Idiopathic Polypoidal Choroidal Vasculopathy in Japanese Patients

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Objective: To describe the vascular nature and clinical features of idiopathic polypoidal choroidal vasculopathy in Japanese patients.

Methods: Patients thought to have idiopathic polypoidal choroidal vasculopathy were examined with binocular ophthalmoscopy, slitlamp biomicroscopy with a contact lens, fluorescein angiography, and indocyanine green angiography.

Results: From January 1993 to December 1997, 35 eyes in 32 patients were diagnosed as having idiopathic polypoidal choroidal vasculopathy. Men were predominantly affected (22 patients [69%]). Most patients were unilaterally involved (29 patients [91%]) and elderly, with a mean age of 65.7 years (range, 44-82 years). Ocular manifestations were relatively mild, with serous or hemorrhagic detachments of the retinal pigment epithelium and neurosensory retina in the posterior pole. Most patients had a favorable course, although some experienced recurrence, and a few eyes developed disciform scarring. In all patients, indocyanine green angiograms demonstrated branching vascular networks with polypoidal dilations at terminals of the network beneath the retinal pigment epithelium. These lesions were mostly in the macula (33 eyes [94%]), with a few in the peripapillary area.

Conclusions: Idiopathic polypoidal choroidal vasculopathy in Japanese patients differs from that in American patients. It seems that this disorder occurs in elderly Japanese patients and should be treated as a distinct clinical entity. It is probably a peculiar form of choroidal neovascularization beneath the retinal pigment epithelium. We propose the term “polypoidal choroidal neovascularization” for this disorder.


AGE-RELATED macular degeneration (AMD) has been increasing in white and Japanese people and in other Asian people. When caring for patients with exudative AMD, demonstration of choroidal neovascularization (CNV) is essential. Fluorescein angiography, however, often does not reveal CNV under the retinal pigment epithelium (RPE). Indocyanine green (ICG) angiography, a recent development, detects occult vessels more clearly.

In 1990, Yannuzzi et al introduced a new clinical entity, “idiopathic polypoidal choroidal vasculopathy” (IPCV). Their paper described a peculiar form of vascular abnormality in the choroid in 11 patients who showed hemorrhagic or serous pigment epithelial detachment (PED) associated with hemorrhagic or serous detachment of the retina in the macular area. A similar disorder was also reported separately by Stern et al, Kleiner et al, and Perkovich et al.

In 1995, Spaide et al used ICG angiography to demonstrate aneurysmal and spheroidal vascular dilation of the choroidal vessels in patients with IPCV. They pointed out that this disorder predominantly affected female African Americans, was mostly located in the peripapillary area, seemed to be a novel choroidal vascular abnormality in the inner choroid, and should be differentiated from typical CNV. They later reported further experiences with this entity and expanded its clinical spectrum. Other more recent cases have also been reported.

The authors described polypoidal vascular lesions in the peripapillary area as well as the macula and periphery, and indicated that these lesions may be an unusual form of CNV—differentiated from typical CNV or AMD. They also noted that this disorder was more common in pigmented and Asian people. Using ICG angiography in elderly patients, Kitamura et al previously described a unique form of CNV that originally appeared as a racemose heman-
PATIENTS AND METHODS

We retrospectively evaluated ICG angiograms taken in our clinic in 3 years (January 1, 1993, to December 31, 1997). Criteria for inclusion were as follows: (1) examination by a physician (M.U. or K.T.) via routine eye examination, binocular indirect ophthalmoscopy, slitlamp biomicroscopy with a contact lens, fluorescein angiography, and ICG angiography; (2) exudative maculopathy; (3) clearly demonstrated evidence by ICG angiography of polyoidal dilations at terminals of the branching vascular networks from choroidal vasculatures in the posterior pole; and (4) diagnosis of IPCV made by ICG findings, indicated previously. As a result, AMD, angioid streaks, high myopia, presumed ocular histoplasmosis syndrome, and other similar abnormalities were excluded.

