

PROPTOSIS IN LEUKAEMIA*†

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ACUTE leukaemia is a common cause of death amongst children and in recent years the emphasis has been centred on the cellular elements involved, especially in relation to treatment and prognosis. Various types of acute granulocytic leukaemia have become recognized, one of which is promyelocytic leukaemia, in which the predominating cell is a primitive precursor of the granulocytic series. Acute promyelocytic leukaemia was described by Bernard, Mathé, Boulay, Céoard, and Chomé (1959) and, in a later communication, Bernard, Boiron, Weil, Lévy, Seligmann, and Najean (1962) reported that they had seen at their Institute a total of 34 cases of acute promyelocytic leukaemia in a series of 497 cases of acute leukaemia between 1956 and 1962. Children and females predominated in the series.

Acute promyelocytic leukaemia is characterized by the presence of a large proportion of cells of promyelocytic type in the bone marrow, associated with the clinical and haematological features of acute leukaemia. Anaemia is intense, thrombocytopenia and hypofibrinaemia are the rule, and death is usually associated with haemorrhagic manifestations, the liver and spleen being the most frequently infiltrated organs.

A fatal case of acute promyelocytic anaemia, which presented with unilateral exophthalmos, is reported below.

A baby girl aged 12 months was seen on April 9, 1963, in the Eye Department at the Royal Infirmary of Edinburgh, with a history of having been hit in the right eye by a young cousin's fist 3 weeks previously. Proptosis had developed almost immediately but no bruising of the skin was noted, the only other sign being some swelling of the right eyelids. Before this time the child had been perfectly healthy. She was the product of a normal full-term delivery and there was no history of any disease of a familial nature.

Examination.—A non-reducible axial proptosis affecting the right eye was noted. Eye movements were full, but there was a suggestion that the right pupil reacted sluggishly to light. The fundus was normal.

Examination under anaesthesia was performed on April 15, 1963, and a hard non-pulsatile mass, probably in the muscle cone, could be felt.

X-ray examination of the orbits was reported as normal.

A blood examination gave the following results: Hb 65 per cent.; erythrocyte sedimentation rate 5 mm. in the first hour; white blood count 7,200 (17 per cent. neutrophils, 83 per cent. lymphocytes).

Though at the time it was felt that the proptosis was either a traumatic haematoma associated with an orbital haemangioma, or a simple localized haematoma, a paediatric opinion was sought because of the anaemia and relative lymphocytosis. Accordingly, she was seen on April 20, 1963, by Dr. D. M. Douglas and the late

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Mr. J. Mason Brown of the Royal Hospital for Sick Children, Edinburgh. They both felt that the proptosis was of traumatic origin and were disinclined, at that stage, to investigate the renal tract to exclude a neuroblastoma. The haemoglobin level was then 77 per cent.

By April 30, 1963, the proptosis had increased and a small subconjunctival haemorrhage was noted above the insertion of the right lateral rectus. No further ocular abnormality was noted, the right pupil reaction having returned to normal. She was admitted to the Royal Hospital for Sick Children on May 4, 1963, for a more detailed examination prior to possible exploration of the right orbit.

Apart from the right proptosis (Fig. 1), no physical abnormality was found.

X ray of the skull now showed a large soft tissue mass in the right orbit with no bone destruction; x rays of the pelvis and long bones showed no definite evidence of bone deposits, though a suspicious area was noted at the lower end of the right femur. Chest x ray was negative.

A blood examination gave the following results: Hb 62 per cent.; packed cell volume 25 per cent.; mean corpuscular haemoglobin concentration 36 per cent.; erythrocyte sedimentation rate 13 mm. in the first hour; white blood count 6,600 (1 per cent. neutrophils, 77 per cent. lymphocytes, of which 12 per cent. were immature lymphocytes and 16 per cent. abnormal cells, ? mononuclears); platelet count 72,000. On the blood film neutrophils were virtually absent, the majority of cells being mature lymphocytes, but there were some more primitive types resembling reticulum cells.

A bone-marrow examination was therefore carried out, and the marrow was found to be totally replaced by sheets of large primitive cells having large nuclei with a fine chromatin network. The nature of these cells was uncertain, but the overall marrow picture was suggestive of acute leukaemia.

Peroxidase blood films showed that many of the immature cells were of the myelocytic series.

Throat, rectal, and nasal swabs gave no pathogens, a Heaf tuberculin test was negative, and serum B₁₂ was within normal limits.

The urine contained no clinical or microscopic abnormalities.

Diagnosis.—A provisional diagnosis of acute myelogenous leukaemia was made.

Treatment.—On May 9, 1963, because of the increasing proptosis, radiotherapy was given to the right orbit and, on the same day, treatment was begun with the anti-metabolic agent 6-mercaptopurine 50 mg./day and vitamin B₁₂ 1 mg./day.

Four days later the proptosis had regressed to about normal (Fig. 2, opposite), but the child's haemoglobin level had fallen to 45 per cent. and she was transfused with one pint of group O Rhesus-positive blood, which brought it up to 94 per cent. On May 20, 1963, the white blood count had dropped to 2,000 and the 6-mercaptopurine was reduced to 25 mg./day. No further proptosis occurred and, apart from



FIG. 1.—Right orbit before radiotherapy.

some bruising affecting both legs and a few palpable glands in the groin, the child remained well, though a repeat marrow examination showed no change from the previous findings. She was discharged home on May 25, 1963, on vitamin B₁₂ 1 mg. on alternate days, and 6-mercaptopurine 25 mg. on alternate days, tetracycline 125 mg. twice a day in view of the low white cell count, and Abidec vitamin complex.

