SCIENTIFIC REPORT

Sub-inner limiting membrane haemorrhage: causes and treatment with vitrectomy

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Background: Preretinal haemorrhages usually occur at the interface between the posterior hyaloid and inner limiting membrane (ILM). Less frequently, they are located between the ILM and the retinal nerve fibre layer. Sub-ILM haemorrhages have been described in a variety of clinical settings and often lead to severe visual impairment because of their predilection for the macular region.

Methods: A consecutive series of five cases in which sub-ILM haemorrhages were clinically suspected and confirmed during early vitrectomy with ILM peeling were reviewed.

Results: Sub-ILM haemorrhages were clinically suspected in five patients (median age 32 years) based on the fundoscopic appearance and clinical setting of Terson's syndrome (n=1), Valsalva retinopathy (n=2), blood dyscrasia (n=1) and blunt facial trauma (n=1). Vision was severely impaired in all patients (to hand movements in four of five) because of a premacular location of the haemorrhage. All patients were treated with early pars plana vitrectomy because of insufficient spontaneous visual recovery after a median of 6 weeks. The sub-ILM location of the haemorrhage could be confirmed intraoperatively in all patients by biostaining of the membrane overlying the haemorrhage. ILM peeling and aspiration of the haemorrhage resulted in excellent visual recovery in all patients. No procedure-related complications were observed.

Conclusions: Sub-ILM haemorrhages often occur in a specific clinical context and can lead to severe visual impairment in young patients. Given the excellent results and low complication rates, timely surgical intervention is justified when spontaneous resorption is insufficient.

Preretinal haemorrhages usually occur at the interface between the posterior hyaloid and inner limiting membrane (ILM). Less frequently, they are located in the superficial retina between the ILM and the retinal nerve fibre layer.^{1–3} These sharply demarcated, dome-shaped haemorrhages show a predilection for the macular region and consequently lead to severe visual impairment.

Sub-ILM haemorrhages have been associated with various different causes, the most common being Valsalva retinopathy⁴ and Terson's syndrome.⁵ However, the sub-ILM nature of the haemorrhage remains difficult to distinguish clinically. We report on five cases in which the sub-ILM location of the premacular haemorrhage was confirmed during pars plana vitrectomy. Independent of the underlying causes, excellent visual recovery was obtained by vitrectomy with ILM peeling and aspiration of the haemorrhage.

CASE REPORTS

Case 1

A 42-year-old woman was referred with bilateral vitreous haemorrhage as a result of Terson's syndrome after

subarachnoidal haemorrhage. Vision improved spontaneously from bilateral light perception to 20/50 OD and 20/200 OS after 4 months. As there was no further improvement, vitrectomy was performed in the left eye, during which a sub-ILM haemorrhage became apparent. An ILM peeling was performed with complete evacuation of the haemorrhage. A vitrectomy of the right eye, performed 3 months later, revealed a similar sub-ILM haemorrhage and was treated correspondingly. Both procedures were successful with postoperative vision of 20/20 OU.

Case 2

A 20-year-old student presented to the emergency room with impaired vision of the left eye after repeated stress-related vomiting. Funduscopy examination revealed two intraretinal haemorrhages, the largest being situated premacularly (fig 1). After exclusion of other causes, a tentative diagnosis of Valsalva retinopathy was made. Considering the premacular location of the haemorrhage without spontaneous resorption after 2 weeks, we decided to perform a vitrectomy. Intracyanine green staining⁶ revealed the sub-ILM location of both haemorrhages, which were subsequently evacuated. Vision improved from hand movements preoperatively to 20/20 after vitrectomy.

Case 3

A 24-year-old construction worker was referred with a vitreous and premacular haemorrhage of the right eye. A sub-ILM haemorrhage was diagnosed during vitrectomy, performed 6 weeks later. Vision improved from hand movements preoperatively to 20/20 after surgery. History revealed repetitive episodes of vomiting as a result of anxiety disorder, suggesting a diagnosis of Valsalva retinopathy.

