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The Value of Bone Marrow Examination in the Diagnosis of Neuroblastoma

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Summary

Sodeinde O, Williams CKO and Folami AO. The Value of Bone Marrow Examination in the Diagnosis of Neuroblastoma. *Nigerian Journal of Paediatrics* **1983; 10: 81.** Two patients in whom the diagnosis of neuroblastoma was first made by cytological examination of the bone marrow are presented. They illustrate the value of this simple diagnostic procedure even when the usual diagnostic criteria prove inconclusive or difficult to apply. Routine bone marrow examination is recommended whenever neuroblastoma is suspected.

Introduction

Delay in diagnosis is one of the major problems presented by neuroblastoma. In an earlier study of the disease in Ibadan, Familusi, Aderele and Williams[1] identified two factors accounting for this: non-familiarity of the physicians with the protean manifestations of the disease and limited diagnostic facilities. In this communication, the value of bone marrow examination in the diagnosis of the disease is illustrated in two patients who were studied recently.

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Case Reports

Case 1

OS, a 6-year old boy, first presented at the Dental Clinic, University College Hospital (UCH), Ibadan, from where he was referred to the Surgical Oncology clinic, UCH. He gave a two-week history of painless swelling in the right lower jaw. He was afebrile and the mucous membranes were normal. There was an ulcerating mass in the right mandible with loose and malaligned teeth. There were no other significant findings. The full blood count was normal. A tumour biopsy was done and the child was started on a course of cyclophosphamide based on a strong clinical impression of Burkitt's lymphoma. The chemotherapy resulted in a partial reduction in tumour size. The biopsy was reported initially as showing small clusters of lymphoid cells not typical of Burkitt's lymphoma and a repeat biopsy, ten weeks later, was reported as showing a poorly differentiated epidermoid carcinoma.

The patient was then referred to the Children's outpatients Department, UCH, six months after the first presentation at the Dental clinic. On examination, he was found to be very pale. Blood pressure was 90/50mmHg. The rest of the cardiovascular and respiratory findings were normal. The spleen was enlarged 3cm below the left costal margin. There were large and firm lymph nodes in the right inguinal and popliteal regions. There were multiple, hard, non-tender nodules in the cranial vault as well as a 5cm-diameter, non-tender swelling in the right mandible with a loose second molar tooth. In addition, there was a large right maxillary swelling with bilateral proptosis which was more marked on the right (Fig. 1). The right optic disc was slightly blurred but the retinae were normal bilaterally. There was no ophthalmoplegia.

The laboratory findings revealed packed cell volume (PCV) of 16%, a white blood cell (WBC) count of $3{,}000/m^3$ ($3x10^9/L$) and reduced platelet count. Since these findings were suggestive of a bone marrow failure, a bone marrow examination was undertaken and this showed extensive infiltration by mononuclear cells, some arranged in rossette-like patterns (Fig. 2), while others showed elongated processes (Fig. 3). A diagnosis of neuroblastoma was made, based on these bone marrow findings. This diagnosis was subsequently supported by the elevated 24-hour urinary excretion of vanillylmandelic acid (VMA) which was 10.5mg/100 ml (0.53 mmol/L) (normal range: 2-7mg/100ml or 0.101–0.353 mmol/L), the presence of fine-speculed calcification in the upper pole of the left kidney in a plain abdominal radiograph and a biopsy of a right inguinal lymph node, which showed neuroblastoma.

Case 2

AS, a 15-month old girl, presented with a 3-month history of a swelling which started as a nodule in the roof of the left orbit and grew to cause proptosis and destruction of the left eye.

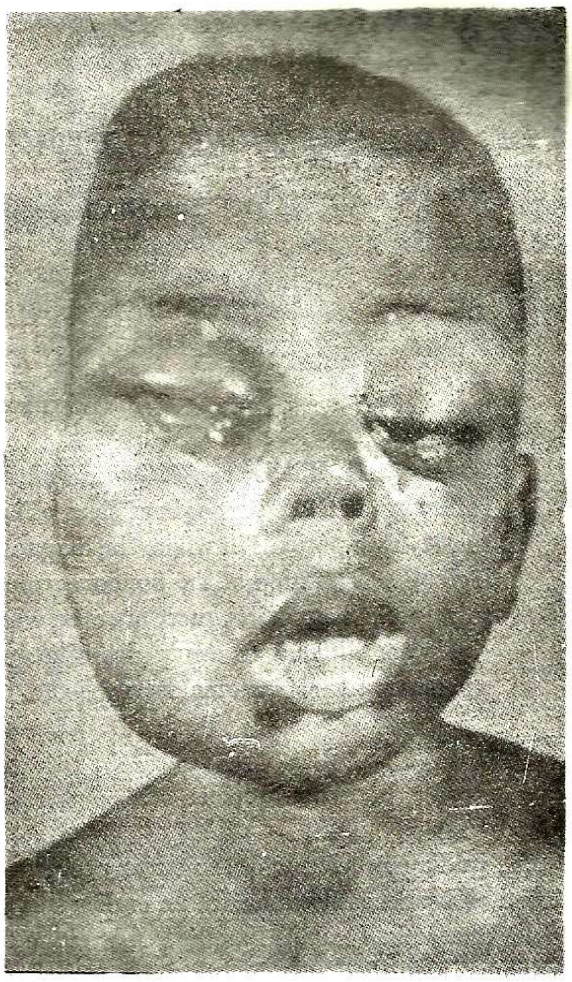

Fig. 1 Photograph of patient – Case 1.

