# NEUROBLASTOMA OF EXTRARENAL ORIGIN

BY

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(RECEIVED FOR PUBLICATION NOVEMBER 28, 1949)

Malignant growths in the Bantu child are uncommon. The Paediatric Service of the Coronation Hospital deals with 1,500 medical paediatric in-patients a year and in five years we have encountered only four cases of embryoma of the kidney, two cases of reticulum cell sarcoma, and only one case of neuroblastoma.

Ladd and Gross (1941), quoting Wyatt and Farber (1941), say that neuroblastoma is the commonest abdominal tumour in childhood. This, our only case of neuroblastoma, was admitted with the diagnosis of ' diarrhoea and an abdominal mass for investigation.' Within four weeks of admission the case showed extensive skeletal changes, including fractures. It is reported because it presents the unusual features of neuroblastoma proved to be of extrarenal origin.

### Case History

The patient, Josephine, was a female Bantu child aged 5, and was admitted to this hospital on February 10, 1949. Questioning the mother revealed that the child became ill about Christmas, 1948, when her feet began to swell and remained swollen for 15 days. She also suffered from diarrhoea by day and by night. She passed as many as five bloodstained soft stools a day and had also passed ' pink ' or bloody urine. Since the onset of illness in December, 1948, the child looked anaemic.

TABLE 1

BLOOD ANALYSIS FINDINGS

| Date | Hb. (g. %) | Red Blood Cells (millions) | White Blood Cells | Percentage | | | | | Description |
|---|---|---|---|---|---|---|---|---|---|
| | | | | P. | L. | M. | E. | B. | |
| 11.2.49 | 1·7 | ·690 | 7,300 | | | | | | Patient given 300 ml. blood. |
| 11.2.49 | 6·4 | 2·150 | 9,300 | 27 | 67 | 3 | 1 | | Plasma cells 2%; E.S.R., 76; P.C.V., 18·5. |
| 12.2.49 | | | | | | | | | Patient given 300 ml. blood. |
| 14.2.49 | 7·5 | 2·540 | 7,300 | 47 | 44 | 3 | 1 | | Myelocytes, 3%; plasma cells, 2%. |
| 22.2.49 | | | | | | | | | 300 ml. blood given. |
| 6.3.49 | | | | | | | | | 250 ml. blood given. |
| 15.3.49 | | | | | | | | | 500 ml. blood given. |
| 17.3.49 | 11 | 3·666 | 7,200 | | | | | | E.S.R. (uncorrected), 61. |
| 19.3.49 | 7·5 | 2·150 | 9,400 | 50 | 37 | 4 | 1 | | ? Myeloblasts, 4%; unidentified, 4%; several neutrophil myelocytes, marked polychromasia. |
| 31.3.49 | 3·5 | 1·410 | 5,400 | 60 | 29 | 1 | 1 | | Myelocytes, 8%. Patient given 500 ml. blood. |
| 1.4.49 | 4·6 | 1·920 | 5,100 | 71·5 | 19 | 3 | 1·5 | | Neutrophil myelocytes, 1%; myeloblasts, 1%; unidentified, 3%. |
| 2.4.49 | | | | | | | | | Patient given 1,000 ml. blood. |
| 4.4.49 | 12·5 | 4·290 | | | | | | | |
| 14.4.49 | | 1·500 | 3,950 | | | | | | Patient given 500 ml. blood. |
| 15.4.49 | | | | | | | | | |
| 19.4.49 | | 1·600 | | | | | | | Patient given 320 ml. blood. |
| 20.4.49 | | | | | | | | | |

