

Retinoblastoma; Bone marrow infiltration - A study of 30 cases

I KHURSHID S NAEEM F BASHIR A LONE N ASLAM A HAYEE I A NAVEED

Department of Haematology, King Edward Medical College, Lahore.

Correspondence to Dr. Irfan Khurshid

Thirty patients of Retinoblastoma presenting in the Haematology Department of King Edward Medical College, Lahore were included in the study to find out the bone marrow involvement. The patients underwent bone marrow aspiration and peripheral blood examination was also done. The aspirates were screened for the presence of tumor cells. Of the patients studied 21(70%) were males while 9(30%) were females giving a male to female ratio of 2.8:1. Maximum number of patients were in the 2-3years age group. Twenty seven patients had unilateral Retinoblastomas while three patients had bilateral disease at presentation. The bone marrow of three patients showed presence of tumor cells.

Key word: Retinoblastoma

Retinoblastoma is the most common malignant intraocular neoplasm of childhood^{1,2,3} and is responsible for approximately 1% of all deaths from cancer in the age group of newborn to 15 years⁴. Retinoblastoma was first described as a specific entity by James Wardrop in 1809 with enucleation as his suggested treatment⁵. The incidence of retinoblastoma in the United States has been almost uniform and the average annual incidence of retinoblastoma is 5.8 per million for children younger than 10 years and 10.9 per million for children younger than 5 years⁶. The retinoblastoma gene (RB1) maps to chromosome 13q14 and encodes a 110 kilodalton variably phosphorylated nuclear protein (Rb)⁷. Retinoblastoma occurs in both familial and sporadic pattern. The presenting findings include poor vision, strabismus, a whitish hue to the pupil, and pain and tenderness in the eye⁸. Distant metastases to bone and bone marrow occur¹. Factors found to be independently associated with the development of metastases include, optic nerve invasion with and without involvement of the resection line, choroidal invasion and enucleation of an affected eye more than 120 days after initial diagnosis⁸. Untreated the tumors are usually fatal, but with early treatment by enucleation, chemotherapy and radiotherapy survival is the rule^{4,9}. The 5 year survival of unilateral Retinoblastoma following adequate treatment is over 90% and slightly less for bilateral cases^{10,11}. The present study was carried out on 30 patients of Retinoblastoma presenting in the Haematology Department of King Edward Medical College for bone marrow aspiration. The objective of the study was to look for the presence of tumor cells in the bone marrow aspirate as the prognosis of patients with carcinoma is determined by whether there is dissemination of the primary tumour at the time of diagnosis¹².

Material and methods

Retinoblastoma cases were collected from the patients presenting for bone marrow aspiration in the Hematology Department of King Edward Medical College. A total of 30 patients were included in the study. The diagnosis of

retinoblastoma was established in the Histopathology department of King Edward medical college.

History of each patient was taken followed by physical examination. Relevant data was also checked from patient's record files. Haemoglobin (Hb) estimation, total leucocyte counts (TLC) and platelet counts were done by Cobos (Minos STE). Erythrocyte sedimentation rate (ESR) of each patient was also recorded.

Peripheral blood smears were stained with May-Grunwald-Giemsa stain. Bone marrow aspiration was performed on the patients from the posterior iliac crests and from tibial tuberosity in patients under two years of age. These were stained by May-Grunwald-Giemsa stain and examined for the presence of tumor cells.

Results

Table I shows age distribution of the patients and figure 1 gives percentage of retinoblastoma patients in different age groups. The maximum number of the patients (30%) were in 2-3 year age group. Of the total patients 90% were between 1 to 5 years of age. The 3 cases with bone marrow involvement were of 3, 4, and 5 years of age. There were 21(70%) male patients and 9(30%) females with a male to female ratio of 2.8:1. Three patients (10%) had bilateral orbital involvement. Bone marrow infiltration was seen in 3(10%) of the total cases. Twenty patients had abnormal CBC examination and the abnormality detected was reduced Hb and raised ESR (Fig. 2). All the patients presenting as bilateral retinoblastoma and with metastatic disease had abnormal CBC reports.

Table I. Age and sex children with retinoblastoma.

Age group	Male	Female	n=
0-1 years	0	0	0
>1-2 years	05	01	06
>2-3 years	06	03	09
>3-4 years	04	02	06
>4-5years	05	01	06
>5 years	02	01	03
Total	21	09	30

Fig.1 Percentage of retinoblastoma patients in different age group.

