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Original Research Article

Incidence of Bone Marrow Infiltration and Hematological Profile in Patients of Neuroblastoma- A Tertiary Care Experience

Dr Sanjay Mishra[1], Dr Mili Jain[1], Dr Atin Singhai[2], Prof A K Tripathi[3], Prof Ashutosh Kumar[4], Prof U S Singh[5]

[1]Assistant Professor, [2]Associate Professor, [4]Professor and Head, [5]Professor,
Department of Pathology, King George's Medical University, Lucknow, Uttar Pradesh, India
[3]Professor and Head, Department of Clinical Hematology, King George's Medical University, Lucknow, Uttar Pradesh

Corresponding Author: Dr Sanjay Mishra

ABSTRACT

Introduction: Neuroblastoma is one of the commonest malignancies of infancy. The clinical presentation of neuroblastoma is very heterogeneous and depends on the stage of disease. Bone marrow infiltration occurs in approximately 50% of the patients at presentation and the procedure can be used in staging of disease. Bone marrow aspiration and biopsy can therefore be utilized as a good method for staging of disease in under resourced laboratories.

Materials and Methods: The patients suffering from proven neuroblastoma by Histopathology and Immunohistochemistry were included in the study. Bone marrow aspiration and biopsy from posterior superior iliac spine was performed in these patients. Only new cases were included in the study.

Result: Total number of 45 patients was enrolled in the study. The study group belonged to age group of 05 months to 18 years. Most common site of involvement was of adrenal medulla. In our study bone marrow infiltration was seen in 53.3% of patients. The predominant pattern of infiltration was diffuse pattern with rosette formation at places. Anaemia was the commonest manifestation (87.5%)

Conclusion: Neuroblastoma is clinically heterogeneous disease with clinical spectrum ranging from asymptomatic individuals to highly symptomatic individuals. The prognosis depends a lot on the stage of disease. Bone marrow aspiration and biopsy is one of the simplest methods of staging the disease in under resourced hospitals.

Key words: Neuroblastoma, Bone marrow aspiration and biopsy, Adrenal medulla, malignancy

INTRODUCTION

Neuroblastoma is one of the commonest malignant neoplasms of infancy. [(1)] It is an embryonal tumour arising from developing and incompletely committed precursor cells derived from the neural crest tissue. [(2)] The tumour presents as a mass lesion arising from the sympathetic nerve ganglia mainly from the adrenal medulla, paraspinal ganglia. [(3)] The tumour is commonly associated with MYCN amplification.

The presentation of neuroblastoma is very heterogenous and ranges from asymptomatic disease requiring little intervention to large abdominal mass requiring multimodality treatment approaches. Frequently the tumour presents as mass lesion in the neck, chest, abdomen and pelvis. At diagnosis, about 50% of the patients present with advanced disease with metastasis to the other sites. [(4)] The common site of metastasis is mainly to the bone marrow and bone. The bone marrow aspiration with biopsy is easy and rapid way of staging the disease.

The prognosis of neuroblastoma patients depends a lot on the stage of

disease. The five years overall survival for stage I without MYCN amplification is approximately 98-100% and for patients with stage IV with MYCN amplification is 20%. [(5)] Bone marrow aspiration and biopsy is an important investigation which can contribute in staging of the disease. The sensitivity of detection of bone marrow can be further enhanced by doing bone marrow from both sides, doing immunohistochemistry, flow cytometry or molecular test. [(6)] However bone marrow proves very rapid and cost effective way in detecting metastasis and staging of the disease. Moreover very few studies have studied the hematological profile of patients with neuroblastoma.