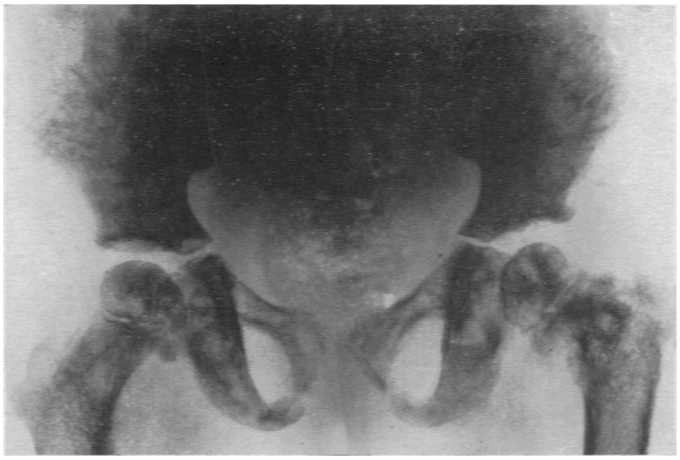

FIG. 1.—Neoplastic changes in the pelvis.

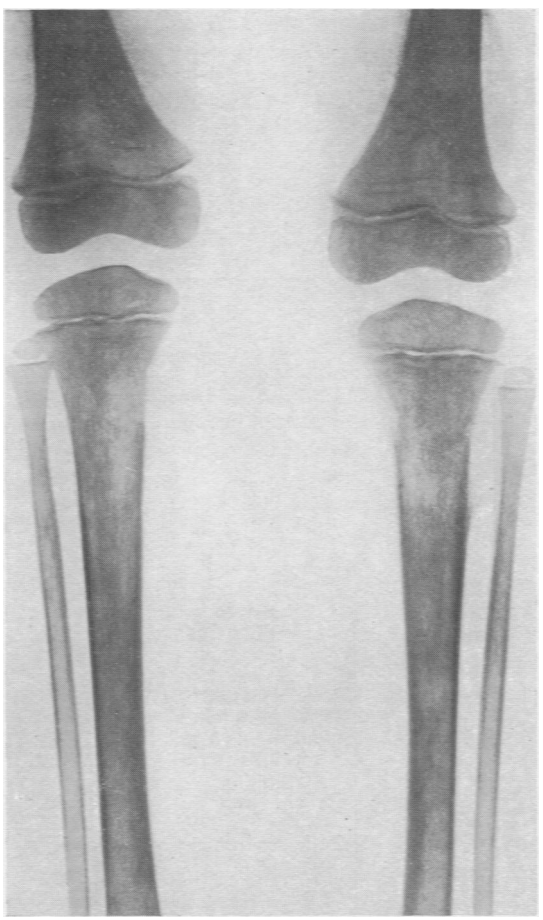

FIG. 2.—Neoplastic changes in the femurs and tibias.

The child was the eldest of three. Nothing abnormal was elicited about her previous health.

Examination revealed an anaemic, co-operative Bantu child. The temperature was 102·6° F. The head was normal in size and shape. Both eyelids were puffy, the conjunctivae were pale, and the mucous membrane of the mouth was also pale. There were no palpable glands in the neck. Both lung fields were clear. The heart sounds were normal. The pulse rate was 120. Abdominal palpation showed that the liver was three fingers below the costal margin and the spleen was palpable. In the umbilical area a firm, untender mass about three inches in diameter was felt. It was slightly movable and seemed to be attached to the posterior abdominal wall. It could be palpated by rectal examination but did not involve the rectum.

There was a lumbar kyphosis. The central nervous system was normal.

**History and Clinical Course.** On admission the patient was given 300 ml. of blood and this was repeated on the following day (Table 1).

A Vollmer tuberculin test was positive. A radiograph of the chest suggested infiltration in the left upper zone, and these findings, together with the fact that the child had a mass in the abdomen, led to a tentative diagnosis of pulmonary tuberculosis with mesenteric glands and renal involvement. The child was accordingly placed on streptomycin.

On her eleventh hospital day the patient had an epistaxis and as time went on this became a frequent and disturbing occurrence, occasionally becoming so severe that nasal plugging was necessary.

Twenty-one days after admission three lumps, ½ in. in diameter, or rather three oedematous areas, appeared on the child's head, one in the right frontal temporal area, one above the nose, and one above the left fronto-parietal area. These masses were semifluctant and the smallest one, that on the left side, was aspirated and a little bloodstained serum obtained.

