Efficacy of cyclosporin A in the treatment of acute posterior multifocal placoid pigment epitheliopathy

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Abstract

Aim of the study is report a case of a female patient with acute posterior multifocal placoid pigment epitheliopathy (APMPPE) in whom remission was obtained after systemic cyclosporin A treatment had been applied. The presented case confirms the efficacy of oral cyclosporin A (Sandimmun Neoral) treatment in selected types of choroiditis including patients with APMPPE resistant to steroid therapy.

Key words: acute posterior multifocal placoid pigment epitheliopathy (APMPPE), systemic steroid therapy, cyclosporin A.

Introduction

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) is a rare idiopathic posterior uveitis [1]. The disease was originally described in 1968 by Gass, who emphasized the typical dotty appearance of the eye fundus [2, 3]. Usually APMPPE is characterized by a sudden, painless loss of vision first in one eye and then bilaterally. Loss of vision is often preceded by flu-like symptoms. Most commonly the disease affects young subjects of both sexes, in the second and third decades of life, from both urban and rural areas. Fundus examination reveals numerous flat yellow-white placoid lesions located in the choroid and/or in the retinal pigment epithelium. The posterior pole findings can be associated with other inflammatory disorders including iritis and vitritis. The disease often runs a self-limiting course. Ocular lesions usually resolve spontaneously over several weeks and visual acuity is recovered to a level slightly lower or equal to that prior to the disease occurrence [1, 4-7]. In most cases treatment is not mandatory. However, in cases of APMPPE with macular involvement, visual acuity may remain markedly lowered due to atrophy of the retinal pigment epithelium. Patients with such a condition often require systemic steroids [6, 7]. In cases where systemic steroid treatment leads to side effects, steroid-sparing immunosuppression could be considered as an alternative.

The aim of the study is to report the case of a female patient with APMPPE with retinal pigment involvement, resistant to steroids, in whom remission has been obtained with systemic cyclosporin A monotherapy.

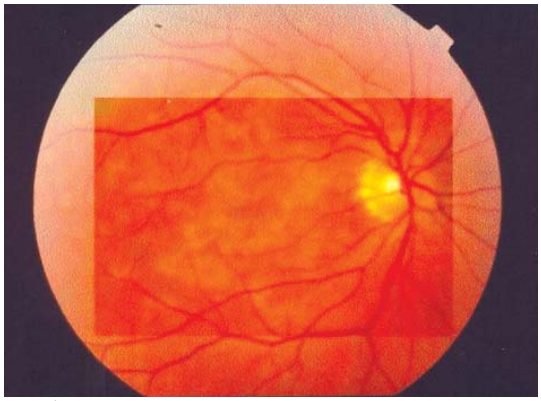
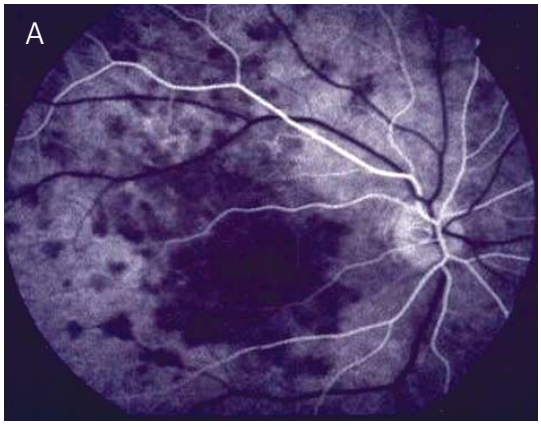


Figure 1. Fundus photography of the right eye. Numerous yellow-white placoid lesions with macular involvement



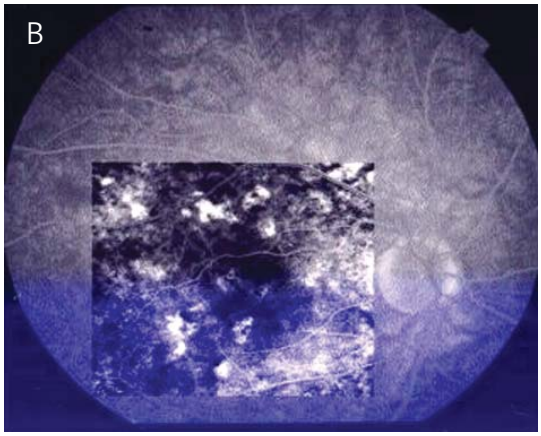


Figure 2. Fluorescein angiography photography: A – early hypofluorescence of pathological changes, B – late staining of pathological changes

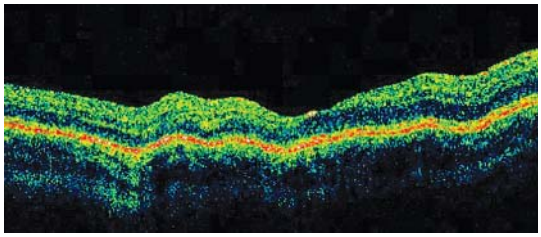


Figure 3. Optical coherence tomography examination: folding in the hyper-reflexive layer of Bruch's membrane and retinal pigment epithelium (RPE), with hyporeflexia of the choroid

