Exudative detachment as a masquerader in hypoalbuminaemic patients

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Introduction

Retinal detachment (RD) is a serious condition that may lead to permanent loss of vision. Most RDs result from a tear(s) in the retina, through which liquefied vitreous enters the sub-retinal space. Rarely, however, exudative retinal detachment (ERD) occurs due to an underlying ocular or systemic condition that produces excess sub-retinal fluid in the absence of tears and/or tractional pull [1]. The ERD may go unnoticed especially if the patient is severely ill and may not complain of symptoms like floaters, flashes of light and peripheral visual field defect. Severe visual deficit occurs once the macula is involved in advanced ERD. Hence, a high level of suspicion is mandatory to detect ERD in these renal and gastroenterological conditions.

We report a series of three patients who had ERD secondary to underlying systemic disease and interestingly were diagnosed only after blurring of vision occurred as their presenting symptom.

Case 1

A 44-year-old female presented to the ophthalmology service with bilateral severe visual loss of 1-month duration. She had a past history of protein C, protein S and anti-thrombin III deficiency, complicated by superior mesenteric and portal vein thrombosis for which she was on warfarin therapy. She had previously been investigated for autoimmune vasculitis as a possible cause of Raynaud’s phenomenon.

Her vision was 6/120 in the right eye and light perception in the left. There was a right inferior quadrant and left total ERD associated with vitreous haemorrhage. Ocular ultrasonography (B scan) did not reveal any underlying posterior scleritis or choroidal tumour. Fundal fluorescein (FA) and indocyanine-green angiography (Figure 1) to visualize the retinal and choroidal vasculature, respectively, for coexistent vasculitis and leakage showed no evidence of any intraocular mass or ocular inflammatory condition causing vasculitis.

During a visit to the ophthalmologist, she was admitted to the medical ward when she was noted to have severe breathlessness from a right-sided pleural effusion and had abdominal distension from portal and superior mesenteric vein thrombosis leading to ascites. Systemic investigations revealed severe hypoalbuminaemia (albumin 10 G/L), elevated serum alkaline phosphatase 124 U/L (32–103 U/L) and gamma-glutamyl transferase 226 U/L (7–39 U/L) levels and total urine protein 0.20 G/day. The gastroenterologist made a diagnosis of protein-losing enteropathy based on the presence of intestinal oedema, which developed secondary to superior mesenteric and portal vein thrombosis.

The vision in her right eye dropped to hand movements progressively over the next 3 months due to rapid progression of ERD, which was treated conservatively in view of her underlying medical condition. The patient became increasingly unwell and defaulted follow-up. In this patient, multiple systemic complications occurred due to venous thrombosis, which eventually led to protein losing enteropathy and rapidly progress to blindness. She subsequently passed away from multi-system organ failure during one of her hospital admissions.

Case 2

A 60-year-old female with no past medical history, presented to the Accident and Emergency Department for bilateral central blurring of vision for 4 days. She also had bilateral ankle oedema. Her visual acuities were 6/30 in the right eye and 6/21 in the left. Fundus examination showed bilateral neurosensory RDs (Figure 2a and b). The clinical picture was suggestive of an underlying systemic condition. She was admitted to the internal medicine department for further investigations. Systemic investigations confirmed a diagnosis of nephrotic syndrome, and kidney biopsy disclosed minimal-change disease. Her 24-h urine protein was 4.83 g/day and serum albumin levels...
were 10 g/L (37–51 g/L). Her autoimmune screen blood profile and ultrasound of the kidneys were unremarkable.

The patient was started on oral prednisolone 50 mg once a day, spironolactone, metolazone and burinex for fluid overload and simvastatin for hyperlipidaemia.

The neurosensory RDs had completely resolved 5 days later, leaving mild residual mottling at the macula (Figure 2c). There was complete resolution of the fluid 5 months after presentation. Her visual acuity improved markedly to 6/12 in the right and 6/9 in the left eye. The patient is on maintenance therapy of cyclosporine and a tailing dose of oral prednisolone therapy. There has been no recurrence of ERD 2 years after the initial presentation.

This case illustrates the importance of detailed systemic evaluation in a seemingly healthy patient presenting with ERD. The diagnosis of neurosensory RD secondary to nephrotic syndrome was supported by the marked improvement with oral steroids. The distinction between this cause from central serous chorioretinopathy (CSCR) was essential since the approach to treatment is completely different. If the underlying condition of serous detachment was due to CSCR, treatment with systemic steroids would worsen the eye condition and the vision. Conversely, ERD due to nephrotic syndrome would respond very well to systemic steroids.

Case 3

A 70-year-old male known to have long-standing poor vision in the right eye due to non-arteritic anterior ischaemic optic neuropathy, presented with sudden onset blurring of vision in the left eye. He was seen elsewhere and was given a provisional diagnosis of Vogt Koyanagi Harada disease (VKH) or bilateral CSCR. He sought a second opinion at our centre.

His visual acuities were 6/120 in the right eye and hand movements in the left eye. Fundus examination showed bilateral ERDs. Clinically, there were no systemic signs of VKH. FA and indocyanine-green angiography did not reveal any underlying choroidal masses but showed multifocal areas of leakages with exudation as seen in Case 2.

During this period, the patient was also seen by a nephrologist for raised serum creatinine levels. He had low albumin levels of 14 g/L (37–51 g/L) and total urine protein was 8.2 g/day. His total cholesterol was elevated at 8.47 mmol/L. Kidney biopsy revealed lesions of focal segmental and global glomerulosclerosis.