Case 4

A 33-year-old man, treated with chemotherapy for acute myeloid leukaemia, was referred with a bilateral vitreous haemorrhage based on severe thrombocytopenia. His vision was severely impaired to bilateral hand movements. A 25-gauge vitrectomy of the right eye was performed after 6 weeks, and revealed a sub-ILM haemorrhage. The roof of the haemorrhagic cyst was excised and sent for pathological examination. Microscopy with histochemical staining confirmed the ILM nature of the excised specimen (fig 2). Postoperative vision improved to 20/50 OD. Vitrectomy of the left eye, performed 3 months later, showed no sub-ILM haemorrhage. Unfortunately, the patient died 8 days later from an intracranial haemorrhage.

Case 5

A 32-year-old patient was referred for sudden visual loss of the left eye after blunt facial trauma. Ultrasound examination of

Abbreviations: ILM, inner limiting membrane; Nd:YAG, neodymium-doped yttrium–aluminium–garnet; OCT, optical coherence tomography

Figure 1 Fundus photograph of the left eye (case 2) showing a large premacular sub-inner limiting membrane haemorrhage.

the left eye showed a vitreous and suprafoveal haemorrhage in the superficial retinal layers. As there was no spontaneous improvement after 6 weeks, a vitrectomy was performed, during which a sub-ILM haemorrhage was also evacuated. Postoperative vision improved to 20/32 OS.

SURGICAL METHODS

All patients underwent general anaesthesia. A standard 20-gauge three-port pars plana vitrectomy was performed in all except one patient (case 4), in whom a transconjunctival sutureless 25-gauge approach was used (see supplemental video file). A posterior vitreous detachment was created if it was not already present. After closure of the infusion line, intracyanine green was introduced into a fluid-filled eye directly into the posterior vitreous cavity over the macula with a blunt canula. Thus, sedimentation of dye occurs at the macular surface. After 2 min, the infusion line was reopened and the excess dye was removed from the vitreous cavity using a backflush canula. ILM peeling was performed and the liquefied blood was aspirated. Prophylactic circular endolaser treatment^{7,8} was applied to the peripheral retina and an air tamponade was used at the end of the surgery. Closure of the

Figure 2 Microscopic image showing the roof of the excised haemorrhage cyst (case 4). The inner limiting membrane (ILM) is clearly visible as a thin acellular layer surrounded by haemorrhagic debris (Giemsa $\times 400$).

conjunctiva was achieved with fibrin glue (Tissucol, Baxter AG, Vienna, Austria), except for the sutureless 25-gauge case.

DISCUSSION

Although various case reports have previously highlighted possible causes of sub-ILM haemorrhages,^{9–14} we are the first to report on a series representing the major causes of sub-ILM haemorrhage. In all six eyes of five patients, the sub-ILM location of the haemorrhage was confirmed during vitrectomy with ILM peeling and resulted in excellent visual recovery.

Causes of sub-ILM haemorrhages

Sub-ILM haemorrhages have been described in a variety of clinical settings. Valsalva retinopathy typically presents as a sudden visual loss in an otherwise healthy individual, caused by a premacular haemorrhage secondary to a Valsalva manoeuvre. The most frequently reported causes of Valsalva manoeuvre include vomiting, coughing, strain and physical activities.^{15–17} A sudden increase in pressure in the intraocular veins, secondary to an increased intrathoracic pressure, causes spontaneous rupturing of perifoveal capillaries. Predilection to the macula is explained by the absence of firm attachments of the ILM to the retina at the posterior pole peripheral from the macular fovea.^{1,3}

Terson's syndrome encompasses any intraocular haemorrhage associated with intracranial subarachnoid haemorrhage and increased intracranial pressures. Premacular haemorrhages have been reported in up to 39% of cases,^{2,12} often with a location beneath the ILM.^{10,12,18} The pathogenesis of Terson's syndrome has been controversial. A mechanism similar to Valsalva retinopathy, in which an increase in intracranial pressure eventually leads to the rupture of retinal capillaries, has been supported by most authors.^{19,20} Although earlier reports had assumed a direct expansion of the intracerebral blood into the intraocular space through the optic nerve sheath, pathological evidence argues against this hypothesis.^{5,21}

Blood dyscrasia has been associated with premacular and sub-ILM haemorrhages in a number of reports.^{13,22} The combination of severe anaemia and thrombocytopenia has been hypothesised to cause, respectively, reduced endothelial cell integrity of the retinal vasculature and reduced coagulability, allowing blood to leak through the jeopardised endothelial barrier.^{22,23} This most often occurs in the clinical setting of haematological malignancies treated with high-dose chemotherapy.