Meanwhile the child's left eye was becoming more swollen and protruded.

Bleeding from the nose became more severe and more frequent until the patient had to be given repeated transfusions. The proptosis increased. Her appetite was not impaired at this time and her general condition remained good. The lumps became stationary under treatment with deep x-ray therapy.

A radiograph taken at the time of the aspiration biopsy showed widespread neoplastic changes in the skull, both femurs and tibias.

The patient was again radiographed one month later, and the vault of the skull was seen to be enlarged and showed very marked increased intracranial pressure. There were multiple areas of osteolysis throughout the skull and a fragment of bone had separated posteriorly at the level of the lambdoid sutures. A sun-ray spicule

effect was observed on the vault of the skull in the frontal and parietal regions. Marked soft tissue swelling accompanied these changes.

Multiple areas of osteolysis were seen throughout the skeleton, most marked in the pelvis and in the lower limbs, periosteal reaction being seen in the femurs. There were pathological fractures of the neck of the left femur, the surgical neck of the right humerus, and in the upper end of the right tibia. Changes were not very obvious in the spine but osteolytic areas could be seen in the dorsal vertebrae. Pleural thickening was apparent in the chest on each side but there were no obvious metastatic deposits in the lungs (Figs. 1, 2, 3, and 5).

The aspiration biopsy of the lumps suggested a malignant growth but no definite diagnosis could be made from the slide. A bone marrow smear made on the twenty-eighth day revealed a collection of syncytial masses (Fig. 4). Although not pathognomonic this finding, according to Kato and Wachter (1938), in addition to those of the radiographs, confirmed the diagnosis of neuroblastoma.

Deep x-ray therapy was begun on March 23 and stopped on April 7, 1949. Aminopterin was given, but abandoned because of the epistaxis and the anaemia.

The veins in the neck became distended, and the patient became dyspnoeic. A hard, but not tender, mass was palpated in the left hypochondrium. The liver and the inguinal glands increased in size as time went on and the lumps on the forehead became larger. The right knee became swollen and tender about the sixth week of the child's illness. She died on the fifty-eighth day after admission.

