ACUTE MULTIFOCAL POSTERIOR PLACOID PIGMENT EPITHELIOPATHY(AMPPPE)

It is not uncommon to find the busy practitioner and student overwhelmed by research publications. *Vision*, in each edition will present summaries of certain clinical research topics highlighting some of the most salient points. This will aid clinicians and students to keep in touch with the latest developments in eye care and related fields.

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INTRODUCTION

Acute multifocal posterior placoid pigment epitheliopathy more popularly known by its abbreviation as the acronym AMPPPE is an idiopathic, typically bilateral inflammatory disorder of the posterior segment seen in otherwise healthy young adults. Typically, there is rapid loss of central or paracentral vision with accompanying multiple, whitish-yellow, creamy inflammatory lesions in the form of flat, large, irregularly shaped discs located at the level of the choroid, RPE and outer retina. This condition is important since the fundus lesions may be confused with drusen and cotton wool spots.

AETIOLOGY

The precise aetiology of AMPPPE is unknown, however some believe that it is secondary to a delayed-type hypersensitivity-induced occlusive vasculitis. Also, genetics are known to play a role in an individual's risk for AMPPPE as several associations have been reported including HLA-B7 and HLA-DR2 genetic haplotypes. The occlusive vasculitis causes non-perfusion of the terminal choroidal lobules in the posterior pole of the eye and inducing secondary ischaemic injury of the overlying retinal pigment epithelium and neuroreceptors. Often, patients report a preceding viral or flu-like illness prior to AMPPPE symptom onset. APMPPE has been described in cases of nephritis, thyroiditis, sarcoidosis, erythema nodosum, granulomatosis with polyangiitis, polyarteritis nodosa, scleritis, ulcerative colitis, CNS vasculitis, and post-vaccination. Other infectious associations include group A streptococcus, adenovirus, influenza, hepatitis B, Lyme disease, mumps, and tuberculosis.

PRESENTATION

AMPPPE can be found in men and women equally. Common onset occurs between the second and fourth decades of life. Generally, a systemic viral illness precedes the onset of ocular signs and symptoms. Patients may complain of tinnitus, stiff neck and headaches, before complaining of blurred vision. Visual acuity can range from 6/9 to counting fingers and may differ between the eyes. Visual field defects correspond to patches-like lesions that borders the macula. When this occurs, near vision is affected, especially when patient is engaged with fine work.

Figure 1. AMPPPE appears as several patchy, cream-coloured lesions in the posterior pole.

PATHOPHYSIOLOGY

The exact pathogenesis of AMPPPE is speculative but it is believed to be due to vasculitic inflammation at the level of the choriocapillaris resulting in hypoperfusion and ischaemia of the RPE and photoreceptors. In later stages, the inflamed choroid and retina manifests with RPE atrophy and hyperpigmentation. AMPPPE falls under the uveomeningeal syndromes (a group of disorders that share involvement of the uvea, retina and meninges).

Evidence suggests that the vascular inflammation causes transient occlusion of these vessels, producing mild ischaemia. Angiography demonstrates a profound delay in choroidal filling time, along with the discovery of extensive areas of choroidal non-perfusion in its acute stages. Recovery of choroidal blood flow following clinical resolution is a hallmark of AMPPPE. The vasculitis associated with APMPPE may affect the long and short posterior ciliary vessels that supply the optic disc. This may result in neural axoplasmic stasis and compression of the central retinal vein, leading to optic neuropathy and central retinal vein occlusion. The perinuclear pattern antineutrophilic cytoplasmic antibody (pANCA), myeloperoxidase (MPOANCA) is often associated with systemic vasculitis, producing systemic and ocular effects.This particular marker is known to be an identifier in the disease process of AMPPPE. The most frequent systemic manifestation associated with AMPPPE is glomerulonephritis. However, inflammation in other tissues of the body along with those detected in ocular structures is possible. A paraneoplastic disorder has been described in patients who have combined optic neuritis and retinitis. This syndrome is defined serologically by the presence of a paraneoplastic IgG autoantibody CRMP-5-IgG. These patients may present with an inflammatory vitritis similar to those seen with AMPPPE. The disease has also been identified as potentially producing neurological sequellae.

