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SEVERE OPHTHALMOLOGIC COMPLICATIONS FOLLOWING FAVISM*

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FAVISM is not uncommon in Greece and every spring quite a few children suffering from variable degrees of acute haemolytic anaemia due to the ingestion of broad beans are admitted to our department.

We have recently had the opportunity to hospitalize two such patients who developed serious ophthalmic complications. Since such complications were encountered for the first time and no relative information was found in the literature we thought it worthwhile to record our experience.

Case Reports

Case 1, a boy aged 3, developed malaise, vomiting, haemoglobinuria, and jaundice on April 27, 1958. He had eaten broad beans the previous day.

On admission on April 28, he was in coma (not responding to light), and deeply jaundiced. The body temperature was 39·6° C., respiration 60/min., pulse 180/min., and blood pressure 75/45 mm. Hg. His lower limbs were spastic and an extensor plantar reflex was easily elicited bilaterally. The liver and spleen were palpated 3 cm. below the costochondral margins. His urine was red and contained large amounts of haemoglobin.

The patient was immediately given a transfusion of 150 ml. whole blood and during the ensuing 24 hrs he received a total of 1,000 ml. whole blood plus 500 ml. of equal amounts of saline and glycose 5 per cent. He was also given prednisone 5 mg., penicillin 200,000 units 6-hrly, and aspirin.

Laboratory Findings (April 29).—Haemoglobin 6 g. per cent., red cell count 2,300,000 cu. mm.; bilirubin 5·8 mg. per cent. (indirect 2 mg. per cent.), blood urea 66 mg. per cent., CO_2 combining power 20·3 mEq/l., Na 148 mEq/l., and K 3·98 mEq/l.

For the next 3 days the patient was given daily transfusions of 150 ml. whole blood, the diuresis gradually became normal, and the urine cleared completely. He was still in coma, and an electro-encephalogram showed irregular slow waves in all leads.

On May 1 he suddenly developed widespread ecchymoses on the buttocks and legs, and vomited "coffee-ground" material. Several times, the blood pressure was 85/45 mm. Hg and the general condition deteriorated.

Laboratory Findings.—Haemoglobin 5·35 g. per cent., white blood cell count 26,000 cu. mm. (polymorphonuclears 74 per cent., lymphocytes 24 per cent., mononuclears 2 per cent.), platelets 26,000 cu. mm., bleeding time 8 min., clotting time within normal limits.

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During the next few days he came gradually out of the coma, the haemoglobin rose to 8 g. per cent. and the platelets to 60,000 cu. mm. New ecchymoses did not appear and the general condition improved considerably, but he was completely blind.

On May 15, 1958, the blood count was normal. Platelets 300,000 cu. mm. Myelogram normal. The patient was receiving large doses of calcium and vitamins C, K, B, and B_2.

Ophthalmological Examinations.—On May 1, 1958, the third day in hospital, the pupils were mydriatic and did not respond to light. Vitreous body clear. In the fundus the discs were prominent with slightly blurred margins, and distended and tortuous veins. There were widespread retinal and pre-retinal haemorrhages mainly in the posterior pole.

On May 8, 1958, the pupils were still mydriatic, and did not respond to light. The fundi could not be seen because of infiltration of the hyaloid body with blood. The patient was quite blind.

On May 15 there was no significant change, but the eyes were now able to distinguish light from darkness.

On May 29, 1958, the fundi were still not visible, although there was some clearing of the vitreous body. Ophthalmological examination every 15 days until the patient's discharge from hospital on August 22 revealed organization of the haemorrhages and only minimal clearing of the vitreous body.

Case 2, a boy aged 6, was admitted to hospital on April 25, 1958, because of sudden onset of blindness. He had had an acute attack of favism 10 days earlier for which he had been hospitalized elsewhere, and had rapidly improved so that he had been discharged on April 21 without receiving any treatment. Two days later he complained of partial loss of sight which rapidly became almost total.

On admission the results of the clinical examination and of the laboratory investigations were essentially normal.

Ophthalmological Examination.—The pupils were moderately enlarged, and responded only very slightly to light. The discs were rather prominent with blurred margins; the retinal vessels, particularly the arteries, were constricted; a few scattered haemorrhages in the proximity of the discs were also present. The visual acuity was hand movements.

