Features of retinal arterial macroaneurysms in patients with uveitis

E Yamanaka, N Ohguro, A Kubota, S Yamamoto, Y Nakagawa, Y Tano

Aim: To determine the frequency and clinical characteristics of retinal arterial macroaneurysms in patients with uveitis.

Methods: A retrospective review of the clinical, photographic, and angiographic records of 1007 patients with uveitis, examined at the Osaka University Hospital uveitis clinic between January 1995 and April 2002, was performed. All of the records were examined to determine whether macroaneurysms were present, and when present, to determine the laterality, type, location, clinical course, and the presence of associated systemic and ocular diseases.

Results: Of the 1007 patients with uveitis, only 14 (1.4%) had macroaneurysms. 12 of these 14 patients had peripheral multifocal chorioretinitis (PMC), and five of these 12 were diagnosed with sarcoidosis and the other seven without sarcoidosis. There was only one case with sarcoidosis without PMC, and the remaining case was uveitis of unknown origin. There were 18 macroaneurysms in all cases and 17 (94.4%) were the exudative type, and the remaining one was the haemorrhagic type. Two patients had been treated for systemic hypertension but the others had no signs of systemic hypertension or cardiovascular disease.

Conclusions: Macroaneurysms are not characteristically found in patients with uveitis, but the majority are found in patients with PMC. The majority of the macroaneurysms were the exudative type, and the conclusion is that patients with PMC should be carefully examined for exudative macroaneurysms.

A}rtial retinal macroaneurysms are fusiform or round dilations of the retinal arterioles that occur in the posterior fundus within the first three orders of arterial bifurcation.1 The supratemporal artery is the most common site, and the macroaneurysms can result in visual impairment.2 The most common clinical symptom of arterial retinal macroaneurysms is a decline in central visual acuity from the posterior fundus within the first three orders of arterial bifurcation.1 The supratemporal artery is the most common site, and the macroaneurysms can result in visual impairment.2 The most common clinical symptom of arterial retinal macroaneurysms is a decline in central visual acuity from the posterior fundus within the first three orders of arterial bifurcation.1 The supratemporal artery is the most common site, and the macroaneurysms can result in visual impairment.2 The most common clinical symptom of arterial retinal macroaneurysms is a decline in central visual acuity from the 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PATIENTS AND METHODS

We reviewed the clinical and photographic records of 1007 patients (average age 40.6 years; range 3–89 years) with uveitis who were seen at the Osaka University Hospital uveitis clinic between January 1995 and April 2002. All patients were examined by NO, SY, or YN, and the clinical and photographic records were reviewed independently by EY and AK after April 2002.

All patients had undergone a standard complete ophthalmologic examination, and 897 patients had fluorescein angiography at least once. Fluorescein angiograms were not only of the macula area but also from as far peripheral as possible. The patients who did not undergo fluorescein angiography were those diagnosed with anterior uveitis, and their fundi were normal by funduscopic examinations.

Macroaneurysms were defined as saccular or fusiform dilations of the retinal arterioles located at the bifurcations or arteriovenous crossings measuring 200 μm or more and located within the first three orders of arterial bifurcation.1 We recorded the laterality, type, location, clinical course, and the presence of associated systemic and ocular diseases for all macroaneurysms. The average duration of follow up of all patients was 48 months (range 1–106 months), and that of patients with macroaneurysms was 33.8 months (range 3–96 months).

All patients had undergone standard laboratory screening tests to evaluate the possible cause of the uveitis. Patients diagnosed with PMC fulfilled all of the following criteria:

Abbreviations: BHL, bilateral hilar lymphadenopathy; PMC, peripheral multifocal chorioretinitis
Retinal arterial macroaneurysms associated with uveitis

Of the 1007 patients, 139 fulfilled the diagnostic criteria for PMC, of which 46 (33.1%) had extraocular findings diagnostic of sarcoidosis. Of the 1007 patients, 139 fulfilled the diagnostic criteria for PMC, of which 46 (33.1%) had extraocular findings diagnostic of sarcoidosis. The diagnoses of the entire series are listed in table 1.

Of the 1007 patients with uveitis, 68 were diagnosed as having sarcoidosis uveitis; 18 had histologically confirmed sarcoidosis and 50 had radiologically confirmed sarcoidosis (hilar adenopathy). Among the 68, 46 (67.6%) had PMC and 22 (32.3%) did not have PMC.

