Medical and surgical management of spontaneous hyphaema secondary to immune thrombocytopenia

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SUMMARY The medical and surgical management of an unusual case of spontaneous 'black ball' hyphaema complicated by secondary haemorrhage, raised intraocular pressure and corneal blood staining, and secondary to immune thrombocytopenia is presented. The literature is reviewed with particular reference to the aetiology and treatment of spontaneous hyphaema and the role of intravenous immunoglobulins in the preoperative management of patients with thrombocytopenia who present for routine or emergency ocular surgery.

Spontaneous hyphaema is relatively uncommon. Only three cases have been reported of its association with thrombocytopenia by Graves in 1837,¹ by Werner and Adlerkreutz in 1931,² and recently by Ackerman *et al.*, who reported a case of spontaneous vitreous haemorrhage associated with thrombocytopenia in which a secondary hyphaema developed.³

Case report

The patient, a 59-year-old Caucasian woman, presented with a three-day history of a red, uncomfortable left eye and diminished left visual acuity. There was no history of trauma. Her visual acuity before onset of symptoms was 6/6 right and 6/9 left. The patient had been referred to the haematology clinic in 1984 with thrombocytopenia. Investigations revealed a leucocyte count $7.1 \times 10^9/l$ and a platelet count $85 \times 10^9/l$. The white cell differential count was normal. Her antinuclear factor was positive and the DNA binding 35 units/ml (normal=1-25). A bone marrow aspirate was of normal cellularity with an increased number of megakaryocytes, consistent with peripheral destruction or sequestration of platelets. Blood coagulation tests gave normal results and there was no splenomegaly. Although indirect immunofluorescence tests were negative for platelet antibodies, these findings were compatible with a

diagnosis of chronic immune thrombocytopenia (ITP), possibly associated with systemic lupus erythematosus, despite the absence of supporting clinical features.

On admission to hospital her visual acuity was 6/9 in the right eye and perception of light in the left eye. There was a subtotal left hyphaema of approximately 80%. The corneal epithelium was oedematous and the intraocular pressure raised (75 mm Hg). The platelet count was $49 \times 10^9/l$.

The patient was advised bed rest and received topical timolol drops and intravenous acetazolamide. Acetazolamide was continued orally. During the first 24 hours there was a modest fall in the intraocular pressure followed the next day by further bleeding into the anterior chamber. The patient developed a total or 'blackball' hyphaema (Fig. 1), with a further increase of the intraocular pressure (70 mm Hg). Six units of platelets were transfused over each of the first three days. On the third day, in an attempt to secure haemostasis and with evidence of further anterior chamber haemorrhage, oral prednisolone (40 mg daily) was begun, together with an intravenous infusion of immunoglobulins over three days (Sandoglobulin 400 mg/kg body weight). Daily platelet counts were obtained, and their changes in relation to treatment are shown in Fig. 2. There was no reduction in the size of the hyphaema and the intraocular pressure remained raised (50 mm Hg). Surgical intervention was indicated with the develop-

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Fig. 1 Total hyphaema shortly after admission.

Fig. 3 Second postoperative day. Small residual blood clots can be seen adherent to the corneal endothelium.

ment of corneal blood staining and evidence of early organisation of the clot.

Prior to surgical evacuation the patient received the antifibrinolytic agent tranexemic acid, 1 g three times a day. A Simcoe irrigation/aspiration cannula was introduced through a 3 mm limbal corneal incision, and approximately 90% of the hyphaema was aspirated. A small peripheral iridectomy was made at the 3 o'clock position directly below the corneal incision. In the initial postoperative period there were several small residual blood clots adherent

to the endothelium, and the cornea was partially decompensated with corneal epithelial oedema (Fig. 3). The intraocular pressure, however, remained normal, and there was no further anterior chamber haemorrhage. The several small residual blood clots adherent to the endothelium were reabsorbed over the ensuing weeks, and at a subsequent review five months later her corrected visual acuity was 6/12. The corneal epithelial oedema had resolved and the intraocular pressure was normal.

Discussion

Anterior chamber haemorrhage is usually associated with ocular trauma. Spontaneous hyphaema is relatively uncommon, being noted mainly in younger patients. Spontaneous haemorrhage may occur from abnormal anterior chamber vessels associated with iris melanoma, retinoblastoma, juvenile xanthogranuloma, or rubeosis secondary to diabetes mellitus or Fuchs's uveitis syndrome.^{4,6} Fibrovascular membranes of retrolental fibroplasia, retinoschisis, and persistent primary vitreous may also bleed into the anterior chamber.⁵ Haemorrhage from iris neovascular tufts near the pupillary frill was first reported in 1973.⁷ Haemorrhage has also been noted in cases of anterior uveitis associated with herpes zoster, diabetes mellitus, and Beçet's syndrome.⁸ Ormerod and Egan in 1987 reported 16 cases of spontaneous hyphaema and corneal haemorrhage as a complication of microbial keratitis.⁹ Spontaneous hyphaema has also been noted in conjunction with blood dyscrasias, notably leukaemia, haemophilia, sickle cell anomalies, and

Fig. 2 Changes in platelet count in response to treatment.

malignant lymphoma.¹⁰ Kzgeler *et al* reported a case of spontaneous hyphaema secondary to ingestion of aspirin and alcohol,¹¹ related presumably to a reduction in platelet function.

