Amyloid can occur as a localized ocular or widespread systemic process. Approximately 4% of amyloid deposits in the head and neck region involve the orbit. Amyloid deposits in ophthalmic structures can occur as a primary or secondary process. Primary deposits (which can be familial or sporadic) occur in the absence of an associated disease. Secondary deposits have been noted after a myriad of processes, including trauma, infection, myeloproliferative disorders, and immune-mediated diseases. Most of the reported ophthalmic cases have been in association with familial amyloidosis with systemic involvement. Some cases have been noted to have only ophthalmic deposition of amyloid without evidence of systemic disease. Amyloid deposits in association with myeloproliferative entities such as lymphomas or plasma cell proliferations can produce paraproteinemias and involve the eye. In our case, the negative study results make this entity unlikely at present. In patients with extrasosseous plasmacytoma, a myeloma develops within 10 years in 10% to 30% compared with 55% in patients with osseous plasmacytoma. Amyloid deposits can also occur in association with rheumatologic diseases, although involvement with systemic lupus erythematosus is distinctly uncommon. Our patient has either a primary amyloid deposit from an extrasosseous plasmacytoma or a focal iris–ciliary amyloid deposit in association with systemic lupus erythematosus. It is conceivable that benign but aberrantly localized plasma cells are part of the systemic lupus erythematosus process in this patient. Alternatively, there is an increase in lymphomas in patients with systemic lupus erythematosus, even when they are not treated with immunosuppression. Amyloid in association with systemic lupus erythematosus is quite rare and usually manifests as renal involvement. Fewer than 20 cases have been reported.

This case illustrates the problem, despite newer diagnostic techniques, of potential diagnostic errors in anterior uveal tumor diagnosis. Our patient is probably at risk for local and systemic recurrence and is being closely observed.

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Acute Posterior Multifocal Placoid Pigment Epitheliopathy With Cerebral Vasculitis: A Multisystem Granulomatous Disease

Typically, acute posterior multifocal placoid pigment epitheliopathy (APMPPPE) is seen along with acute binocular visual disturbance (ie, visual blurring, metamorphopsia, or scotomas) in young adults of whom approximately one third experience a flulike illness at onset. The clinical course is usually self-limited, with remarkable visual recovery. A few cases with cerebral vasculitis or meningoecephalitis have been reported. Although circumstantial evidence for a choroidal vasculitis is gathering, the exact pathological origin of APMPPPE remains unknown. Herein we report a case of APMPP-associated cerebral vasculitis with angiographic, radiologic, and, to our knowledge, for the first time in the literature autopsy findings that include both ocular and cerebral histopathological descriptions.

Report of a Case. Clinical History. A 23-year-old white man developed acute loss of vision in the right eye. There was no history of a flulike illness and his medical history only denoted resection of nasal polyps. On examination visual acuity was confined to perception of a waving arm at a distance of 1 m OD and 20/40 OS. Fundoscopic examination showed multiple creamy white lesions just below the retinal pigment epithelium (RPE) in both eyes. Besides a slightly raised C-reactive protein level, findings from other routine blood tests (including antiglucosaminidase enzyme, anti-nuclear antibody, and antineutrophil cytoplasmic antibody screening) were normal. A fluorescein angiogram (Figure 1) showed early-stage hypofluorescence and late-stage hyperfluorescence consistent with APMPPPE in both eyes. Next he developed bilateral anterior uveitis, and 3 days later, he had acute pain behind the right eye and severe headache. Results of neurological examination showed a left-sided hemiparesis and hypesthesia. He developed a tonic-clonic status epilepticus that did not respond to intravenous treatment with clonazepam and phenytoin sodium.

A magnetic resonance imaging study of the brain and magnetic resonance angiography (Figure 2) revealed occlusion of the left medial cerebral artery and narrowing of the right posterior cerebral artery with infarctions in these vascular territories. Massive swelling of the left hemisphere with midline shift and temporal herniation resulted in death.


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Pathological Findings. In the lungs and enlarged paratracheal hilar lymph nodes, noncaseating granulomas were observed that contained a large number of Langhans or foreign-body-type multinucleated giant cells without asteroid or Schaumann bodies. Ziehl-Nielsen stain and a combination of rhodamine and auramine stain for mycobacteria were negative. Using polarized light no foreign-body material was found. Small noncaseating granulomas were also found in the heart, liver, and spleen. In the choroid there was a granulomatous inflammation with Langhans multinucleated giant cells and focal disruption of the RPE (Figure 3A and B). In these specimens no signs of vasculitis were observed.

