CASE REPORTS

AN UNUSUAL CASE OF ACUTE LEUKAEMIA

BY

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During the five-year period 1942-6 twelve children suffering from acute leukaemia were admitted to Alder Hey Children's Hospital, Liverpool. They were classified as follows:

Lymphatic leukaemia	7 cases
Monocytic	2 "
Myelocytic	3 "

Eleven were boys, and one girl; three of these children were under the age of four years and nine were over four. Ramsay (1927) in a much larger survey (one hundred cases) found that roughly twice as many occurred during the first four years of life as during the subsequent four years and the incidence steadily declines in adolescence. The condition is commoner in males (63 per cent.). The average duration of life is two to four months (Ramsay, 1927; Court and Edwards, 1939). Acute lymphatic leukaemia accounts for 75 per cent. of the cases described by Ramsay; in a smaller series of the same condition reported by Falkenstein and Fowler half the number were aleukaemic. Monocytic and myeloblastic types are much less common.

The case of acute leukaemia now recorded presented several unusual clinical features and a special problem of diagnosis.

Case History

J.H., a boy aged 2 years 9 months, was admitted to Alder Hey Children's Hospital on Oct. 25, 1947, with a three weeks' history of pallor and listlessness. There had been swelling of the left cervical glands for one week preceding admission. He had not lost weight and his appetite was good. His birth and subsequent progress had been normal; he had had no serious illness.

Family history. He was the fifth child of healthy parents. All the siblings living were healthy. The first baby died as a result of birth injury.

Clinical examination. On admission the child was extremely pale but otherwise well-nourished, weighing 30 lb. The temperature was 101° F., the pulse rate 120 per minute, and the respirations 24 per minute. There was bilateral enlargement of the posterior and anterior cervical, axillary, and inguinal glands. The liver edge was one inch below the right costal margin, and the tip of the spleen was

just palpable. No abnormal physical signs were found in the nasopharynx, ears, eyes, lungs, heart, or central nervous system.

A blood count made shortly after admission was as follows: haemoglobin less than 28 per cent. (3.6 g. per cent.); red blood cells 1,040,000 per c.mm. of blood; white blood cells 19,900 per c.mm., of which the majority appeared to be blast cells. Platelets were greatly reduced in number. A transfusion of one pint of compatible blood was given on the evening of admission.

Course. Two days after admission a few petechiae were found on the trunk, and small areas of bruising appeared behind the left ear and around the right orbit. This latter area increased in size during the following week with the gradual onset of proptosis and right ophthalmoplegia. An ophthalmological report stated that there was conjunctival oedema, corneal infiltration, and proptosis of the right eye equivalent to 10 mm., but no movement. The optic fundus could not be seen.

Following the blood transfusion the haemoglobin increased to 34 per cent. (4.7 g. per cent.); the red blood cells numbered 1,810,000 per c.mm. and the white blood cells 3,600 per c.mm. of blood. On Nov. 7, 1947, however, the haemoglobin had again fallen to 26 per cent. (3.6 g. per cent.). On this date sternal puncture showed a very cellular marrow with the following differential count: myeloblasts 4.4 per cent.; premyelocytes 1.6 per cent.; myelocytes 28.0 per cent.; metamyelocytes 7.2 per cent.; polymorphonuclears 2.8 per cent.; normoblasts 17.6 per cent.; lymphocytes 4.4 per cent.; smear cells 1.6 per cent. The remaining 32.4 per cent. were cells 7 to 10 μ in diameter, with scanty dark blue cytoplasm devoid of granules, and an oval or round nucleus, sometimes indented with rather coarse chromatin threads and up to three indistinct nucleoli. These were finally considered to be atypical myeloblasts.

Proptosis steadily increased and there was much distress, probably due to pain. Early on the morning of Nov. 8, 1947, the night nurse was alarmed to find that the right eye had been extruded and was lying on the pillow. The eyelids were inflamed and oedematous and there was a little purulent discharge from the socket. These local conditions responded rapidly to a course of systemic penicillin (500,000 units daily in six divided doses; total amount given: 5,000,000 units).

Immediately after the loss of the eye the child's general condition improved considerably. The temperature, which previously had ranged between 99° and 100° F., now settled and remained at 98° F., until the terminal phase of the illness. The cervical glands became much smaller and the axillary and inguinal glands and spleen were no longer palpable. The child was happy and contented, interested in his toys and talkative. He remained well for three weeks and gained 1 lb. in weight.

The following investigations were made during this period: the Mantoux reactions, blood Wassermann reaction, and Widal reaction were all negative. Blood urea was 24 mg. per 100 c.cm. Skull and chest radiographs were normal, and urine analysis was also normal (no Bence-Jones protein). Total white blood counts from Nov. 7 to Nov. 27 varied between 2,900 and 8,000 per c.cm. of blood with 40 to 50 per cent. polymorphonuclears, a similar number of lymphocytes, and only scanty immature myeloid cells.