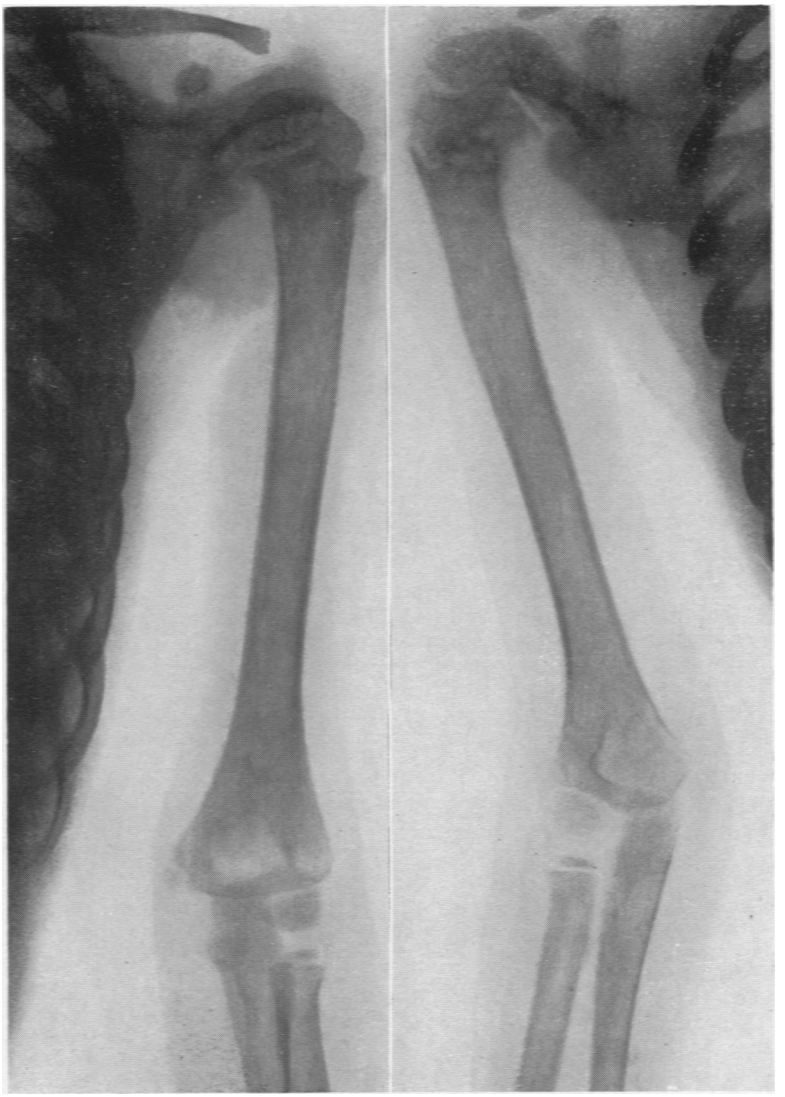

FIG. 3.—Neoplastic changes in the humeri.

**Necropsy.** The body was well developed but emaciated. The soles of the feet and palms of the hands were very yellow. The head was grossly enlarged and there were obvious lumps in the parietal and occipital areas which on section proved to be haemorrhages. A large swollen purple mass covered the frontal area and extended to the base of the nose. Incision showed little subcutaneous fat.

In both pleural cavities there was bloodstained fluid with very few adhesions between the lungs and the chest walls. The heart and pericardial sac were normal.

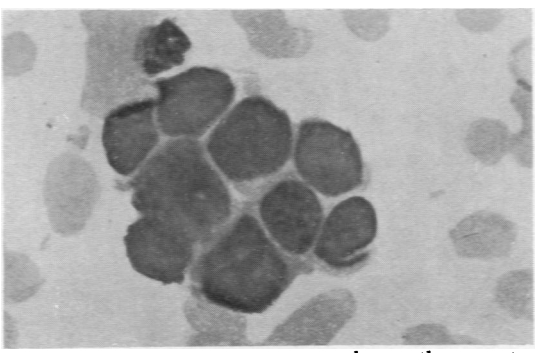

FIG. 4.—Bone marrow smear made on the twenty-eighth hospital day.

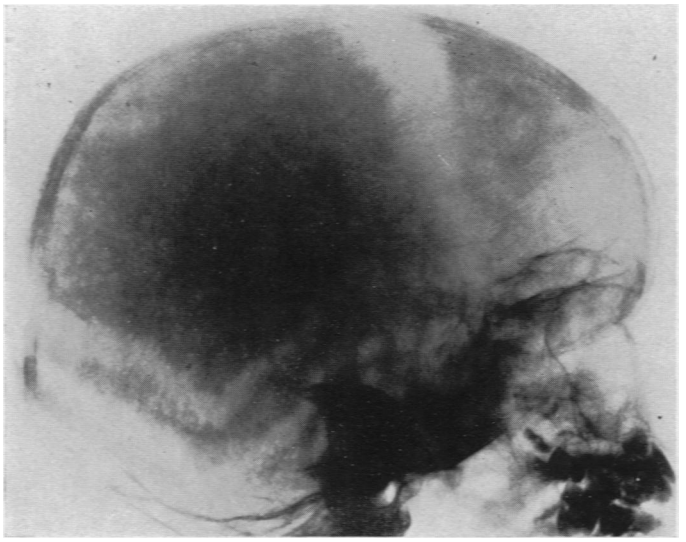

FIG. 5.—Neoplastic changes in the skull.

All but the first three ribs were invaded by new growth, which replaced much of the bony structure.

The peritoneal cavity contained bloodstained fluid. The liver was markedly enlarged and extended 5 in. below the costal margin and was studded with many nodules of secondary growth, the largest being about ¾ in. in diameter.