In addition to patients being older than 50 years, criteria for exudative AMD were the macula showing (1) serous and/or hemorrhagic detachment of the sensory retina; with or without serous and/or hemorrhagic PEDs; (2) serous PEDs with CNV; (3) subretinal fibrovascular membranes; (4) subretinal fibrous scarring; (5) evidence of CNV demonstrated via fluorescein and ICG angiography; and (6) no evidence of aneurysmal dilations at terminals of branching vascular networks from choroidal circulation via ICG angiography.

Indocyanine green angiography was performed using a scanning laser ophthalmoscope (Rodenstock Co, Munich, Germany). Indocyanine green was given intravenously in 50 mg doses, and a double injection of this dose was given routinely 20 minutes after the initial injection. This double-injection method is useful in disclosing the precise localization of abnormal findings in relation to the retinal vessels and for polyoidal vascular lesions and branching vascular networks.

In some patients in this series, particularly the early ones, moderate intense laser photocoagulation was applied directly to the polyoidal dilated terminals and in a few eyes, to the feeder vessels using a dye and argon laser (Coherent Radiations Co, Palo Alto, Calif). Laser photocoagulation was applied in selected cases involving recurrence of subretinal hemorrhages and increased serous retinal detachment.

REPRESENTATIVE PATIENTS

Case 1: A 58-Year-Old Woman

This patient noticed blurring of vision and a central scotoma in her left eye 2 weeks before her visit. She had no previous history of eye problems and was generally healthy. Visual acuity in her left eye was 0.8 with correction. An ophthalmoscopic examination revealed a large hemorrhagic PED surrounded by a subretinal hemorrhage at the macula, temporoinferior to the fovea. Several reddish-orange, small nodular elevations of RPE were found nasosuperior to the fovea. No drusen were observed (Figure 1).

Fluorescein angiography demonstrated a hemorrhagic PED but no CNV. Nodular elevations of RPE showed nodular hyperfluorescences in the middle phase of fluorescein angiography. Indocyanine green angiography clearly demonstrated, in the very early phase, a branching vascular network nasosuperior to the fovea. At terminals of the branches, several polyoidal dilations of the vessels were seen (Figure 2).

During 1-year follow-up, hemorrhages in the PED and subretinal space gradually resolved, but degeneration of the RPE remained, and a flat serous minimal retinal detachment persisted at the macula. Thereafter, her retinal manifestation was stable. Visual acuity in the left eye improved to 1.0. However, the nodular elevations of RPE, nasosuperior to the fovea, persisted for 15 months (Figure 3). Indocyanine green angiography revealed polyoidal swellings of the vessels at terminals of the branching vascular network (Figure 4), almost identical to those from the Japanese; 22 (69%) were men and 10 (31%) were women. Their ages ranged from 44 to 82 years (average, 65.7 years). The affected eyes were unilateral in 29 patients (91%) and bilateral in 3 patients (9%), for a total of 35 eyes. In unilaterally affected patients, the right eye was affected in 13 patients and the left eye in 16. The systemic condition of all patients was healthy, except for mild chronic hypertension. None of the patients had an exceptional family history of retinal disease.

OCULAR MANIFESTATIONS

AT THE FIRST EXAMINATION

Subjective Symptoms

Thirty-one patients complained of a mild decrease in visual acuity, a central scotoma, or blurring of vision in affected eyes. Four eyes of 3 bilaterally affected patients were asymptomatic.

Visual Acuity

Eighteen eyes (51%) had relatively good visual acuity, but severe visual loss to less than 0.2 was noted in 6 eyes (17%) (Table 1).
first examination and corresponding to the nodular elevations of RPE. Findings in the right eye were not remarkable.

Case 2: A 58-Year-Old Man

This patient was generally healthy, and had no previous notable medical history. Two months before the initial examination, he noticed blurring of vision and a metamorphopsia in his left eye; visual acuity was 0.3 with correction. His left eye had a large hemorrhagic PED and a widespread subretinal hemorrhage in the macula. Several reddish-orange nodular elevations of RPE were seen temporosuperior to the fovea. There were no drusen (Figure 5).

