of two diseases are characterized

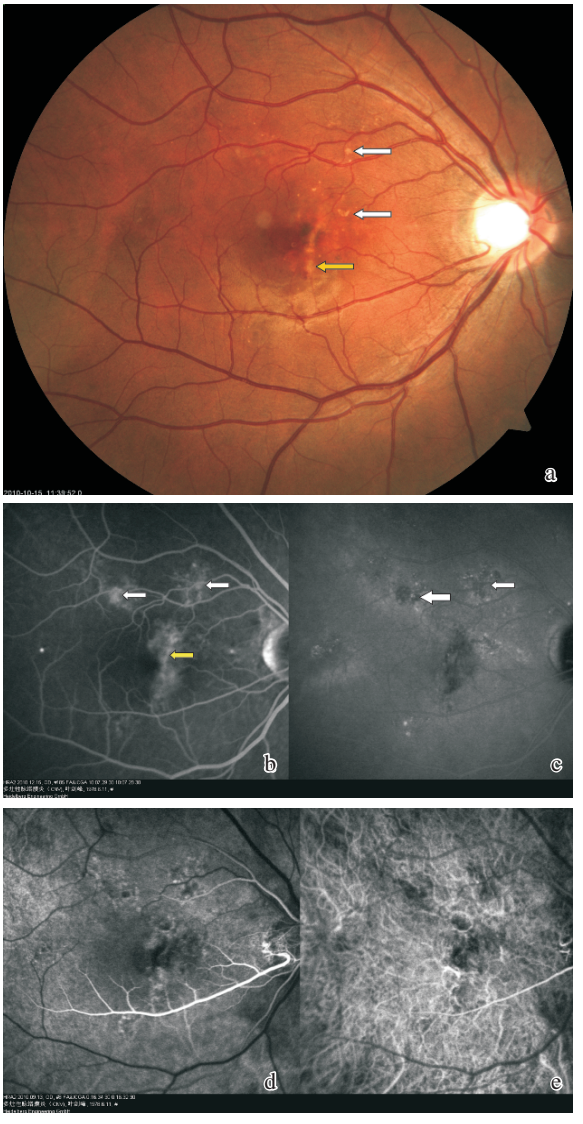


**Figure 1** (a) Fundus color photography of a 34-year old female PIC patient. Multiple, samll, yellow chorioretinal lesions in macula, typically 100–300 μm in size(white arrows). A gray subretinal fibrosis is seen juxtafoveal (yellow arrow). (b) In the early phase of FA, the PIC lesions can have a variable fluorescence pattern. In the scarred and healed lesions the choriocapillaris is damaged, there is hypofluorescence (hollow white arrows). While purely RPE atrophy there is window defect with hyperfluorescence (white arrows). Irregular hyperfluorescence is seen at the site of CNV (yellow arrow) (c) In the early phase of ICGA, clearly shows the areas of poor blood flow in the choriocapillaris. In the area of the lesions there is hypofluorescence (white arrows). (d)In the late phase of FA, there is staining of the lesions, making them appear hyperfluorescent (white arrows). Mild leakage of dye from CNV(yellow arrow). (e) In the late phase of ICGA, hypofluorescence still can be seen in the site of atrophic choriocapillaris, around the hypofluorescence, there are hyperfluorescence areas associated with the localized vasculitis of choriocapillaris (white arrows).