MANAGEMENT

Diagnosis is made via clinical presentation and 90D and BIO fundoscopic examination. No specific laboratory tests exist for AMPPPE diagnosis. However, fluorescein angiography and Indocyanine Green angiography are typically performed in confirming the diagnosis. Optical coherence tomography and fundus autoflourescense may also have a role in diagnoses. Characteristic findings of these diagnostic procedures include:

- Optical coherence tomography (OCT): Hyper-reflectivity from the outer plexiform layer to the RPE with normal retinal thickness in acute lesions. Hyper-reflectivity of outer layers resolve along with resolution of the lesion.
- Fundus autoflourescense (FAF): Early and late hypo-autoflourescence correspond to the placoid lesions. Hypo-autoflourescence may persist at borders after lesion resolution.
- Fluorescein Angiogram (FA): Early hypofluorescence (blockage) correspond to the placoid lesions followed by late, irregular hyperfluorecent staining.
- Indocyanine Green (ICG) Angiogram: Early and late hypofluorescence correspond to the placoid lesions.

Corticosteroids are often prescribed for AMPPPE and its benefits clearly demonstrated in the management plan. The optometrist can manage the accompanying signs like uveitis, episcleritis and conjunctivitis. However, referral to a retinal specialist is warranted. Since the patient is often placed on steroids, IOP must be monitored regularly.

AMPPPE has generally good prognosis with the majority of affected patients achieving a visual acuity of 20/40. Visual recovery typically takes 4 weeks, but can extend to 6 months in some patients. Foveal involvement confers a worse visual prognosis. All patients with a new diagnosis of AMPPPE should receive a full neurologic and systemic work-up to evaluate for CNS vasculitis and other associated systemic conditions.

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CLINICAL PEARLS

- AMPPPE is seen as patchy inflammatory defects in the choriocapillaris, retinal pigment epithelium (RPE) and outer retina the basic underlying mechanism is believed to be an obstructive vasculitis.
- Patients typically notice a rapid onset of blurred vision associated with central and paracentral scotomas.
- Photopsias have been reported prior to vision loss.
- Symptoms are usually bilateral, asymmetric and can occur several days apart. Visual acuity can range from 6/9 to counting fingers depending on the extent of foveal involvement.
- Anterior segment exam is usually normal, though anterior uveitis can be present. There may be mild vitritis present in 50% of cases.
- Fundoscopic examination typically shows multiple bilateral yellow-white placoid lesions at the level of RPE and choroid 1-2 disc diameters throughout the fundus, posterior to the equator.
- New lesions may appear in the periphery up to 3 weeks following onset (radially or linearly). Older lesions are replaced with RPE atrophy or hyperpigmentation. There are reports of associated retinal vasculitis, vein occlusion, subhyaloid haemorrhage, optic disc oedema, and rare choroidal neovascular membrane formation.
- White-Dot syndromes can resemble AMPPPE. These include, but are not limited to: multiple evanescent white dot syndrome, serpiginous choroiditis (especially in chronic, recurrent cases), relentless placoid choroiditis, multifocal choroiditis and panuveitis, punctate inner choroidopathy,birdshot chorioretinopathy. Other infectious uveitis (tuberculosis, fungal disease, syphilis), choroidal metastases, and lymphoma may present with placoid lesions as well and should be ruled out with appropriate tests if clinical suspicion is high.
- One should consider the diagnosis of primary ocular-CNS lymphoma in patients with unilateral or bilateral vitritis and intermediate uveitis with or without neurological findings.

CONCLUSION

Acute multifocal posterior placoid pigment epitheliopathy (APMPPPE) typically affects healthy young adults and is characterised by rapid loss of central vision and multiple inflammatory yellow-white lesions deep within the sensory retina at the level of the retinal pigment epithelium as well as classic fluorescein angiography (FA) findings. AMPPPE shares important differential diagnosis with drusen, AMD and white dot syndromes and therefore needs to be understood. The subretinal lesions block most of the background choroidal fluorescence in the early phases of FA.