Fluorescein angiography revealed a large PED; however, demonstration of CNV was not clear. Indocyanine green angiography demonstrated in the very early phase (15 seconds) a branching vascular network and a feeder artery (Figure 6, top). In the early phase (32 seconds), aneurysmal dilations at terminals of the branching network were demonstrated in the fovea (Figure 6, bottom). Findings in the right eye were not remarkable.

We performed laser photocoagulation for the feeder vessel and polypoidal lesions. After laser photocoagulation treatment, new dilated vessels were visible beneath the RPE at the fovea. Three months after photocoagulation treatment, a marked subretinal hemorrhage appeared in the macula, and thereafter, the subretinal hemorrhage was gradually resorbed. However, 3 months later, a massive vitreous hemorrhage occurred and then spontaneously resolved. The macula remained in a degenerative condition, and visual acuity was 0.02. Laser photocoagulation treatment for IPCV showed a worse outcome in this case.

Case 3: A 64-Year-Old Man

This patient was referred to us for a large disciform subretinal fibrovascular membrane at the macula in his left eye, similar to that seen in AMD. The patient had no problem in the right eye, which had a visual acuity of 1.2. Ophthalmoscopically, there were some small nodular orange elevations of the RPE around the fovea (Figure 7).

Fluorescein angiography revealed a branching vascular network and polypoidal swellings at the terminals (Figure 8). Indocyanine green angiography demonstrated a branching vascular network in the fovea and aneurysmal dilations at terminals of the branching in the early phase (90 seconds) (Figure 9, top). Polypoidal hypofluorescence was well demonstrated in the middle phase (Figure 9, bottom).

During 29-month follow-up, the patient’s right eye was asymptomatic, retinal findings did not progress, and visual acuity remained at 1.2. He had disciform scarring in the macula of his left eye, whereas the polypoidal lesions in his right eye were asymptomatic and stable.

Case 4: A 62-Year-Old Man

This patient complained of slight blurring of vision in his right eye, and ophthalmoscopy revealed many confluent soft drusen in the macula. His left eye showed widespread degeneration of the RPE in the macula, with many large serous PEDs at the border, particularly in the area superotemporal to the macula. The PEDs were reddish-orange and seemed to be small choroidal hemangiomas (Figure 10).

Indocyanine green angiography demonstrated branching vascular networks in the early phase and many large polypoidal dilations at terminals of the vascular network (Figure 11).

Macular findings persisted for 1 year without change, and his retina appeared stable. Among patients in this series, this man had the largest vascular network and the greatest number of polypoidal dilations; he was reported on in a previous article.9

Findings of Fundus Examination

Patients showed disorders in the macula, with a shallow serous retinal detachment (43%); subretinal hemorrhages (17%) (Figures 1 and 5) in thin or thick amounts, associated with large serous PEDs (17%) (Figure 10); hemorrhagic PEDs (17%) (Figures 1 and 5); or diffuse RPE degeneration (Figure 10 and Table 2). These macular lesions measured 2 to 3 times disc diameter. None of the eyes were remarkable in the anterior segment, media, or fundus, except for the macular involvements, and none had drusen in the macula.

In the macula, small nodular elevations of the RPE were found in 13 eyes (37%) at the first examination. They were bright reddish-orange (Figures 1, 3, 5, 7, and 10) and 0.3 to 0.5 disc diameters, with a yellowish white margin that seemed to be small serous PEDs and were described previously as “polypoidal lesions.”11

Findings of ICG Angiography

Indocyanine green angiography revealed branching vascular networks in 97% of patients (34 eyes) (Figures 2; 4; 6, top; 9, top; and 11) and polypoidal or aneurysmal dilations at terminals of the branches (Figures 2; 4; 6, bottom; 9; and 11). The vascular network had an umbrella-like appearance and spread to 2 to 3 disc diameters beneath the RPE. A feeder artery originated from the choroidal circulation and supplied the center of the branching vascular network in 86% of patients (30 eyes) (Figure 9, top). Each polyp measured 0.3 to 0.5 disc diameters (range, 2-7 polyps; average, 4 polyps in each eye). Polypoidal dilations were found in the macular area in 33 eyes (94%) but in the peripapillary region in only 3 (9%). In 1 eye, lesions were seen in both the macular and peripapillary areas.

