CASE REPORT

Long-term fundus changes in acquired partial lipodystrophy

Joyce Jansen,¹ Lien Delaere,² Leigh Spielberg,³ Anita Leys²

¹University Hospitals Leuven, Leuven, Belgium

²Department of Ophthalmology, University Hospitals Leuven, Leuven, Belgium

³Oogziekenhuis, Rotterdam, The Netherlands

Correspondence to

Dr Joyce Jansen,
joyce.jansen@uzleuven.be

SUMMARY

We describe long-term fundus changes in a patient with partial lipodystrophy (PL). Retinal pigment alterations, drusen and subretinal neovascularisation were seen without evidence for membranoproliferative glomerulonephritis. Fundus alterations similar to those seen in age-related macular degeneration can occur at an earlier age in patients with PL, even without renal disease. Dysregulation of an alternative complement pathway with low serum levels of C3 has been implicated as a pathogenetic mechanism.

BACKGROUND

This patient was known to have partial lipodystrophy (PL), a rare disorder characterised by the loss of subcutaneous fat, most commonly involving the face, trunk and the upper limbs. PL is often associated with membranoproliferative glomerulonephritis (MPGN-II), also known as dense-deposit disease or mesangiocapillary glomerulonephritis. MPGN-II is a rare kidney disorder that usually presents in early adulthood with proteinuria, haematuria and renal impairment. There are several reports of pigmentary fundus changes associated with this renal disease. The patient in this case report had no renal impairment but the typical fundus changes as we see them in MPGN-II were detected.

CASE PRESENTATION

A 48-year-old man was referred to our institution for the loss of vision in the right eye due to choroidal neovascularisation. At the age of 6, he was diagnosed with facial lipodystrophy (figure 1). There was no associated renal dysfunction at that time. His medical history revealed that he suffered from arterial hypertension, diabetes mellitus type 2 and hypertriglyceridaemia. At the age of 47, he was treated for acute pancreatitis.

INVESTIGATIONS

At examination, the best-corrected visual acuity was 20/32 in the right eye and 20/20 in the left. Fundus biomicroscopy showed bilateral diffuse granular pigmentation and extensive small drusen at the maculae (figures 2 and 3). In the right eye, a classic subretinal membrane subfoveal and nasal to the fovea was seen on fluoroangiography and optical coherence tomography (figure 4).

There was a depletion of complement C3 factor (0.98 g/L).

Figure 1 Facial lipodystrophy.

DIFFERENTIAL DIAGNOSIS

The fundus changes are similar to those seen in age-related macular degeneration (AMD), but develop at an earlier age.

TREATMENT

At that time, photodynamic therapy (PDT) was the only available treatment for neovascularisation. Unfortunately, the antivascular endothelial growth factor (VEGF) treatment was not yet available for ophthalmological use. Three PDT treatments over a period of 6 months were performed in the right eye. An occult subretinal membrane papillomacular in the left eye developed at the time of the third treatment in the right eye. The left eye also received one PDT treatment.

OUTCOME AND FOLLOW-UP

Thereafter, the lesions stayed inactive for 6 years with a stable vision of 20/50 in the right eye and

Figure 2 Fundus examination at age 48. Bilateral red-free fundus photography with pigment epithelial alterations and wide spread small drusen. (There's subretinal membrane subfoveal and nasal to the fovea in the right eye.)

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Figure 3 Fundus examination at age 48. Bilateral red-free fundus photography with pigment epithelial alterations and wide spread small drusen. (There's subretinal membrane subfoveal and nasal to the fovea in the right eye.)

20/20 in the left during follow-up. There were slowly increasing widespread pigment epithelial alterations and multifocal atrophic lesions with little active occult neovascularisation in both eyes (figures 5 and 6). Visual field testing showed normal peripheral borders and no remarkable central defects.