MATERIALS AND METHODS

The study was conducted in the hematopathology section of Department of Pathology at King George's Medical University, Lucknow and total of 45 cases were enrolled In the study from Jan 2014 to Dec 2017. All cases were diagnosed as neuroblastoma by fine needle aspiration cytology / histopathology and were further subjected to cytochemistry and immunohistochemistry for confirmation. The diagnosed cases simultaneously underwent bone marrow aspiration with bone marrow biopsy from posterior superior iliac spine and examined for evidence of metastasis. The slides were stained with May-Grubwald Giemsa and Hematoxylin and eosin. The patient's clinical, hematological profile, bone marrow aspiration / biopsy findings were recorded and analyzed for evidence of metastasis.

RESULT

The study was conducted from Jan 2014 to Dec 2017 in the hematopathology unit of Department of Pathology at King George's Medical University. Total number of patients enrolled for the study was 52 of which 07 patients were excluded from the study as they either refused bone marrow aspiration and biopsy or they were on chemotherapy before the procedure. Therefore 45 patients were enrolled for data analysis. The diagnosis was confirmed by histopathological examination and immunohistochemistry.

The patients included in the study belonged to age group of 05 months to 18 years. 82% of these patients belonged to poor socioeconomic status. 31/45 (68.9%) of the patients were male and 14/45 (31.1%) were female. Male to female ratio is 2.21:1. The most common site of involvement was adrenal medulla (48.9%; 22/45) and paraspinal ganglion (35.6%; 16/45). All patients underwent complete blood counts, peripheral blood smear examination along with bone marrow aspiration with biopsy and imprint smears and were subsequently examined for marrow infiltration.

The patient's complete blood count showed that 87.5% (39/45) of cases were anaemic with mean hemoglobin of 8.2 gm% (4.7 - 9.6gm %). Majority of them were normocytic normochromic type suggesting anaemia of chronic inflammation. Anaemia was seen even in cases with uninvolved bone marrow. Total Leukocyte count was reduced in 22.2% of patients (10/45). Total leukocyte count ranged from 1300-33,800/cumm. The differential leukocyte count was intact in all cases. The leukocytosis was because of neutrophilia. Thrombocytopenia was observed in 22.2% (10/45) cases and thrombocytosis was observed in 20.0% (9/45) cases. The platelet count ranged from 21,000 - 666,000/cumm. The morphology of the platelets was normal in all cases. None of the patients presented with bleeding manifestations. Pancytopenia was seen only in one case. This case showed extensive infiltration in the marrow.

Bone marrow infiltration was present in 53.3% (24/45) of patients with evidence of infiltration seen in bone marrow aspirate as well as bone marrow biopsy in 20/24 (83.3%) cases. 4/24 cases showed infiltration only on biopsy and had patchy involvement. Most common pattern of infiltration was diffuse (14/24; 58.3%) followed by interstitial (7/24; 29.2%) and patchy (3/24; 12.5%). The classical rosette

pattern was seen in 70.8% (17/24) cases. Reticulin staining was done in all cases and showed evidence of fibrosis in 31/45 cases (68.9%) ranging from grade 1-2

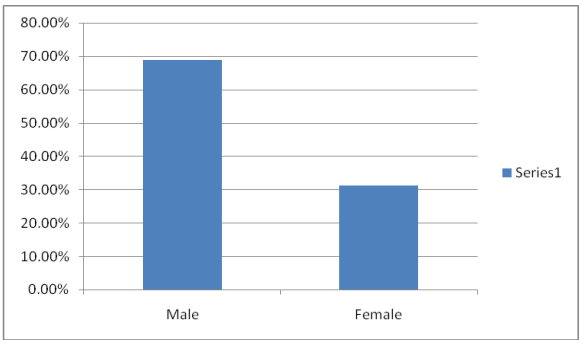


Table 1: Male and female ratio amongst the study group.