Progress.—A week later she was seen again because of a large fungating tumour in the mouth growing from the left maxillary region (Fig. 3), which was treated by further radiotherapy. By June 12, 1963, she was complaining of pain in her legs and refused to put her feet to the ground. There was a pulp infection of the right thumb, but the mass in the mouth had greatly decreased in size. She was started on erythromycin 100 mg. three times a day in addition to the previous therapy, but by June 15, 1963, the haemoglobin level had dropped to 50 per cent. with a white blood count of 1,600 and a platelet count of 50,000.

She was re-admitted to hospital 4 days later because the haemoglobin had dropped to 36 per cent., widespread bruising had appeared again all over her back, and the spleen was firm and enlarged 1½ finger-breadths below the left costal margin. On June 26, 1963, after a further blood transfusion, treatment with prednisolone 60 mg./day was given and the 6-mercaptopurine was discontinued. At this stage a hard firm swelling developed below the right eye; this gradually became larger until on July 5, 1963, it measured 2.5 × 1 cm. The child was extremely miserable and was kept sedated with pethidine and Largactil.

Termination.—On July 8, 1963, she developed melaena, epistaxis, and subconjunctival haemorrhages with widespread bruising, and widespread enlarged lymph nodes were found in the axillae, inguinal region, and neck. She died on July 11, 1963, of hypostatic pneumonia.

Post-mortem Examination

The bone-marrow picture was the same as before; there was an enlarged spleen, moderately enlarged liver, and marked erosion of the lower end of the right femur from the medullary cavity. There was little evidence of tumour within the muscle cone of the right orbit or in the left maxillary region, and a biopsy was taken from the mass under the right eye. This proved to be inconclusive and consisted of sheets of undifferentiated cells, which were considered to be haemoblasts.



FIG. 2.—Right orbit after radiotherapy.

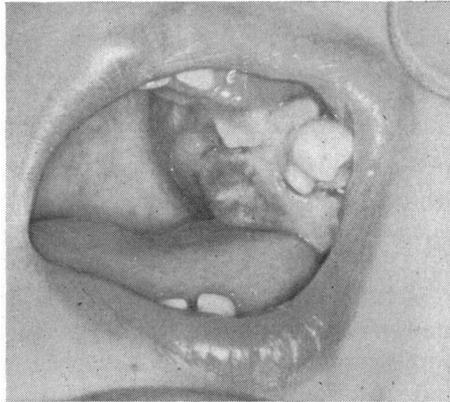


FIG. 3.—Fungating tumour in left maxillary region.

A report on the marrow film by Prof. D. L. Mollin of the Department of Haematology, Royal Postgraduate Medical School, London, was as follows:

"The marrow is hyperplastic, the great majority of the cells being primitive leukaemic cells, which contain azurophil granules. The cells resemble the promyelocytes seen in a normal marrow. The condition could be called acute promyelocytic leukaemia."

Discussion

It is unusual for proptosis to be the presenting feature of acute leukaemia in children, although it may occur later in the course of the disease. Crawford (1952) found six cases of proptosis due to leukaemia in a survey of 131 children with proptosis. In the case reported above it is difficult to pinpoint the exact nature of the proptosis in the first instance, but the most likely explanation is that it was due to a haemorrhage caused by the reported trauma, into a deposit of leukaemic cells. That a deposit of cells did exist seems beyond doubt, since the proptosis responded so rapidly to radiotherapy.

In this child no ocular abnormality was noted, though the fundus is frequently involved in myelogenous leukaemia. Porterfield (1962), in a survey of 214 cases of orbital tumour in children, found twelve of haematopoietic origin, and six of these occurred in the age group 1 to 5 years. In this same age group, it is interesting to note that only three cases of metastatic neuroblastoma occurred; indeed, only three were found in the whole series. It is significant that, among the malignant orbital tumours in childhood in Porterfield's series, malignancies of haematopoietic origin were second only to rhabdomyosarcomata. Discussing this point, Porterfield stated that rhabdomyosarcomata, acute leukaemia, and undifferentiated reticulum cell sarcomata are much more important orbital neoplasms of childhood than has generally been appreciated in the past.

In our case the blood count was the clue to the diagnosis, though an indirect one, since the original routine blood count showed only a relative anaemia and lymphocytosis. In all cases of orbital proptosis, even if the peripheral blood count and film are not greatly abnormal, a bone-marrow biopsy should be performed and supra-vital staining techniques carried out. Only in this way can an early leukaemia in the aleukaemic phase be diagnosed.

Summary

A fatal case of acute promyelocytic leukaemia in a baby girl, who presented with proptosis, is described. A plea is made for full haematopoietic investigations in young children with proptosis.

I should like to thank Prof. G. I. Scott of the Department of Ophthalmology, The Royal Infirmary of Edinburgh, and Dr. D. M. Douglas of The Royal Hospital for Sick Children, Edinburgh, for permission to publish this case.

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