Two further blood transfusions (half a pint on each occasion) were given on Nov. 8 and 13, and by Dec. 4 the haemoglobin was 92 per cent. (12.9 g. per cent.).

Despite the child's general well-being, however, his parotid and submaxillary salivary glands began to increase in size. The mouth and nasopharynx appeared healthy, but haemolytic streptococci (group A) were grown from a throat swab. A further course of systemic penicillin was given (500,000 units daily: total 9,000,000 units).

During the first fortnight in December the haemoglobin level remained fairly constant, but the white cell picture gradually changed, and a count made on Dec. 17 gave 76 per cent. blast cells in a total of 16,700 white cells per c.mm. of blood. Scanty nucleated red blood cells were also present. Sternal puncture on Dec. 9 showed greatly increased cellularity with approximately 95 per cent. blast cells. The peroxidase reaction, morphology, and cell distribution in marrow and peripheral blood indicated that the leukaemia was of myeloblastic type.

During the last two weeks of December his condition began to deteriorate rapidly. Parotid, submaxillary, and cervical glands increased in size and the spleen was felt three inches below the left costal margin. The white cell count rose to 50,000 per c.mm. of blood on Dec. 29, and the cells were practically all myeloblasts. A supply of nitrogen mustard was obtained and treatment started (dose: 0.1 mg. per kg. body weight per day for three days) but the child died on Jan. 1, 1948.

Post-mortem examination. Unfortunately, permission was given for only a limited examination (excluding the brain).

GLANDS. Submaxillary, cervical, and tonsillar glands were enlarged and hard. There was no structural destruction. The thyroid was normal.

CHEST. Heart and lungs appeared normal.

ABDOMEN. The pancreas was enlarged and hard. The kidneys were enlarged and pale, with numerous capsular and subcapsular haemorrhages. The right kidney weighed 256 g. (normal 48 g.); the left weighed 251 g. (normal 49 g.). The spleen was enlarged and hard, weighing 100 g. (normal 37 g.). The liver and alimentary tract appeared normal.

HISTOLOGICAL REPORT. Throughout the kidney, pancreas, and submaxillary glands there was a heavy infiltration of small cells with little cytoplasm and a deeply-stained round, oval, or indented nucleus. Occasional myelocytes and polymorphonuclears were present. In the liver a similar infiltration was largely confined to the periportal areas. In the lymph nodes, and to a lesser degree in the spleen, there was replacement of the normal follicular structure by a uniform infiltration of these cells. The appearances supported the diagnosis of acute leukaemia.

RIGHT EYE. There was complete necrosis of all structures, which included the ciliary body, iris, and parts of the sclera and cornea. There was no evidence of gross inflammatory reaction or tumour.

Discussion

An unusual feature of this case was the loss of an eye. Proptosis occurred as a presenting symptom in three other cases admitted to this hospital, but in none was the process so rapid and extensive that the eye was actually cast off. In the present case the eye appeared normal on admission and the total length of time from the onset of the peri-orbital ecchymosis to extrusion of the eye was twelve days.

Proptosis due to leukaemic infiltration has been reported by Leber (1869) and Werner (1905). Lagrange (1904) collected twenty-five cases and pointed out that the symmetrical nature is a fundamental characteristic. In the case recorded no infiltration of the left orbit was observed. The corneal oedema and infiltration precluded examination of the right fundus. This feature is unusual, but could be accounted for by raised intra-ocular tension due to orbital venous congestion. No case can be found in the literature of spontaneous expulsion of an eyeball due to leukaemic proptosis.

A provisional diagnosis of acute leukaemia was made on admission but was later reconsidered in view of the apparent initial response to treatment, with remission of symptoms and normal blood picture four weeks after admission. Alternative diagnoses were then suggested. Septicaemia or toxæmia were first considered in view of the fact that either condition could depress bone marrow activity and produce a leukaemoid blood picture. The apparent response to penicillin and blood transfusion lent further support to this possibility. Consideration was also given to the possibility of suprarenal neuroblastoma, with secondary deposits in the eye and bones; chloroma; Hand-Schüller-Christian disease; or multiple myelomatosis, all of which might inhibit haemopoietic function. A diagnosis of acute infective mononucleosis, as a

cause of generalized lymphadenopathy and splenic enlargement, was considered unlikely as the mononuclear cells were mainly primitive cells and did not resemble the abnormal type usually found in this condition. The enlargement of parotid and submaxillary glands raised the question of sarcoidosis or Mikulicz syndrome. Syphilis was excluded on the negative Wassermann reaction. Finally, lymphosarcoma could not be disproved until histological sections confirmed the original diagnosis of acute leukaemia.

Summary

A case of acute leukaemia occurring in a male child aged two years is described. An unusual and interesting feature is the loss of one eye, which, beginning with peri-orbital ecchymosis, progressed over a period of twelve days to spontaneous extrusion. The differential diagnosis is discussed.

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