The average age of patients with sarcoidosis was 47.7 years (range 24–84 years), and that of patients with PMC was 55.3 years (range 29–83 years).

Of the 1007 patients, 14 patients (1.39%; 10 women and four men with an average age of 60.7 years; range 47–82 years) had macroaneurysms; 12 were diagnosed with PMC, one without PMC, and one of uveitis of unknown origin. Of these 12 patients with PMC, five were also diagnosed with sarcoidosis and the other seven without sarcoidosis. The clinical characteristics of patients with macroaneurysms are presented in table 2.

The macroaneurysms were unilateral in 12 patients and bilateral in two patients for a total of 16 eyes with macroaneurysms. One eye had three macroaneurysms while the other eye had one for a total of 18 macroaneurysms. All but one (17 of 18, 94.4%) were exudative macroaneurysms, and the remaining one was a haemorrhagic type. Seven of the macroaneurysms were in the superotemporal artery, five in the macular artery, three in the inferotemporal artery, two in the inferonasal artery, and one in the superonasal artery. Five macroaneurysms were symptomatic and caused visual loss. Spontaneous regression occurred in 10 macroaneurysms, while in seven exudative macroaneurysms lipid exudates from the macroaneurysms threatened the fovea and laser photocoagulation was performed. The typical appearance of a retinal arterial macroaneurysm in a case of PMC with sarcoidosis uveitis is shown in figure 1.

Among the 14 patients with macroaneurysms, two patients had been treated for systemic hypertension but none had other cardiovascular diseases. Others had no signs of systemic hypertension or cardiovascular disease.

DISCUSSION

Our results confirmed the high association of macroaneurysms with PMC (12 of 14 cases), and this high incidence was not seen in uveitis in general. We also found a significant association between PMC and sarcoidosis as previously reported.

### Table 1 Diagnosis of uveitis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behcet’s disease</td>
<td>98</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>68</td>
</tr>
<tr>
<td>Vogt-Koyanagi-Harada disease</td>
<td>64</td>
</tr>
<tr>
<td>Bacterial uveitis*</td>
<td>25</td>
</tr>
<tr>
<td>Fungal uveitis†</td>
<td>23</td>
</tr>
<tr>
<td>Cytomegalovirus retinitis</td>
<td>21</td>
</tr>
<tr>
<td>Eales’ disease</td>
<td>18</td>
</tr>
<tr>
<td>Acute retinal necrosis</td>
<td>12</td>
</tr>
<tr>
<td>Toxocariasis</td>
<td>11</td>
</tr>
<tr>
<td>Other specific uveitis entities</td>
<td>72</td>
</tr>
</tbody>
</table>

*Uveitis caused by bacterial infection. Endogenous metastatic bacterial endophthalmitis is included, but exogenous bacterial infections are excluded.
†Endogenous fungal endophthalmitis.
‡Those that did not fulfill any distinct clinical diagnosis criteria. 110 cases of anterior uveitis and 93 cases of peripheral multifocal chorioretinitis (PMC) are included here.