DISCUSSION

MPGN-II is known to be associated with typical subretinal changes including small drusen and pigment epithelial alterations.¹ Partial lipodystrophy (PLD) can also be associated with these fundus changes in the absence of renal disease. Patients are initially asymptomatic, but in time, the drusen become more numerous and there is a slow evolution to either geographic atrophy and/or subretinal neovascularisation very similar to the changes seen in AMD. Fluoroangiography of these patients is characterised by the presence of numerous, small, tightly packed basal laminar drusen throughout the posterior pole.² These fluoresce brightly on FA, giving a starry sky appearance. The changes are located within Bruch's membrane, the

Figure 5 Examination at age 54 with the best-corrected visual acuity of 20/50 in the right eye and 20/20 in the left. Progressive bilateral pigment epithelial alterations with extensive fine drusen at the macula and in the periphery with islands of atrophic spots in between. There's a small bleeding in the right eye at the level of the superior vascular arch.

choriocapillaris and the retinal pigment epithelium (RPE). However, PLD and MPGN-II-associated drusen appear at a younger age. Retinal pigmentary epithelial changes were seen at the maculae but the fovea was unaffected in the left eye and only partially affected in the right. The central vision was preserved in the left eye and reduced to 20/50 in the right eye. No peripheral field or central field defects were detected. This suggests a good visual prognosis if the fovea is not involved.

The pathogenesis of fat loss and the frequent association with MPGN-II in patients with APL is not completely understood but a complement involved mechanism is implicated.³ Mutations and polymorphisms in the major complement regulator, factor H predispose to four different diseases: MPGN II, PLD, recurrent atypical haemolytic uraemic syndrome, and AMD.³ APL is frequently associated with hypocomplementaemia and is often associated with an Ig antibody called C3

Figure 4 Optical coherence tomography imaging of the subretinal membrane in the right eye after the photodynamic therapy treatment.

Figure 6 Examination at age 54 with the best-corrected visual acuity of 20/50 in the right eye and 20/20 in the left. Progressive bilateral pigment epithelial alterations with extensive fine drusen at the macula and in the periphery with islands of atrophic spots in between. There's a small bleeding in the right eye at the level of the superior vascular arch.

nephritic factor, which binds to and stabilises the enzyme C3 convertase.^{4–6} This combination leads to the activation of the alternative complement factor pathway and excessive consumption of C3. Adipocytes and similarly renal cells produce complement protein, factor B and factor D (fD) (adipsin). Regional differences in adipocyte fD production can explain the predominant facial involvement of APL. Deposition of activated components of complement in adipose tissues results in the destruction of adipocytes in areas high in fD content (adipsin).^{3 4 6 7} Because we know that patients with PL are prone to develop mesangiocapillary glomerulonephritis, patients should be assessed from a renal point of view. Hypocomplementaemia can sometimes precede nephritis by many years and those who become C3 nephritic factor positive can be initially asymptomatic.⁷ The ophthalmologist can play a crucial role in the early referral of these patients to the nephrology department and should be aware that several other autoimmune diseases, in par-

ticular diabetes mellitus, hypertriglyceridaemia, lupus erythematosus and dermatomyositis are often associated with APL.^{4 8 9} Both diabetes and hypertriglyceridaemia were present in our patient. Ophthalmological follow-up of these patients is important to detect choroidal neovascularisation early and treat it accordingly. The analogy of the pathophysiology with AMD, suggests that treatment of choroidal neovascularisation with anti-VEGF agents, may also be indicated in patients who develop neovascularisation due to PL.^{10 11}

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Learning points

- ▶ Partial lipodystrophy is a rare disorder in which typical fundus changes, similar to those in age-related macular degeneration (AMD) are seen at an early age. These fundus changes have been described in partial lipodystrophy associated with membranoproliferative glomerulonephritis, but can also occur in the absence of renal damage.
- ▶ Ophthalmologists should be aware of this association since visual loss can occur at an early age due to choroidal neovascularisation. It would be interesting to conduct further investigation concerning complement factors in the pathogenesis of these diseases to assess their role as a possible therapeutic target.
- ▶ The treatment and follow-up of these patients can be conducted in the same way as for AMD. The antivasular endothelial growth factor treatment may also be indicated.

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