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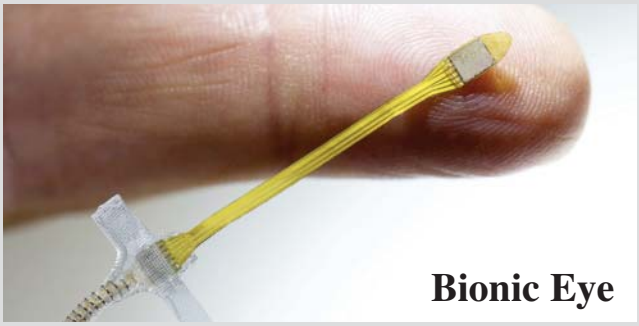

Bionic Eye

A blind woman fitted with a "bionic eye" has spoken of her joy after she was able to tell the time for the first time in more than six years.

Rhian Lewis, 49, was given the retinal implant as part of an ongoing trial at Oxford's John Radcliffe hospital. Surgeons at the Oxford Eye hospital implanted a tiny electronic chip at the back of her right eye's retina in an attempt to help her see.

The mother of two, from Cardiff, has suffered from retinitis pigmentosa – an inherited disorder – since she was five. The condition causes gradual deterioration of photo-receptors, the light-detecting cells in the retina, which can lead to blindness. One in 3-4,000 people in the UK have the disease, for which there is currently no cure.

Lewis is completely blind in her right eye and has virtually no vision in her left eye. The implant, made by a German firm, Retina Implant AG, was placed in Lewis's eye in June in an operation that can last six to eight hours.

During follow-up tests, Lewis was asked to look at a large cardboard clock to see whether she could tell the time. She had not been able to tell the time with her right eye in 16 years or with her left eye for about six years.

She said "Oh my god" when she realised she had managed to recognise it was three o'clock. She added: "Honest to god, that felt like Christmas Day."

The implant – a 3mm sq array of around 1,500 light sensors which sends pulsed electrical signals to nerve cells – is connected to a tiny computer that sits underneath the skin behind the ear. This is powered by a magnetic coil on the skin. From the outside, it looks like a hearing aid.

When the device is first switched on, patients see flashes of light, but over a few weeks the brain learns to convert those flashes into meaningful shapes and objects. The images can be black and white and grainy but still have the power to transform lives.

Describing the moment the device was turned on, Lewis said: ***"They said I might not get any sensation and then all of a sudden within seconds there was like this flashing in my eye, which has seen nothing for over 16 years, so it was like, oh my god, wow!"***

Lewis was then taken to the cloisters of New College, Oxford, to see whether she could make out its features. She said: "I walked up the street, and the lady from social services said to me to point out anything I thought might or might not be there. And the first thing I thought 'there might be something there,' there was a car, a silver car, and I couldn't believe it, because the signal was really strong, and that was the sun shining on the silver car.

"And I was just, well, I was just so excited, I was quite teary. The enormity of it didn't hit me until I'd actually got home, thinking 'Oh my god, what have I done? I've actually spotted something out that I haven't been able to do.'"

Lewis is able to manipulate the implant using dials on a small wireless power supply held in her hand. This helps her adjust sensitivity, contrast and frequency.

"The problem with having no sight is that you also lose your confidence because you lose your mobility," Lewis said. "It's simple things like shopping, clothes shopping, you don't know what you look like.

"It's been maybe eight years that I've had any sort of idea of what my children look like. Now, when I locate something, especially like a spoon or a fork on the table, it's pure elation. I just get so excited that I've got something right."

The "bionic eye" has been tested as a treatment for retinitis pigmentosa since 2012. Lewis is the first patient outside Germany to be fitted with a newer second-generation device.

Prof Robert MacLaren, who is leading the research at Oxford, said the technology had huge potential benefits. "It's an amazing process because what Rhian and others are trying to do is reactivate a part of the brain that hasn't been doing anything for the last 10 years or so," he said. "There is a lot of rehabilitation because basically they are learning to see again."

George Freeman, the minister for life sciences, said: "This groundbreaking research to create the world's most advanced bionic eye highlights the crucial role of the NHS as a test bed for 21st-century medicine."