The neoplastic mass in the abdomen was attached to the lumbar vertebra. The sigmoid colon was adherent to the anterior surface of this mass and the second part of the duodenum was also adherent to the superior surface of the main tumour mass. The tumour was found to consist of a central portion 2½ in. × 5 in., which was whitish-yellow in colour and studded with a few haemorrhagic areas and two lateral masses about 2 in. × 1 in., made up of deeply purple cysts and whitish areas. The bilateral masses proved to be the ovaries (Fig. 6).

The main mass compressed the right ureter, and in its upper two-thirds the ureter was dilated above the site of compression which was due to a nodule of neoplastic tissue invading the lumen of the ureter. The left ureter ran around the mass and was not involved in the new growth. Both kidneys were large. The adrenals were thin and orange in colour and seemed normal.

The inguinal glands were enlarged. The iliac chain of glands was replaced by growth and many of the glands were haemorrhagic. The cut surface of the larger growth showed haemorrhagic areas surrounded by yellowish tissue. The ovaries were mainly haemorrhagic.

The heart, lungs, trachea, oesophagus, and alimentary canal were normal. The long bones were not examined.

The scalp was very swollen. When it was peeled back it showed areas of bleeding in the sub-periosteal area. The skull cut easily and the cut surface was at least ½ in. thick and haemorrhagic. The growth seemed to be on both surfaces of the cranial bones.

Only the petrous part of the temporal bone was free from invasion.

## Discussion

In view of the extent of the disease and the impossibility of treating the whole area involved

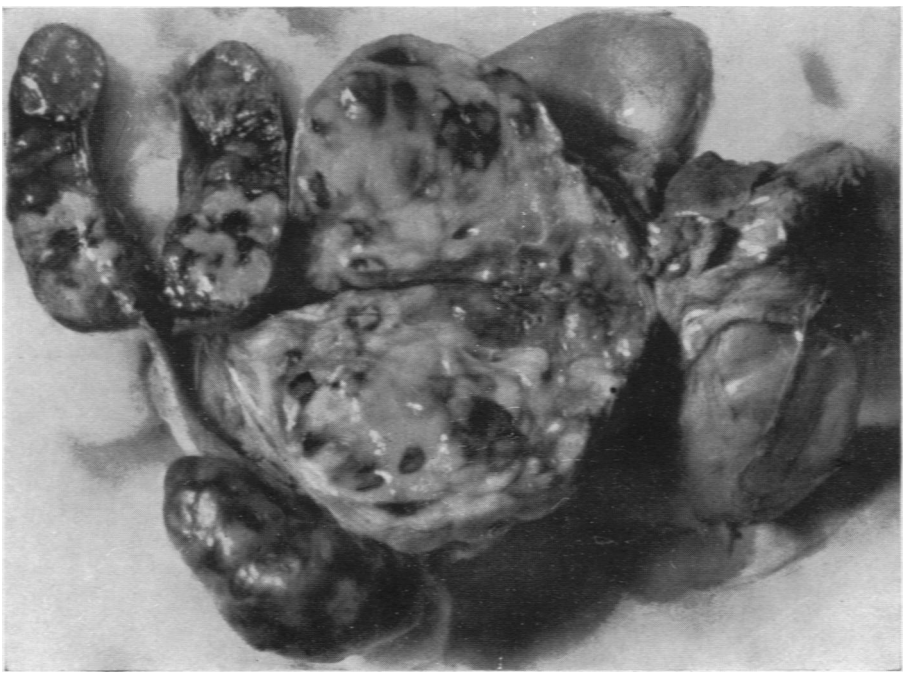

FIG. 6.—Cut surface of the main mass and ovaries.

simultaneously, it was decided to treat the patient in sections. Treatment was started on March 23, 1949. Since it was considered that the immediate threat to life was the cerebral deposits, the first treatments were directed to the skull. For this purpose high voltage Röntgen rays generated at 180 KV constant potential (filtration ½ mm. Cu. and 1 mm. Al, half-value layer 0·9 mm. Cu., and a target-skin distance of 40 cm.) were applied through a 10 × 20 cm. applicator. Anterior and posterior fields were treated on alternate days, 500 r being delivered at each treatment. Initially the fields were centred on the cranial vault, and at each succeeding treatment the fields were shifted caudad a distance of 5 cm. (half the field width). By this 'moving strip' method the skin received a total dose of 1,000 r without any gaps due to faulty field contiguity. Any given point in the coronal plane of the body, therefore, was irradiated for four successive days, and received an estimated dose of 120 r. The proposed plan of treatment was not completed as the patient's condition deteriorated rapidly in the third week.

