LYMPHOCYTIC LEUKÆMIA CAUSING PONTINE HÆMORRHAGE

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The symptoms and signs associated with lymphocytic leukæmia are numerous, and depend principally upon five factors which may be thus summarized:—

1. Changes in the circulating blood.
2. Pressure from enlargement of lymphoid structures, or from deposits and infiltrations of lymphoid cells.
3. Infiltrations of various organs interfering with their functions.
4. Hæmorrhage, which may be due to blood changes, weakening or infiltration of the vessel walls.
5. Metabolic disturbances not covered by the factors mentioned already, such as pyrexia, and due probably or possibly to the poisonous effects of the disease itself. Such pyrexia will occur with new growths, such as carcinoma and sarcoma, as well as in leukæmias.

Considering the relative commonness of leukæmia and the extensive literature upon it, it is none the less apparent that involvement of the nervous system is amongst its rarer manifestations. It is for this reason, and also because of the typical syndrome which was produced, that the following case is recorded.

Case report.

B.S., a girl of ten and a half years, was sent by her doctor to the Birmingham Children's Hospital with the history that she had been limping slightly for three days, and on the night before being sent up to hospital, had suddenly become paralysed all down the left side. For three weeks previous to this she had been languid, and for a fortnight had been coughing and expectorating frothy sputum. A fortnight before admission she had developed bilateral subconjunctival hæmorrhages, for which she attended an eye hospital, where the condition was attributed to coughing.

On admission she was conscious, rational and spoke clearly. She was well-nourished and rather pale: there were hæmorrhages under both conjunctivæ and bruising of both upper eyelids. There were slight cough and some dyspnoea, but no stridor.

Physical examination revealed a general enlargement of the glands in both axillæ, both groins and in the neck. Her spleen was enlarged down to the pelvis and her liver almost to the umbilicus. No ascites was present.

There was a large pleural effusion on the left side, sub-manubrial dullness was absolute, and the sign known as paravertebral tracheophony was present as far down as the fifth dorsal vertebra on both sides.

Examination of the central nervous system revealed a left hemiplegia in which the face, tongue and masticatory muscles of the same side shared,

FIG. 1.—Brain after sagittal section showing hæmorrhage into the pons Varollii.

The eye movements were normal, both pupils reacted to light and were central and circular, the right one being a trifle more dilated than the left. The fundi were pale, but showed no pathological change.

The diagnosis was made of lymphocytic leukæmia, complicated by a left pleural effusion, and intra-cranial hæmorrhage. The fact that the whole of the left side was paralysed made it probable that the lesion lay at a point where the pyramidal tract could be injured en masse in a small area such as the internal capsule or pons. As large a cortical hæmorrhage as would have been needed to paralyse an entire side would certainly have caused other and severe manifestations.

A complete blood count was unfortunately not done at the time, and was thus lost as she died next day. A smear taken on admission showed a marked white-cell increase, about 90 per cent. of the white cells being lymphocytes.

For twelve hours there was no change, then she quite rapidly became comatose. Her temperature rose to 106°, and she developed pin-point pupils. The location of her hæmorrhage was now no longer in doubt. She died a few hours later.

FIG. 2.—Pons under low power showing infiltration.

AUTOPSY. At autopsy there was found marked enlargement of all the lymph glands. The mediastinum was one mass of growth in which the aorta, trachea and œsophagus were buried. There was a large amount of fluid in the pericardium and a large effusion into the left pleural cavity.

The spleen was greatly enlarged, soft and to the naked eye appeared homogenous; the liver was large and pale, having many small whitish areas scattered about its cut surface.

On examining the contents of the skull there was no sub-arachnoid hæmorrhage and no gross change in the cerebrum or cerebellum. The pons was bulging on both sides and section revealed a large hæmorrhage involving chiefly the right side, but in part also the left. Fig. 1 shows the appearance on hemisection of the brain.

Microscopical examination of the liver showed periportal lymphocytic infiltration. There was well-marked infiltration of the spleen, kidneys and mediastinal structures. Microscopy of the pons showed it to be heavily infiltrated all round the area of hæmorrhage with lymphocytes; the appearance is shown in the microphotographs (Figs. 2 and 3).