Both hemispheres showed diffuse swelling and infarcts, which were more pronounced on the left side. The sections through the origin of the left medial cerebral artery showed occlusion by a blood clot, eccentric hyperplasia of the intima, as well as a granulomatous inflammation of the vessel wall with degeneration (Figure 3C and D), and the presence of Langhans-type multinucleated giant cells at the level of the lamina elastica interna, which also showed degeneration (Figure 3E). Bi-refringent material inside the giant cells was not found. Parenchymatous granuloma was not found in the central nervous system.
Comment. There have been a number of reports of aseptic meningitis and cerebrovascular accidents in association with APMPPE.\textsuperscript{2-10} Cerebral angiographic findings in some of these cases were suggestive of vasculitic changes. In our case a focal granulomatous vasculitis affecting large cerebral arteries was demonstrated. The inflammation contained Langhans-type multinucleated giant cells at the level of the lamina elastica interna, which also showed fragmentation. This latter feature is frequently seen in giant cell (temporal) arteritis, and it is hypothesized to be the primary site to which the immunologic response is focused.\textsuperscript{11} These findings are in agreement with the only other documented histopathological study of cerebral vasculitis in association with APMPPE. Those authors reported a multifocal, granulomatous arteritis of medium arteries with fibrinoid necrosis, not dissimilar to the microscopic findings in temporal arteritis.\textsuperscript{7} As temporal arteritis is one of the large-artery vasculitides that does not affect intradural vessels, and most of the patients are older than 50 years of age, it is unlikely that the findings in our and the mentioned case are due to “classic” temporal arteritis.

In his initial description, Gass\textsuperscript{12} proposed APMPPE to be primarily a disease of the RPE. Buskirk et al\textsuperscript{13} proposed a focal choroidal vasculopathy to explain the slow, irregular filling of the early hypofluorescent areas on the fluorescein angiogram. Various fluorescein angiographic studies confirmed malperfusion of the lamina choriocapillaris.\textsuperscript{4,8,14,15} However, ocular pathological characteristics of APMPPE have not been reported. In our case we found granulomatous inflammation and focal disruption of the retinal pigment epithelium (hematoxylin-eosin [HE], original magnification ×100). B, Magnification of the 2 granulomas in the choroid. These are not situated in or near vessels (HE, original magnification ×200). C, Section through the left medial cerebral artery showing granulomas in the vessel wall with degeneration (HE, original magnification ×40). D, Magnification of the inset in part C of the granulomas in the left medial cerebral artery, which shows Langhans-type multinucleated giant cells (HE, original magnification ×200). E, Elastin staining of the left medial cerebral artery. Langhans-type multinucleated giant cells with inclusions of elastin. Degeneration of the internal elastic lamina (original magnification ×100).
lomas just beneath the RPE. None of these intraretinal granulomas were situated near arterioles, capillaries, or venules. The choirocipallaris itself did not show any sign of acute or chronic vasculitis. Furthermore, generalized granulomas were found in lung parenchyma, lymph nodes, heart, liver, and spleen. One could argue that the generalized granulomas with multinucleated giant cells are in line with advanced sarcoidosis. In favor of this idea are 2 case reports of APMPPE with probable sarcoidosis and posterior choroiditis. The granulomas in our patient contained no characteristic asteroid bodies or Schaumann bodies, which can be seen in sarcoidosis. Furthermore, the occurrence of stroke in sarcoidosis is extremely rare and the fluorescein angiogram shows a different pattern.

The absence of any signs of previous or present vasculitis in the choriocapillaris does not support the hypothesis that APMPPE is caused by a choroidal vasculitis of the lamina choriocapillaris. Instead, our findings indicate that APMPPE is caused by choroidal granulomas and can be part of a generalized granulomatous disease. The granulomas resemble those seen in sarcoidosis. However, its clinical presentation and the occurrence of a cerebral granulomatous vasculitis of large and medium arteries instead suggests that it may be a distinct multisystem granulomatous disease.

Recognition of this syndrome is important and our case illustrates that it can be rapidly fatal. Because cerebral vasculitis associated with APMPPE usually responds well to corticosteroid therapy, we propose that patients with APMPPE complicated by central nervous system manifestations should be treated immediately with intravenous corticosteroids.

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