The unusual radiosensitivity of this tumour is well illustrated by comparison between the treated and the untreated lesion. The section from the ovary (Fig. 7), which had received only an insignificant amount of scattered radiation, showed the typical structure of this vigorously growing anaplastic tumour. Large round and pear-shaped cells, uniform in size and staining characters, each containing a single large, spherical nucleus, replaced the normal tissue and showed little tendency to form any recognizable structure, although a few characteristic rosette formations could be identified.

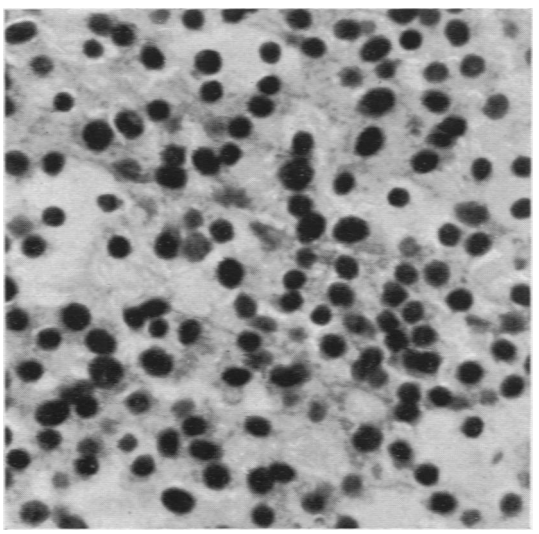

FIG. 7.—Ovary untreated.

The section from the skull which had received an estimated dosage of 1,200 r about four weeks before death (Fig. 8), showed radiation damage. The relatively sparse islets of recognizable tumour still present in the necrotic and haemorrhagic tissue, consisted entirely of non-viable cells. There was gross variation in cell size and shape, many cells being swollen with vacuolated cytoplasm, some obvious giant cells and many in the process of dissolution. Nuclei were all abnormal. Some were in the process of aberrant mitosis, and others showed the effects of completed abnormal mitoses: multinucleated cells, grossly enlarged nuclei, pyknotic staining, nuclear fragments and micronuclei, and much nuclear debris, often in the form of chromatin dust.

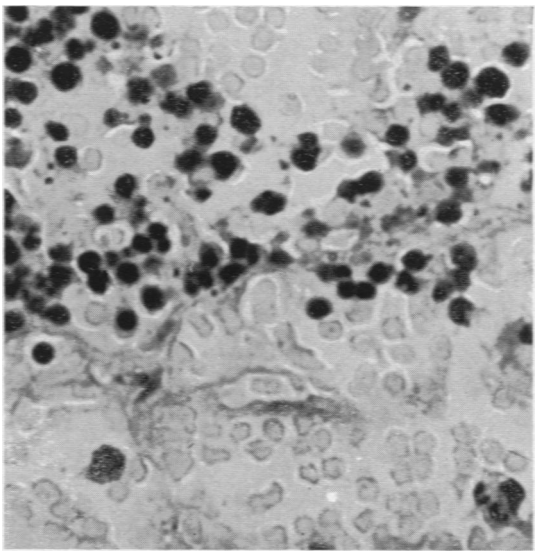

FIG. 8.—Skull treated.

**Summary**

A case of neuroblastoma in a Bantu girl, of interest because of the extrarenal origin of the tumour, is presented. Although the tumour was radiosensitive, its marked malignancy and the rapid appearance of its metastases in the skeleton resulted in death. The problems of treating such a case are discussed.

My thanks are due to Dr. Lionel Cohen for his report on the microscopic slides and on the deep therapy.

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