Sections taken from the various areas of the cerebrum and cerebellum showed no abnormality.

Discussion.

The nervous manifestations of leukæmia have been classified by Tapie and Cassar¹, who in recording a case of hæmorrhage due to leukæmic infiltration of the internal capsule describe the following varieties:—

1. Medullary degeneration: small foci of sclerosis or capillary hæmorrhage in the brain or cord.
2. Leukæmic infiltration: this may or may not cause symptoms.
3. Hæmorrhages into nerve centres.
4. Nerve lesions due to compression.
5. Zoster.

The case here described will, under this classification, come into both the second and third types, being due to hæmorrhage, itself probably caused by the leukæmic infiltration.

FIG. 3.—Pons under high power showing infiltration.

The child had, as before mentioned, been limping for three days previously to the onset of hemiplegia. Whether the initial limping was due to the infiltration alone, or to a small and earlier effusion of blood it is impossible to say; Tapie and Cassar themselves say that the infiltration may or may not cause symptoms. It seems, however, more probable that the infiltration alone was responsible, as in such an area a hæmorrhage would have to be very small, and occur very gradually not to cause some sudden change in the reactions of the central nervous system. The sequence of events which seems to explain the symptoms is as follows: first, a gradual infiltration of the pons, eventually causing slight involvement and resulting in a limp; then a hæmorrhage, which resulted in a sudden hemiplegia; finally an increase in the hæmorrhage causing coma, the pontine syndrome and death.

The relative rarity of nervous complications in the leukæmias of childhood has already been mentioned. Ramsay², in an analysis of a hundred cases of leukæmia in children under eight years of age, does not mention one in which the nervous system (apart from the fundus oculi) was involved. He states that 'The patient may die with hyperpyrexia suggesting some toxic action on, or a leukæmic infiltration of, the pons Varollii.' He does not, however, describe or quote an actual case.

Munro³ describes a case of a female in the twenties, whose symptoms and signs suggested meningitis, and whose cerebro-spinal fluid was blood-stained and under increased pressure. Post-mortem examination revealed the fact that she had myeloid leukæmia. The vessels of the meninges showed marked engorgement, and there was acute œdema of the brain and cord. No gross hæmorrhage was found.

The case described here was not investigated by lumbar puncture, but autopsy revealed no hæmorrhage into the meninges.

Bass⁴, in a review of the cases of leukæmia in children at the Mount Sinai Hospital from 1911-1921, found four to have shown involvement of the brain. The first, which soon died, had hepatic and splenic enlargement, and signs of meningeal irritation. Post-mortem examination revealed a large hæmorrhage over the surface of the brain and the usual systemic appearances of leukæmia. The second, third, and fourth cases all died with convulsions, delirium and coma; these are not so fully described as the first case.

He quotes another case, in which he performed a necropsy and found large, brick-red masses, up to the size of a cherry, involving the brain; these proved to be leukæmic deposits. There had been no nervous disturbances until a few days before death. He states that leukæmic infiltration of the brain may affect considerable areas before causing symptoms.

He quotes Munro's case, already mentioned, and states that he has seen altogether six cases with symptoms referable to the central nervous system. Of these, four were examples of cerebral hæmorrhage. Three of these were verified post mortem; two had also been lumbar punctured; and the last had been diagnosed clinically but was not verified after death.

The case recorded here in no way resembled any of these clinically, and post-mortem examination revealed what macroscopically appeared to be simply a pontine hæmorrhage.

Allbutt and Rolleston⁵ record a case of leukæmia with multiple cerebral and cerebellar hæmorrhages. They conclude that the hæmorrhages were probably due to badly nourished vessels becoming thrombosed, the condition most likely beginning in the small veins.

The case that has been described agrees with the statement of Tapie and Cassar that infiltrations may or may not cause symptoms; this having caused none until four days before death. It also provides an example of the termination of life with hyperpyrexia mentioned by Ramsay.

Summary.

A case of hæmorrhage following leukæmic infiltration of the pons Varollii is recorded and compared with other examples of disease of the central nervous system due to leukæmia.

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