### Table 2 Clinical characteristics of patients with macroaneurysms

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Laterality</th>
<th>Type</th>
<th>Hypertension/ cardiovascular disease</th>
<th>Clinical course/treatment</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>62</td>
<td>Sarcoidosis with PMC (BHL)</td>
<td>RE</td>
<td>Exudative</td>
<td>no</td>
<td>PC†</td>
<td>M*</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>49</td>
<td>Sarcoidosis without PMC (BHL)</td>
<td>LE</td>
<td>Exudative</td>
<td>no</td>
<td>PC</td>
<td>PC</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>55</td>
<td>Sarcoidosis with PMC (BHL)</td>
<td>LE</td>
<td>Exudative</td>
<td>no</td>
<td>SR†</td>
<td>S-T</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>56</td>
<td>Sarcoidosis with PMC (BHL)</td>
<td>LE</td>
<td>Exudative</td>
<td>no</td>
<td>SR</td>
<td>S-T</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>65</td>
<td>Sarcoidosis with PMC (BHL)</td>
<td>LE</td>
<td>Exudative</td>
<td>Hypertension</td>
<td>PC</td>
<td>I-T†</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>62</td>
<td>Sarcoidosis with PMC (BHL)</td>
<td>LE</td>
<td>Exudative</td>
<td>no</td>
<td>SR</td>
<td>S-T</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>59</td>
<td>PMC†</td>
<td>LE</td>
<td>Exudative</td>
<td>no</td>
<td>PC</td>
<td>S-T</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>82</td>
<td>PMC</td>
<td>LE</td>
<td>Hemorrhagic</td>
<td>no</td>
<td>PC</td>
<td>S-N†</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>54</td>
<td>PMC</td>
<td>LE</td>
<td>Exudative</td>
<td>no</td>
<td>PC</td>
<td>S-T</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>64</td>
<td>PMC</td>
<td>LE</td>
<td>Exudative</td>
<td>no</td>
<td>SR†</td>
<td>I-N†</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>70</td>
<td>PMC</td>
<td>LE</td>
<td>Exudative</td>
<td>Hypertension</td>
<td>SR</td>
<td>M</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>71</td>
<td>PMC</td>
<td>LE</td>
<td>Exudative</td>
<td>no</td>
<td>SR</td>
<td>S-T</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>54</td>
<td>PMC</td>
<td>LE</td>
<td>Exudative</td>
<td>no</td>
<td>SR</td>
<td>I-T†</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>47</td>
<td>Unknown aetiology</td>
<td>LE</td>
<td>Exudative</td>
<td>no</td>
<td>PC</td>
<td>M</td>
</tr>
</tbody>
</table>

Interestingly, all but one macroaneurysm (17 of 18) was the exudative type. The largest study of arterial macroaneurysms consisted of 40 patients, and the authors reported that haemorrhagic macroaneurysms were the major type, and hypertension and systemic vascular disease were prominent features. In contrast, all but one of the macroaneurysms in our patients were the exudative type. This particularly high incidence of exudative macroaneurysms is a distinctive characteristic of macroaneurysms in patients with PMC.

The high systolic blood pressures in patients with haemorrhagic macroaneurysms may have led to the vascular haemorrhages because of the increased transmural tension and greater pulsation amplitude. In comparison, the vascular damage due to inflammations and chronic vasculopathy may have led to the formation of macroaneurysm in the PMC cases, and a leakage through weak vascular walls may have contributed to the exudative process. However, the very high incidence of exudative macroaneurysms in cases of PMC, and not in uveitis in general, needs further explanation.

Previous studies have shown that retinal branch vein occlusions were frequently associated with macroaneurysms, and they were commonly associated with non-haemorrhagic macroaneurysms. As in sarcoidosis uveitis, PMC is also frequently associated with vasculitis, and more specifically, periphlebitis. While periphlebitis usually does not induce significant vascular occlusions, it occasionally causes occlusive retinal vascular disease, which may contribute to the macroaneurysm formation. A better understanding of the development of retinal macroaneurysms in PMC will require a more intensive observation, especially in relation to the region and the severity of inflammation including periphlebitis and the location of the macroaneurysm during the clinical course of PMC.

Although the exact incidence of retinal macroaneurysms in cases of systemic hypertension or cardiovascular disease has not been reported, more than 60% of patients with macroaneurysms have been reported to have hypertension. Of our 14 uveitic patients with macroaneurysms, only two patients (14.3%) had been treated for systemic hypertension and the others had no signs of systemic hypertension or cardiovascular disease. This indicates that PMC itself may have had a role in the formation of the macroaneurysms in our patients. However, not all of our uveitic patients in this study were followed regularly throughout the 7 year period of review, and some macroaneurysms might have spontaneously regressed before the time of a follow up examination. In addition, the presence or absence of systemic hypertension and cardiovascular diseases was determined by patient report and unidentified hypertension and cardiovascular disease could not be ruled out in our study.

We must also consider the ageing process as an important factor in macroaneurysm formation in PMC, because patients with PMC were older than patients with other uveitis. Moreover, because we did not perform fluorescein angiography on patients with anterior uveitis, there was a possibility that we missed some macroaneurysms in these cases. Therefore, a prospective, long term, and precise observation of both the systemic and ophthalmological conditions of a larger number of cases will be necessary to confirm our finding of the high incidence of macroaneurysms in cases of PMC, and not in uveitis in general.

Although the mechanism of macroaneurysm formation in PMC still remains unclear, our observations demonstrated that patients with PMC should be carefully examined for exudative retinal macroaneurysms.

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