The vascular network was demonstrated in the early phase of ICG angiography. With a double injection of ICG, localizations of the vascular abnormalities were confirmed precisely in relation to polypoidal dilations.

Half of the polypoidal vascular lesions found by ICG angiography were seen in the macula as reddish-orange nodular elevations of RPE, which were described previously, by ophthalmoscopy and slitlamp biomicroscopy with a contact lens. However, half were not seen by ophthalmoscopy because they were covered by subretinal hemorrhages, exudations, or PEDs.
Findings of Fluorescein Angiography

Most polypoidal dilations were detected as spotty hyperfluorescence, and some showed slight leakage from the lesions (Figure 8). The branching networks were not seen on fluorescein angiography, except in a few eyes in which networks were visible as hyperfluorescence through atrophic RPE.

Findings in Fellow Eyes

The fellow eyes in 20 patients (63%) were not remarkable. Four eyes had manifestations of disciform subretinal scarring that resembled typical disciform lesions in AMD, 2 showed soft drusen, 2 showed degeneration of the RPE, and 3 showed polypoidal vascular lesions, as detected by ICG angiography.

CLINICAL COURSE

All eyes were followed up for an average of 20 months (range, 1-60 months). In evaluation of the clinical course, 17 laser-treated eyes were excluded. Thus, the remaining 18 eyes were evaluated for natural course. Twelve eyes (67%) showed a stable clinical course (Figures 3 and 4). In eyes with serous or hemorrhagic retinal detachments, the subretinal serous fluid and blood were spontaneously resorbed. In 5 eyes (28%), slight serous and hemorrhagic detachments of the macula recurred (Table 3). In 2 eyes, massive submacular hemorrhages recurred and developed massive vitreous hemorrhages. In
LASER PHOTOCOAGULATION TREATMENT

According to the indication for the treatment described previously, laser photocoagulation was applied in 17 eyes. Afterward, 12 eyes (71%) showed a favorable course—the hemorrhage and subretinal fluid were gradually resorbed and the lesions became dry. Four eyes (24%), however, showed a less favorable outcome—the subretinal serofibrinous exudations and hemorrhages increased and the lesions became enlarged and persisted for a prolonged period. In 2 eyes, disciform scarring developed after laser treatment (Table 4).

VISUAL OUTCOME

Visual acuity of the affected eyes at the final examination is noted in Table 1. Seventeen eyes (49%) maintained good visual acuity (>0.8) with mild abnormalities in the macula, whereas 10 eyes (29%) showed poor visual acuity (<0.2). The main causes of poor visual acuity in those eyes were massive vitreous hemorrhages (2 eyes) and the formation of disciform subretinal fibrosis, which resembled the disciform lesions of AMD (4 eyes).

One of 35 eyes was followed up for only 1 month and was excluded on the evaluation of visual outcome.
at the final examination. Thirty-four eyes were followed up for at least 3 months (average, 20 months; range, 3-60 months).

Visual acuity at the final examination was compared with that at the first visit and is shown in Figure 12, in which outcomes of laser-treated or untreated eyes were separately made marks. Outcomes in untreated eyes were better than those in treated eyes. Visual outcome in this disorder was relatively good, except for 3 eyes treated by laser photocoagulation.

**COMMENT**

We saw 32 patients and 35 eyes (a relatively large number) with IPCV. The clinical features of this disorder in Japanese patients were characterized as hemorrhagic and/or serous neurosensory retinal detachments associated with serous and/or hemorrhagic PEDs at the posterior pole, and recurrences of these events. Results of ICG angiography demonstrated polyplike vascular dilations with branching vascular networks. The clinical course of this disorder was relatively stable, and the prognosis was relatively favorable. These ocular manifestations were consistent with those in American patients and our observations support previous reports that IPCV may be common in Asian people.

Most of our patients with IPCV were affected unilaterally, and polypoidal vascular lesions were present in the macular area. Men and elderly people were predominantly affected. These epidemiological features differed from those of American patients.