In view of the possible diagnosis of bilateral CSCR, the patient opted for oral corticosteroids to be withheld as part of his treatment. He was started by the renal
physician on an immunosuppressant (cyclosporine A 50 mg bid). At last visit 2 months after initial presentation, the patient’s exudative detachments had resolved. His visual acuity was 6/12 in the left eye after cataract surgery was performed and 6/60 in the right, with a presence of moderately dense nuclear sclerosis cataract.

Discussion

ERDs are common and may be seen in ocular as well as systemic conditions. Ocular causes include CSCR, intraocular tumours and posterior scleritis [2]. In CSCR, the detachment may be precipitated or worsened by glucocorticoids [3]. The increased permeability of the choriocapillaries results in detachment of the neurosensory retina [2, 3]

A common systemic cause is VKH, which is an autoimmune condition characterized by neurological involvement, bilateral exudative detachments and cutaneous changes [4]. There have also been a few reports on bilateral exudative detachments secondary to pre-eclampsia during pregnancy [5]. Exudative detachments secondary to renal conditions have been widely described in literature as single case reports describing detachments due to hypertensive retinopathy, complications during haemodialysis or as a result of corticosteroid therapy [6–9]. However, to date, larger case series describing exudative detachments secondary to hypoalbuminaemia in conditions like protein-losing enteropathy and nephrotic syndrome as demonstrated in our three patients have, to the best of our knowledge, been under-reported (Table 1 [10–12]).

There are various mechanisms involved in maintaining adhesion of the neurosensory retina to the retinal pigment epithelium (RPE). Postulated mechanisms include oxygenation of the retina, mechanical apposition of the retina by the vitreous, as well as adhesion between the retina and RPE by matrix material [1].

Another major contributing factor is the force that drives a net outward movement of fluid across the retina. This comprises the intraocular pressure, osmotic pressure and the active ion-fluid transport pump of the RPE cells [13–15]. Any disruption between the osmotic pressure and intraocular pressure such as in conditions like VKH and posterior scleritis can result in fluid being drawn from the choroid through the retina and into the vitreous leading to retinal separation from the RPE [15]. Similarly,
Exudative retinal detachment

Table 1. Publications reporting exudative retinal detachment in hypoalbuminemic patients

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Description</th>
<th>Reference</th>
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<tbody>
<tr>
<td>Venkatramani et al. [10]</td>
<td>A 47-year-old female with protein-losing enteropathy diagnosed on biopsy presented with bilateral exudative detachments. She had very low serum albumin levels of 1.4 g/dL.</td>
<td>Single case report</td>
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<tr>
<td>De Benedetto et al. [11]</td>
<td>A 24-year-old female who presented with generalized oedema secondary to nephrotic syndrome had bilateral blurring of vision with exudative detachments that resolved with diuretic therapy.</td>
<td>Single case report</td>
</tr>
<tr>
<td>Hoger and Wiegand [12]</td>
<td>A 52-year-old patient with atypical plasmacytoma and nephrotic syndrome presented with serous retinal detachment and pigment epithelial detachment.</td>
<td>Single case report in German</td>
</tr>
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Direct damage to the ion channels (RPE pump) on the surfaces of the RPE cells in conditions like malignant hypertension and pre-eclampsia also leads to accumulation of sub-retinal fluid and exudative detachment [1]. Both protein-losing enteropathy and nephrotic syndrome have characteristically low serum albumin levels. In the former, there is an abnormal loss of protein from the digestive tract or an inability of the digestive tract to absorb proteins [16]. The latter is defined as urine total protein excretion >3.5 g/day or total protein-creatinine ratio >3.5 g/g, low serum albumin level, high serum cholesterol level and peripheral oedema [17]. Animal studies have shown evidence of albumin in the retinal, choriocapillaris and larger choroidal vessels [18]. In conditions where there is an overall decrease in serum albumin, which was a common pathology in all our three patients, the osmotic pressure in the choroidal vessels is decreased, and there is transudation of fluid into the sub-retinal space. This leads to accumulation of fluid in the sub-retinal space. However, not all patients with renal failure or gastroenterology problems have associated complications of exudative detachments. Care has to be taken by the ophthalmologist to differentiate if the ERDs are a result of a complication of the systemic disease or are primarily an ocular pathology. Zalts et al. [19] reported a case of VKH associated with renal failure while Anadol et al. [20] reported a case of mesenteric ischaemia with VKH. In these two cases, the exudative detachments are part of the triad of VKH and not a result of the renal failure or mesenteric ischaemia.

Another important reason for differentiating if the cause of the exudative detachment is due to a primary ocular pathology or secondary to a systemic illness is that the management can be difficult. While most cases of exudative detachments secondary to a systemic illness improve with treatment of the underlying disease with high-dose systemic steroids and immuno-suppressants, primary ocular pathologies like central serous retinopathy (CSR) are worsened by systemic steroids [3]. In Case 2, it was a clinical judgement call by the attending ophthalmologist to treat the condition as an exudative detachment. The patient was monitored closely with the intention to stop systemic steroids if she got worse. If a CSR is suspected, the attending ophthalmologist should inform the treating physician as alternative medications other than systemic steroids may be required. The diagnosis of hypoalbuminaemia leading to exudative detachment should be that of exclusion, after a thorough history and investigations. The patient should also be informed of the possible ocular complications that can ensue with systemic immunotherapy.

Teaching points

(i) Hypoalbuminaemia from systemic diseases like protein-losing enteropathy or nephrotic syndrome is a rare cause of ERD.
(ii) With early recognition and treatment of the medical condition, the exudative detachments can resolve with good visual prognosis.
(iii) In patients with gastrointestinal and kidney disease presenting with blurring of vision, it is advisable to refer to the ophthalmologist for eye screening.

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References


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