On May 8, 1958, the discs were pale with persisting blurring of the margins. The narrowing of the arteries was still present, but the haemorrhages round the discs were almost completely absorbed. Visual acuity was counting fingers.

On May 15, 1958, the discs were pale with the margins better defined. The arteries were narrow but the haemorrhages were completely absorbed. The visual acuity was counting fingers at 1 metre.

On May 22, 1958, there was no change.

On June 6, 1958, the discs were very pale but with well-defined margins. The retinal vessels were still narrow. The visual acuity was 1/10 in the right eye and 1/20 in the left. The visual fields were difficult to examine because of the patient's age, but central scotomata were observed and peripheral loss, particularly downwards. The patient was discharged from hospital on June 25, 1958, and has not been seen since.

Discussion

Although both patients showed severe ophthalmological complications after an acute attack of favism, only one developed generalized haemorrhagic phenomena simultaneously. It therefore appears reasonable to assume that the mechanism responsible for the ocular complications was different in each case.

Case 1.—Drinker and Brittingham (1919) described a patient who developed a haemorrhagic syndrome following a large transfusion of incompatible blood. Krevans, Jackson, Conley, and Hartmann (1957) reported two similar cases in which hypofibrinogenaemia, hypoprothrombinaemia, and thrombocytopenia were observed; there was no evidence of increased fibrinolytic activity and in one patient accelerin activity was reduced.

Disturbances of blood coagulation resulting in haemorrhagic phenomena were also described by Crosby and Stefanini (1952) in patients with paroxysmal nocturnal haemoglobinuria following plasma transfusions.

All these authors consider that an intravascular coagulation, presumably initiated by the thromboplastin-like activity of the haemolysed red blood cells, is the most likely explanation for the haemorrhagic diathesis. Such a concept appears to apply to our first patient, who developed an acute haemorrhagic state with prolonged bleeding time and thrombocytopenia following an extensive haemolysis due to favism. The possibility that the patient was transfused with incompatible blood can be ruled out. The retinal and pre-retinal extravasation which occurred might be easily attributed to the generalized haemorrhagic state. Similar retinal haemorrhages have been also described in idiopathic thrombocytopenic purpura.

If the haemorrhages are restricted to the retina, the prognosis is usually good because they may be absorbed without causing any permanent damage. However, when the haemorrhages into the hyaloid body are extensive and diffuse, the prognosis is poor, because of the ensuing organization which eventually leads to retinal detachment.

Case 2.—The pathogenesis of the ophthalmological findings in the second patient (oedema and blurred margins of the discs as well as constriction of the retinal vessels with small haemorrhages), is obscure. To the best of our knowledge no such ocular findings associated with favism or any other acute haemolytic syndrome have been reported in the literature. The blurring of the disc margins, slight papilloedema, narrowing of the retinal arteries, and small haemorrhages round the discs as well as the later changes (secondary optic nerve atrophy, marked narrowing of the arteries, disturbances of the visual fields), and the sudden bilateral loss of vision 7 days after an acute haemolytic syndrome, resemble the clinical picture sometimes observed after acute haemorrhage.

Haemorrhages from the gastro-intestinal tract or uterus may be followed by severe visual disturbances and occasionally by blindness (Pincus, 1919; Terrien, 1921; Barr, 1934; Traquair, 1938; Bamford and Barber, 1940; Unger, 1955); these complications usually appear 3 to 7 days after the onset of haemorrhage and may progress to complete blindness within a few hours. The fundus appearances are similar to those observed in our case. The prognosis is usually poor, 50 per cent. of the cases never improving and only 10 per cent. recovering completely.

The pathogenesis of these post-haemorrhagic complications is not known. Many authors consider anaemia to be the main factor, while others believe that some other systemic factor is essential for these changes to develop.

In our cases the anaemia following an episode of acute haemolysis may be regarded as similar to post-haemorrhagic anaemia, and this (together with a toxic factor, possibly that responsible for the haemolysis) may have caused the severe ocular involvement.

Summary

Severe ophthalmological complications followed an attack of favism in two children.

The visual loss in the first patient is attributed to a generalized haemorrhagic diathesis. The visual disturbances in the second patient are considered to be similar to those which may follow a severe haemorrhage.

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