Results of ICG angiography revealed umbrellalike branching vascular networks with a feeder artery supplied to the center of the vascular network. Polyplike, spheroidal, and aneurysmal dilations at terminals of the

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**Table 1. Visual Acuity in 35 Eyes**

<table>
<thead>
<tr>
<th>Visual Acuity</th>
<th>Eyes, No. (%)*</th>
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<tbody>
<tr>
<td>0.8</td>
<td>18 (51)</td>
</tr>
<tr>
<td>0.3-0.7</td>
<td>11 (31)</td>
</tr>
<tr>
<td>0.2</td>
<td>6 (17)</td>
</tr>
</tbody>
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*Because of rounding, percentages do not total 100.
†Final examinations were performed after an average of 20 months (range, 1-60 months).

**Table 2. Ocular Manifestations at the First Examination in 35 Eyes**

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>Eyes, No. (%)*</th>
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</thead>
<tbody>
<tr>
<td>Serous retinal detachment at the macula</td>
<td>15 (43)</td>
</tr>
<tr>
<td>Subretinal hematoma at the macula</td>
<td>6 (17)</td>
</tr>
<tr>
<td>Retinal pigment epithelial detachment</td>
<td></td>
</tr>
<tr>
<td>Serous, large (≥2 disc diameters)</td>
<td>6 (17)</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>6 (17)</td>
</tr>
<tr>
<td>Retinal degeneration</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Polypoidal vascular lesions</td>
<td>13 (37)</td>
</tr>
</tbody>
</table>

*An eye can have more than 1 manifestation.

**Table 3. Clinical Course of Patients Without Laser Treatment (18 Eyes)**

<table>
<thead>
<tr>
<th>Course</th>
<th>Eyes, No. (%)*</th>
</tr>
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<tbody>
<tr>
<td>Favorable</td>
<td>12 (67)</td>
</tr>
<tr>
<td>Vitreous hemorrhage</td>
<td>2 (11)</td>
</tr>
<tr>
<td>Subretinal hemorrhage, recurrence</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Serous retinal detachment, recurrence</td>
<td>2 (11)</td>
</tr>
<tr>
<td>Disciform scarring</td>
<td>1 (5)</td>
</tr>
</tbody>
</table>

*An eye can have more than 1 course.

**Table 4. Outcome of Laser Photocoagulation Treatment (17 Eyes)**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Eyes, No. (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved</td>
<td>12 (71)</td>
</tr>
<tr>
<td>Worsened</td>
<td>4 (24)</td>
</tr>
<tr>
<td>No follow-up</td>
<td>1 (6)</td>
</tr>
</tbody>
</table>

*Because of rounding, percentages do not total 100.
vascular networks were demonstrated in all eyes. The polypoidal dilations appeared as reddish-orange nodular elevations of RPE ophthalmoscopically and seemed to be beneath the RPE when observed by a slitlamp biomicroscope with a contact lens. Such findings in ICG angiography and biomicroscopy are characteristics of IPCV, and demonstration of both signs are essential to a correct diagnosis of this disease, particularly, reddish-orange nodular elevations of RPE in the macula. This finding seems to be a small serous PDE. However, on ICG angiography, hyperfluorescence of polypoidal vasculature was noted, but true serous PED shows hypofluorescence on ICG angiography.

Although the histopathologic evidence of IPCV is not yet clear, it seems that ophthalmoscopic and biomicroscopic findings suggest that vascular abnormalities of IPCV are between the RPE and Bruch membrane and are a peculiar form of CNV.

Clinically, this disease usually shows serous and/or hemorrhagic detachment of the sensory retina associated with serous and/or hemorrhagic PEDs, which likely originate from vascular abnormalities under the RPE and on Bruch membrane. These findings also support our concept of IPCV.

Yannuzzi et al\textsuperscript{1} and Spaide et al\textsuperscript{5} originally indicated that vascular abnormalities were in the inner choroid; their following articles\textsuperscript{6,8} report that these may be a peculiar form of CNV. Gass\textsuperscript{10} indicated that this disorder is a type of CNV beneath the RPE. Our observations showed them between the RPE and Bruch membrane.