Immune thrombocytopenia (ITP) is a heterogeneous syndrome of unknown aetiology characterised by a reduction in the platelet count, normal or increased number of bone marrow megakaryocytes, and a shortened platelet life span. In a variable proportion of patients (3-16%) it may be an early manifestation of systemic lupus erythematosus (SLE).¹² An increased frequency of HLA DRW2 and a high female predominance also link the two diseases.¹³ There is evidence that peripheral destruction of platelets is responsible for the thrombocytopenia in SLE.¹⁴ The mechanism may involve either antiplatelet antibodies or immune-complex mediated destruction by reticuloendothelial cells.

Conventionally the primary treatment of ITP has been systemic corticosteroids giving a remission rate of up to 80%. There is a high relapse rate, and in these patients together with those refractory to steroids splenectomy is sometimes indicated. More recently commercial preparations of intravenous immunoglobulins have been introduced as a novel treatment of patients with ITP. Preliminary studies by Imbach *et al*¹⁵ showed that some children with ITP respond to large doses of immunoglobulins, and this was confirmed by Bussel *et al*.¹⁶ High doses of intravenous immunoglobulins have also been shown to produce a rapid and predictable rise in the platelet count of adults with acute or chronic immune thrombocytopenia.^{17,18} The exact therapeutic mechanism remains uncertain, though a number of interesting theories have been proposed, of which the most popular is the blockade, by immunoglobulins, of the macrophage Fc receptors.¹⁸⁻²⁰

The medical management of uncomplicated hyphaema has been a subject of a number of studies. Edwards and Layden in 1973 reported no difference between monocular and binocular patching.²¹ Bed rest and sedation confers no statistically significant benefits on reabsorption of hyphaema or secondary bleeding rates.^{22,23} The reported incidence of the secondary bleeding rate varies widely (6-38%), with an overall approximate rate of 25%.²² The incidence is directly related to size of hyphaema, indirectly related to the patient's age, and is associated with concurrent aspirin ingestion.²⁴ The antifibrinolytic drugs aminocaproic acid and tranexamic acid have been recently advocated to reduce the incidence of secondary haemorrhage.^{25,26} They act principally through competitive inhibition of plasminogen activator, preventing conversion of plasminogen to plasmin, maintaining the integrity of the fibrin clot, and reducing the opportunity of the damaged vessels

to bleed again. Systemic steroids²⁷ and oestrogens²⁸ have been largely discarded in the routine management of hyphaema.

There was a modest transient rise in the platelet count in response to the initial platelet transfusions. However, with the continued anterior chamber haemorrhage and the prospect of surgery it became apparent that intravenous immunoglobulins were indicated to secure and maintain adequate haemostasis. The sustained rise in platelet count was almost certainly directly attributable to the intravenous immunoglobulins. Transfused platelets in the setting of immune thrombocytopenia have a very short lifespan,²⁹ and steroids often take up to two weeks to induce a rise in platelet count.³⁰ There is also evidence of a cumulative effect of combining steroids and immunoglobulins in producing a higher and more sustained rise in the platelet count.³¹ The ability of commercial high-dose preparations of immunoglobulins to produce a dramatic correction of thrombocytopenia enables otherwise hazardous emergency surgical procedures to be carried out safely.^{17,32,33}

For small hyphaemas conservative medical management provides the best overall results, but for larger hyphaemas the indications for surgical intervention are: (1) sustained elevation of the intraocular pressure unresponsive to treatment; (2) microscopic corneal blood staining; and (3) evidence of organisation of the clot, with the potential for the formation of peripheral anterior synechiae.^{34,35}

Surgical evacuation of hyphaema may present difficulties. It has been suggested that the optimum time for evacuation is four days, which allows for optimal clot retraction while avoiding the problems of clot organisation and integration with adjacent structures.³⁶ Many different surgical procedures with varying degrees of success have been described, including, irrigation with fibrinolytic agents, cryo-extraction, viscoelastic extrusion, ultrasonic emulsification, and the use of vitrectomy instrumentation.³⁶⁻⁴¹ The use of the Simcoe irrigation-aspiration cannula introduced through a small corneal incision proved to be very satisfactory. The risk of prolapse of intraocular contents was reduced by the small incision. The variable infusion pressure ensured the maintenance of the anterior chamber depth to protect the corneal endothelium. In addition there was the opportunity to tamponade any subsequent haemorrhage by alteration of the infusion flow rate.

CONCLUSIONS

A haemorrhagic diathesis should be considered in all cases of atypical spontaneous hyphaemas. If a surgical procedure is indicated, in the presence of immune thrombocytopenia, intravenous immunoglobulins may have a useful role in the management.

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