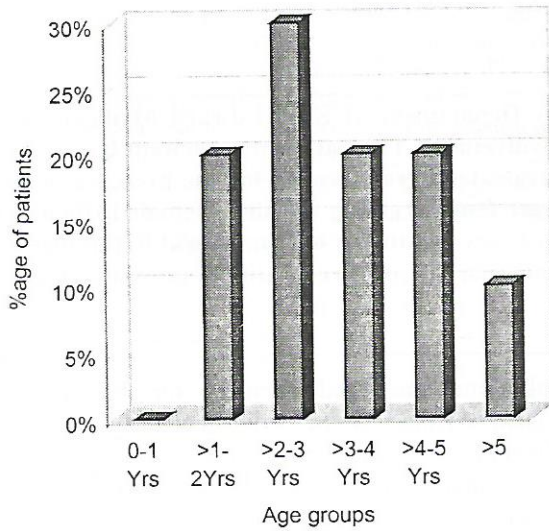


Fig.2: Percentage of normal and abnormal CBC reports

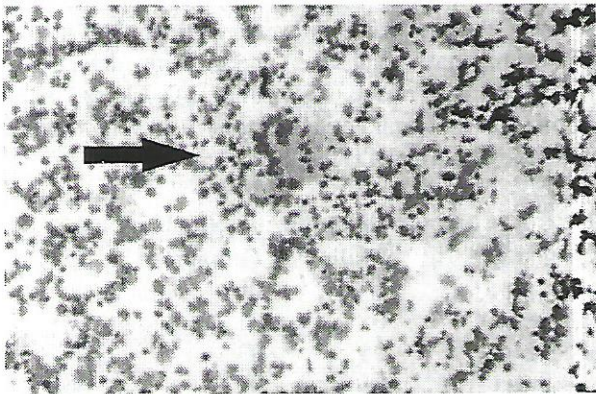
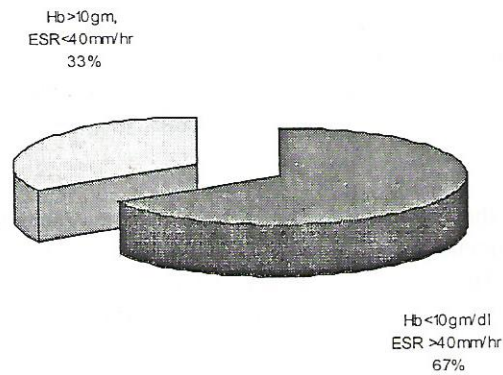


Fig.3. The tumour cells in bone marrow aspirate showing an attempt for rosette formation (Gmay-Grunwald-Giemsa, 10x).

Discussion

Retinoblastoma (RB) is the most frequent malignant intraocular tumor in childhood¹³, in which distant metastases to bone and bone marrow occur¹. We have found that 90% of the cases were unilateral at the time of presentation and 10% of the cases bilateral . All the patients with metastatic and bilateral disease had abnormal CBC reports and bone marrow infiltration was found in 10% of the cases from our study. The type of the treatment chosen for any retinoblastoma patient depends upon the stage of the disease and the prognosis of patients is determined whether the primary tumour has metastasised at the time of diagnosis¹⁰. Chemotherapy plays an important role in therapy for patients with extraocular and metastatic retinoblastoma^{14,15,16}. The means available to screen for retinoblastoma metastases, including bone marrow aspiration, lumbar puncture, and radionuclide scans, offer variable usefulness at different stages of the disease¹⁷. Patients with metastatic retinoblastoma have a poor outcome. Hope that early detection of extraocular spread will improve survival has led to routine monitoring with bone marrow and cerebrospinal fluid (CSF) examinations¹⁸. The study the has been carried out by Karcioglu-ZA et al indicates a good interrelation between the positivity of diagnostic tests (bone marrow and bone scan) and higher stages of the disease (stages III and IV) and choroidal involvement in enucleated eyes, with statistically significant correlation; correlation with lumbar puncture and liver scan were not significant¹⁷. Our study did not established the correlation of the diagnostic test – bone marrow aspiration with histopathologic findings. However other studies showing the correlation of diagnostic tests with the histopathologic findings showed that with no choroidal involvement, no positive diagnostic tests were encountered¹⁹. Moreover in those studies correlation between positive diagnostic test results and the level of optic nerve involvement failed to indicate any trends. In study carried by Pratt et al report that that demonstrable bone marrow involvement is so infrequent an event at diagnosis in patients without symptoms, signs, or histologic evidence of tumor dissemination (stages I-II) as to support a recommendation that these studies need not be performed routinely in such patients¹⁹. If, after enucleation, there is evidence of extraglobar extension, or if patients have symptoms or signs of CNS or systemic spread (stages III or IV), both bone marrow and CSF examination should be performed to accurately stage disease and provide baseline measurements of tumor involvement for monitoring of response to chemotherapy and /or irradiation¹⁸. These results show importance in terms of justification of invasive work-up of most affected children, as the staging investigations are not without risk and trauma to the patient, emotional stress on parents and financial cost to the community^{19,20}.

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