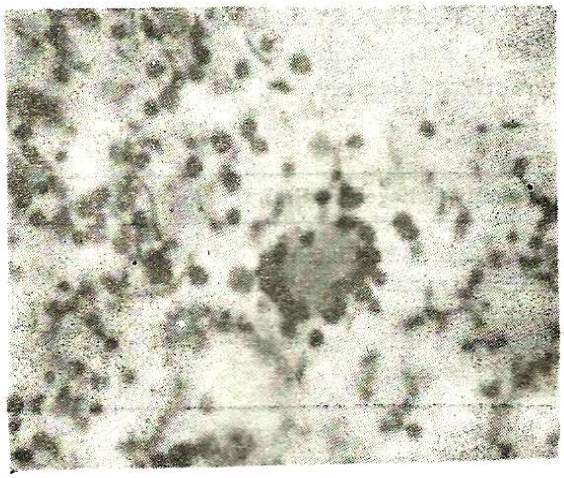

Fig. 2 Photomicrograph of bone marrow aspirate showing typical rossette of neuroblastoma cells.

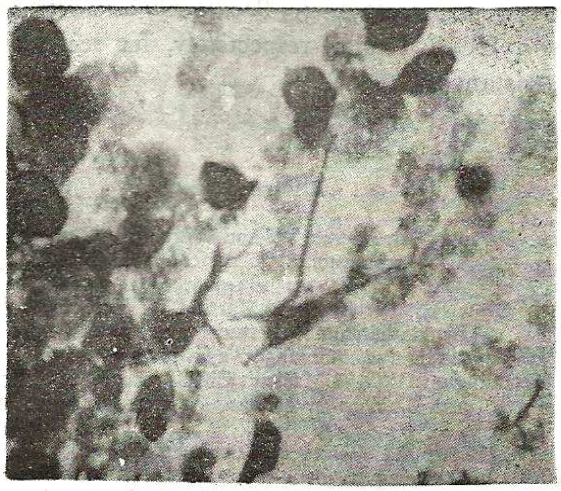

Fig. 3 Photomicrograph of bone marrow aspirate showing cells with elongated processes suggestive of neuro-axonal differentiation.

It also produced a huge swelling in the surrounding frontal and maxillary areas of the face with extension into the mouth. The right eye was normal. Nasal involvement caused noisy breathing, while her blood pressure was 100/60mmHg. The respiratory and cardiovascular systems were otherwise normal. The liver edge was palpable, 3cm below the right costal margin. A hard, irregular, non-tender, deeply seated, non-mobile mass was palpable in the left upper quadrant. Neurological examination was normal apart from the destroyed left eye.

A full blood count revealed a PCV of 22%, WBC of 8,500/mm^3 (8.5x10^9/L), with normal differentials. The serum electrolytes and urea as well as the serum creatinine were normal. Intravenous urography revealed a mass above the left kidney displacing the bowel loops downwards and the stomach laterally.

Three attempts to collect 24-hour urine for VMA estimation were unsuccessful. Similarly, several attempts to obtain a tissue diagnosis through a surgical biopsy failed over a period of several weeks because of various logistic problems. A bone marrow examination was therefore undertaken and this revealed a total replacement by cells showing features similar to those in Figs. 2 and 3. A diagnosis of neuroblastoma was made and this was subsequently confirmed histopathologically by a lymph node biopsy.

Discussion

Two cases of neuroblastoma are presented, in which the usual diagnostic criteria of tissue histopathology and endocrine markers proved initially inconclusive or difficult to apply, but in which the diagnosis was made by bone marrow cytology. In both cases, the traditional procedures subsequently confirmed the diagnosis earlier made from bone marrow cytology.

Neuroblastoma often presents at the metastatic stage even in developed countries where patients tend to attend hospital early and extensive facilities for investigation are available.[2] In Nigeria, further delay is sometimes caused by initial misdiagnosis—most commonly as Burkitt's lymphoma,[1] a tumour which occurs more frequently than all other childhood tumours put together.[3] For the resolution of this diagnostic problem, several tests are available. Elevation of the urinary excretion of catecholamine metabolites such as VMA is probably the most discriminatory of the diagnostic tests for neuroblastoma and this occurs in 76% of cases at diagnosis.[4] Determination of VMA is a non-invasive procedure but its use requires skilled laboratory manpower and expensive equipment. Furthermore, urine collection may present problems as happened with one of our cases.

Bone marrow aspiration on the other hand, although an invasive procedure, carries little risk, if a careful sterile technique is employed. Since the smears can be processed as a sideroom procedure, results can be obtained within a few hours of obtaining the marrow aspirate. In addition, it can lead to the diagnosis in up to 70% of new neuroblastoma cases.[5,6] Routine tissue biopsy, by contrast, would require at least, one week to process in most centres and VMA estimation is available in only a few hospitals. Differentiation from Burkitt's lymphoma with which neuroblastoma is most frequently confused

on clinical grounds, is readily achieved on the basis of differences in cytological and cytochemical characteristics of the bone marrow smears.

Bone marrow aspirates were examined in only three of the 31 neuroblastoma patients reported by Familusi *et al.*[1] Thus, it would appear that this simple but very useful diagnostic tool is still grossly underused. In conclusion, it is recommended that the examination of stained smears of bone marrow aspirates be undertaken in all children suspected of having malignant disease, especially when other diagnostic procedures are not readily available.

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