Other causes of sub-ILM haemorrhages described in case reports include ruptured retinal macro-aneurysms,¹¹ blunt or penetrating ocular trauma²⁴ and shaken baby syndrome.¹² In some patients, no obvious cause can be identified and the sub-ILM haemorrhage is assumed to be idiopathic.¹³

Diagnosis of sub-ILM haemorrhages

Sub-ILM haemorrhages funduscopically appear as sharply demarcated, dome-shaped haemorrhages at the posterior pole. A glistening light reflex reflected from the ILM overlying the haemorrhage can often be observed. However, it is usually difficult to distinguish clinically between a sub-ILM and a subhyaloid haemorrhage.^{9,25} Whereas the latter tends to move slowly towards the bottom of the eye after a change in the patient's head position, the former is immobile. The use of optical coherence tomography (OCT) to identify the plane of the haemorrhage has been investigated in patients with Valsalva retinopathy.^{1,4,9} OCT performed just above the level of sedimented blood can demonstrate two distinct membranes: a highly reflective band immediately above the premacular haemorrhage, corresponding to the internal limiting membrane, and an overlying patchy membrane with low optical reflectivity consistent with the posterior hyaloid. Although a

useful diagnostic tool in most patients, OCT can be misleading. Despite its high resolution and ability to differentiate the retinal layers, misinterpretation of the level of the haemorrhage can occur because of high blood reflectivity in recent haemorrhages.²⁶ At present, the only method to confirm the sub-ILM location of an intraretinal haemorrhage remains intraoperative biostaining of the membrane overlying the haemorrhage and pathological examination of the excised membrane. This kind of histological confirmation has already been reported for patients with Valsalva retinopathy^{1 4 9} and Terson's syndrome.^{2 10 12 18}

Treatment of sub-ILM haemorrhages

Spontaneous resorption of the sub-ILM and associated vitreous haemorrhages depends on their severity and tends to be slow in extensive haemorrhages. Prolonged contact of the retina with haemoglobin and its catabolites can possibly cause toxic retinal damage, which may be irreversible.^{2 27} Other potential complications of longstanding intraocular blood persistence include cataract, epiretinal membranes and other macular abnormalities, glaucoma, retinal detachment, proliferative vitreoretinopathy, and amblyopia and myopia in infants.^{2 12 28}

Puncturing the ILM by means of pulsed neodymium-doped yttrium–aluminium–garnet (Nd:YAG) laser has been used in Valsalva retinopathy to cause immediate drainage of the haemorrhage into the vitreous cavity. It is an effective procedure in fresh cases less than 21 days.²⁹ It achieves rapid resolution of premacular subhyaloid haemorrhages with restoration of visual function, preventing the need for vitreoretinal surgery.^{29–31} Complications of Nd:YAG laser membranotomy include macular hole, retinal detachment,²⁷ epiretinal membrane formation⁹ and a persistent premacular cavity.¹ Argon and krypton laser membranotomy have also been tried with some success.³² Other modalities include pneumatic retinopexy (with or without tissue plasminogen activator), displacing the haemorrhage from the fovea.^{33 34}

Treatment with vitrectomy has been shown to result in significant and immediate visual improvement and may also prevent blood-related complications.² Common complications of vitrectomy are increased intraocular pressure, cataract and retinal detachment, although none of these occurred in our patient series. Recurrent haemorrhage after vitrectomy has also been described recently in the particular setting of a retinal artery macro-aneurysm.³⁵

CONCLUSIONS

In our opinion, the premacular location of sub-ILM haemorrhages causing severe visual impairment in young patients justifies a timely surgical intervention when spontaneous resorption is insufficient. Moreover, the exact location of the haemorrhage can be ascertained. We did not encounter any surgical complications in our case series, and complication rates reported in the literature are low, including a retinal tear, retinal detachment and cataract.² We found vitrectomy to be a safe and effective alternative to observation and Nd:YAG laser treatment, offering rapid visual recovery in patients with extensive sub-ILM haemorrhages.

Video file is available at <http://bjophth.com/supplemental>

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