Yannuzzi et al\textsuperscript{1} and Spaide et al\textsuperscript{5} also indicated that IPCV may not be a typical CNV or be associated with AMD. They point out that few patients developed disciform scarring and that there were no soft drusen. In our series, however, some eyes developed disciform scarring, and drusen are not frequently seen in elderly Japanese people, even those with AMD.

The epidemiological features of IPCV in Japanese patients are similar to those of exudative AMD in Japanese patients, and the clinical manifestations of IPCV are the same as those of AMD. In Japanese people, AMD was predominant in men (74\%) and unilaterally affected in 81\%\textsuperscript{11} (Table 5). Table 5 lists the clinical features of exudative AMD and IPCV in American and Japanese patients. We cannot differentiate the 2 diseases without ICG angiography.

The results indicate that IPCV probably belongs in the same category as AMD. Other articles also described the association with inflammatory reaction\textsuperscript{12} and severe hypertension.\textsuperscript{13} We believe this entity may be a peculiar form of CNV and is probably associated with exudative AMD.

The natural course of this disorder varied in each patient. In most eyes, macular manifestations, particularly hemorrhagic or serous retinal detachments, were gradually resorbed and disappeared after several months. Thereafter, they persisted in a stable state for a prolonged period with a relatively favorable prognosis. Polypoidal vascular lesions also persisted for a prolonged period without apparent change in manifestation (Figures 3 and 4). In a few eyes, a massive or mild subretinal hemorrhage recurred, along with vitreous hemorrhages and the development of disciform subretinal fibrovascular lesions (Table 3). However, exudative AMD usually shows a downhill course, and subretinal neovascularization develops extensive serosanguineous, exudative retinal detachment, and finally, disciform scarring. These clinical manifestations and courses in IPCV support the findings of Yannuzzi et al\textsuperscript{1}, Spaide et al\textsuperscript{2} and others, which state that IPCV should be treated as a distinct clinical entity, showing a mild manifestation and a favorable prognosis with different management than that used for AMD. Also, the difference between American and Japanese patients must derive from differences in genetic backgrounds.

Figure 12. In most eyes, the visual prognosis was stable and favorable, except in 3 eyes that underwent laser photocoagulation treatment. Final examinations were performed after an average of 20 months (range, 3-60 months).

Table 5. Clinical Features of Exudative AMD and IPCV in American and Japanese Patients\textsuperscript{*}

<table>
<thead>
<tr>
<th>Feature</th>
<th>Exudative AMD</th>
<th>IPCV</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>Elderly</td>
<td>Middle aged to elderly (60.1 y)</td>
</tr>
<tr>
<td>Sex</td>
<td>60% Women</td>
<td>82% Women</td>
</tr>
<tr>
<td>Affected eye</td>
<td>Bilateral</td>
<td>Bilateral (80%)</td>
</tr>
<tr>
<td>Soft drusen</td>
<td>Common</td>
<td>None</td>
</tr>
<tr>
<td>Location</td>
<td>Macula</td>
<td>Peripapillary area</td>
</tr>
</tbody>
</table>

\textsuperscript{*}AMD indicates age-related macular degeneration; IPCV, idiopathic polypoidal choroidal vasculopathy.

\textsuperscript{†}Data are from the present study.
To treat IPCV, we applied laser photocoagulation to the polypoidal lesions of the early patients in this series. Most eyes improved with this treatment, but in some, the lesions deteriorated (Figure 12). In Figure 12, laser-treated eyes showed worse outcome than untreated eyes. Spaide et al also reported similar results with photocoagulation treatment. Recent patients in this series were not treated in this way, but they remained in stable condition. We do not recommend laser photocoagulation as the first choice of treatment for IPCV. However, in this series, patient selection was not randomized, so further study is needed to draw a definitive conclusion about laser treatment.

We conclude that Japanese patients with IPCV have some dissimilarities to American patients, and that polypoidal vascular lesions may be a peculiar form of CNV. This disorder may be in the same spectrum as AMD in Japanese patients. We propose the term polypoidal dilation of subretinal pigment epithelial choroidal neovascularization and the abbreviated name polypoidal choroidal neovascularization for this entity.

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REFERENCES


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