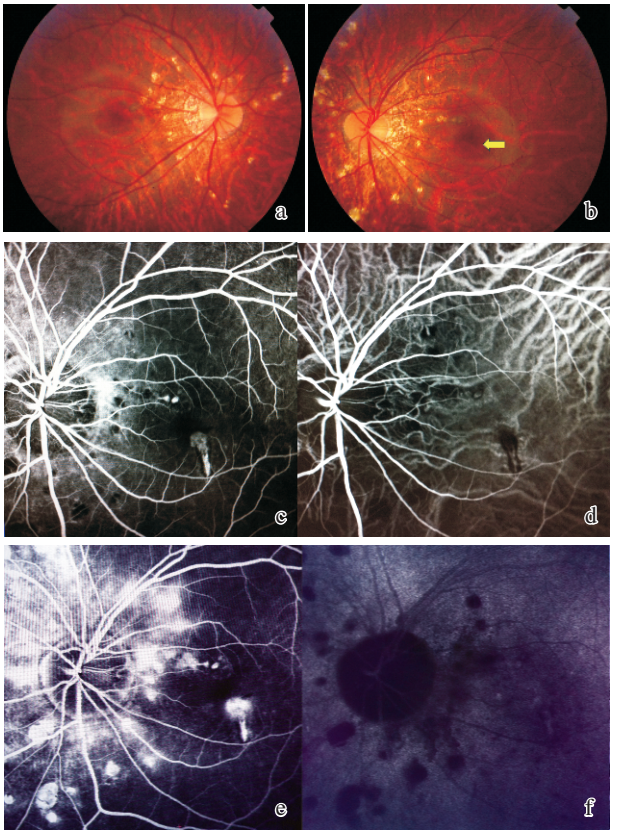


**Figure 2** (a) (b)Fundus color photographies of a 24-year old male MFC patient, bilateral eyes areaffected, CNV can be seen inferior to fovea (yellow arrow). (c) In the early phase of FA, the the scarred lesions display hypofluorescence (white arrows), active lesions with hyperfluorescence leakaging from injured blood-renital barrier (white arrows hollow). Irregular hyperfluorescence is seen at the site of CNV (yellow arrow). (d、f) Obvious hypofluorescence (white arrows) in the early and late phase of ICGA, corresponded to the localized choroidal hypoperfusion. (e) In the late fhase of FA, demostrates multiple small ares of hyperfluorescence due to stain of MFC lesions (white arrow), leakage from an active CNV is detected (yellow arrow), mild leakage and stain from retinal vessel walls is the evidence of intraocular inflammation.

by small, yellow-white, retinal pigment epithelial and choriodal lesions in the posterior pole that lead to pigment chorioretinal scars in acute phase. However, MFC and PIC may have distinguishable characteristics as follows: (1) Ages of MFC patients are generally older than those of PIC. (2) MFC typically affects women with high myopia while PIC often attacks women with moderate and low myopia. (3) MFC and PIC vary in terms of distribution and size of lesions. MFC lesions are mainly locate in macula and around optic disc, while PIC lesions are noted mainly in macula. MFC spots measure 300-1000 μm in diameter compared 100–300 μm of PIC spots (Figures 1a, 2a). Some investigators consider that when lesions with greater than 300 μm in diameter were observed on a fundus photograph, the case could be diagnosed as MFC even in the absence of intraocular inflammation[8,9]. (4) Previous studies suggest that both MFC and PIC associate with a high incidence of CNV, as high as 32 to 46%[10,11] for MFC cases and 27–40%[7,10] for PIC patients. In our study, PIC patients presented a higher frequency of CNV (55.6%) than MFC (21.6%), which may be related to the racial differences. Most subjects enrolled in foreign researches were Caucasians, while all participants in this investigation were Mongoloids. Furthermore, selection bias may affect the outcomes to some degree. PIC patients without CNV have good visual acuity, so it is possible that those patients will not go to hospital until CNV and poor vision occur. Therefore, PIC patients with CNV might be more likely to be admitted to our hospital compared with those without CNV. (5) Most MPC patients present signs of intraocular inflammation such as aqueous flare, keratic precipiate, iris conglutination, vitreous inflammatory cells, while PIC patients are absent of similar complications. (6) Visual acuity is more severely impaired in MFC patients than PIC subjects. (7) The vision loss between two groups ascribes to different factors. CNV is the dominant factor causing visual impairment in PIC patients, and all PIC with BCVA≤0.3 have been involved in CNV. However, intraocular inflammation and related complications mainly cause a decline in visual acuity of MFC patients, and only 42.1% of those cases with BCVA≤0.3 are complicated with CNV. (8) PIC and MFC share similarities in both FA and ICGA. It is difficult to distinguish PIC and MFC by the angiographic photographs alone. However, for MFC patients, increased retinal vascular permeability appearring in course of FA can be considered as an evidence of intraocular inflammation.

Although both MFC and PIC have been reported in clinical practice, misdiagnosis rate is 72% in MFC patients and even 87% in PIC subjects. Most cases

were misdiagnosed as pathological myopia, AMD and idiopathic CNV. In spite of the distinct clinical characteristics presented by MFC and PIC, it is debatable if PIC is belongs to a subtype of MFC or they are two independent diseases among physicians. Hiroyuki Shimada et al studied the pathological findings of CNV surgically resected from MFC or PIC eyes. CD20-positive B lymphocytes were found in CNV from MCF eyes with intraocular inflammation, while no trace of B lymphocytes infiltraiton was noted in PIC eye. However, no differences were observed in histopathological findings between MFC eyes without intraocular inflammation and PIC eyes[12].

Our study suggested that MFC and PIC have similar ocular expressions, but they have significantly different clinical characteristics regarding ages of onset, refractive status, spots morphology, intraocular inflammation, complications and vision loss. It is beneficial for clinical diagnosis and differential diagnosis of these two diseases. In order to determine whether MFC and PIC share the same etiology and pathogenesis, more intensive investigations should be conducted.

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