Case report

A 31 year-old female presented with a sudden bilateral onset of impaired vision which was preceded by flu-like symptoms and headache. She had never been referred to or treated by an ophthalmologist. On the day of admission her visual acuity was 0.1 in the right eye and 0.05 in the left eye. The examination of the anterior segment of the eye was normal and the values of intraocular pressure measurements were within normal limits. Fundus examination revealed numerous yellow-white placoid lesions bilaterally, with macular involvement (Figure 1). Additional examinations: fluorescein angiography (FA) revealed hypofluorescence in the early phase and subsequently late hyperfluorescence located in choroid lesions (Figure 2). Optical coherence tomography (OCT) showed folding in the hyperreflexive layer representing Bruch's membrane and pigment epithelium, with marked hyporeflexia of the choroid (Figure 3). Her general health condition was normal and additional neurological examination did not reveal any abnormalities. Based on the clinical findings and the results of the fluorescein angiography and OCT the diagnosis of acute posterior multifocal placoid pigment epitheliopathy (APMPPE) was established. Regarding the fact of bilateral intensive changes of the retinal pigment epithelium and severe visual acuity loss, prednisolone treatment was applied at a daily dose of 1 mg/kg body weight. The dose was reduced by 10 mg every seven days. Following two months of treatment, visual acuity improved to 0.4 in both eyes. Fundus examination still revealed active foci of retinal and choroid lesions. Ineffectiveness of the applied therapy and occurrence of side effects, i.e. arterial hypertension of 160/100 mm Hg and obesity, made it necessary to modify the treatment and apply cyclosporin A at a daily dose of 5 mg/kg body weight (Sandimmun Neoral 100 mg *p.o.* twice a day). Initially, cyclosporin A was administered as an element of prednisolone conjugated therapy. Due to worsening of steroid-related side effects, prednisolone was discontinued and cyclosporin A was continued in monotherapy at the same dose. No side effects of cyclosporin A treatment in this patient were observed.

Following three months of treatment with cyclosporin A, improvement was achieved in visual acuity, which reached 1.0 in the right eye and 0.8 in the left eye. Lesions in the fundus were resolved completely. The control FA and OCT showed normal structure of the retina layers. No recurrence of the disease in the following three months was observed, which allowed the dose of cyclosporin A to be gradually reduced until it was withdrawn. At present, the patient attends her follow-up visits and no immunosuppressive treatment is required.

Discussion

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) remains a disease with unknown aetiology. Occurrence of lesions observed in the fundus are usually explained by two hypotheses. One of them, originally put forward by Gass, suggests the role of inflammatory mechanisms in development of the disease and its retinal pigment epithelium (RPE) and choroid involvement. The other hypothesis, which was presented by Van Buskirk, postulates the existence of primary inflammatory lesions in the choriocapillaris as a result of the immune response to external antigens. As a consequence of the inflammation, ischaemic followed by atrophic lesions develop in the retinal epithelium [4, 6, 8].

Occurrence in the majority of patients of flu-like symptoms which precede ocular lesions and reports of documented cases of developing similar fundus after anti-viral vaccinations could support the immune background [6, 7]. Some authors suggest a genetic predisposition towards APMPPE. It has been reported that HLA-DR2 antigen occurs in 56% of patients with APMPPE and HLA-B7 in 40% of patients [3, 6, 7].

Acute posterior multifocal placoid pigment epitheliopathy has been described in association with some systemic diseases, including cerebral vasculitis, erythema nodosum, Wegener's granulomatosis and polyarteritis nodosa. Taking this into account, it is advisable to perform neurological examinations in patients with APMPPE [6, 9].

In the cases of APMPPE with non-typical course, associated retinal findings such as vasculitis, optic disc oedema or exudative retinal detachment are frequently found. Although APMPPE usually occurs bilaterally, asymmetric involvement can also be observed [4, 10].

Fluorescein angiography and indocyanine green angiography as well as optical coherence tomography are useful examinations in confirming the diagnosis [1, 3, 5, 8, 11].

Reports of APMPPE cases which have been presented so far suggest that older age of patients at presentation and macular involvement of the disease are factors influencing the extent of recovered visual acuity [12]. Fundus lesions resolve spontaneously in the majority of cases. Occurrence of lesions in pigment epithelium or in the macula and atypical cases of APMPPE are indications for systemic steroids. Systemic corticosteroid treatment is usually effective in inducing remission and results in a better visual prognosis [4, 6]. When no improvement has been achieved with steroids, non-steroidal anti-inflammatory immunosuppressive drugs should be applied, e.g. cyclosporin A. Cyclosporin A represents a family of cyclic peptides of 11 amino acids with a broad spectrum of biological activities including immunosuppressive, anti-inflammatory, anti-fungal, anti-parasitic and anti-allergic effects. Of all the family representatives, cyclosporin A (Sandimmun, Neoral) has been investigated most thoroughly. The main target cells of the drug are the T lymphocytes, and its action results in inhibiting gene transcription for the key cytokines IL-2, IL-3 and IL-4 as well as GM-CSF and TNF-α. Inhibition of gene transcription is precisely correlated with the immunosuppressive activity of cyclosporin A, which has been confirmed in both *in vivo* and *in vitro* studies [13]. Patient tolerance of therapy with cyclosporin A is usually good and the number of adverse reactions as observed in our patient, i.e. arterial hypertension, is smaller compared to steroid treatment [14].

Cyclosporin A is not a standard therapy in the treatment of APMPPE [6]. In this case, standard corticosteroid treatment was instituted first and only discontinued due to side effects. Complete remission of the disease occurred with cyclosporin A, suggesting that it may be beneficial in other cases of APMPPE where steroids are not effective or tolerated. To the best of our knowledge, successful treatment of APMPPE with cyclosporine A monotherapy has not previously been reported.

In conclusion:

1) cyclosporin A (Sandimmun Neoral) seems to be a potential alternative to corticosteroid treatment, especially in cases of APMPPE resistant to steroids,
2) applying cyclosporin enables steroids to be reduced or, in some cases, withdrawn totally, which reduces the risk of local and systemic side effects associated with steroid therapy,
3) the beneficial effect of cyclosporin A treatment in APMPPE strongly supports the immune background of the disease.

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