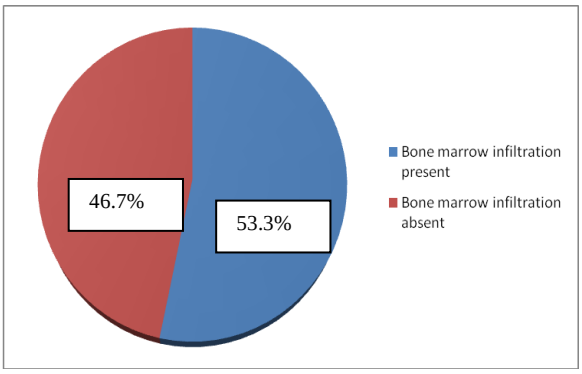
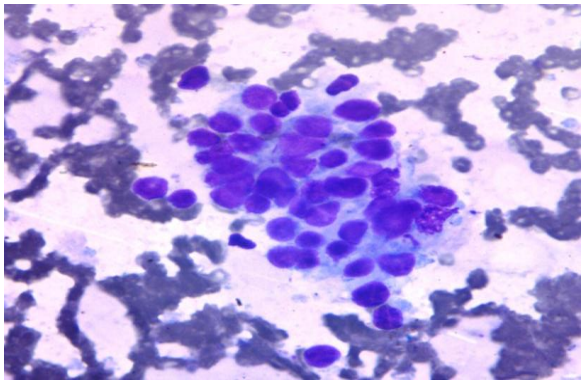
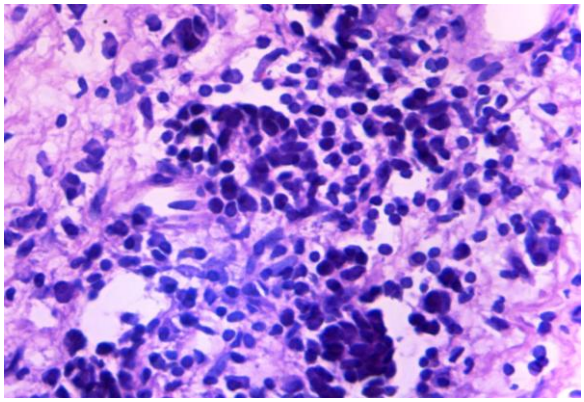


Table 2: Number of patients present with bone marrow infiltration.





DISCUSSION

Neuroblastoma is one of the commonest embryonal malignant neoplasms of infancy arising from developing and incompletely committed precursor cells derived from the neural crest tissue. The tumour presents as a mass lesion arising from the sympathetic nerve ganglia mainly from the adrenal medulla, paraspinal ganglia. The tumour is commonly associated with MYCN amplification. The clinical presentation is very heterogeneous with most patients looking very ill, malnourished and having pain. Patients usually present with mass, most commonly abdominal (35%) and paraspinal ganglia (35%). Other sites of involvement are posterior mediastinum, pelvis and neck. Intrathoracic tumours are incidentally discovered on chest X-ray.

Approximately half of the patients present with distant metastasis and such patients have systemic symptoms and look quite ill. These patients present with malaise, anorexia, weight loss, fever, anaemia and skin lesions. Neuroblastoma also has a peculiar tendency to metastasize to orbit with bruising and proptosis termed as "Raccoon eyes". [(7)] Bone marrow metastasis if present suggests poor prognosis and dismal outcome of the patient. Bone marrow involvement causes cytopenia in the peripheral blood as well.

In our study most common site of involvement of neuroblastoma was adrenal medulla and paraspinal ganglia. Bone marrow infiltration was seen in 53.3% of patients. The findings are similar to Cozzutto C et al [(8)] (58.3%) and Rastogi P et al [(9)] (54.5%). Franklin at al [(10)] reported marrow infiltration by malignant cells in 48.9% cases. The patient's complete blood count showed that 87.5 % of patients had anaemia. The discordance between the number of patients with marrow infiltration and anaemic patients can be explained by anaemia of chronic inflammation. Moreover, most of the patients in our study population were of poor socioeconomic

status predisposing them for nutritional deficiency.

In the present study, bone marrow aspiration and biopsy was done for staging of the neuroblastoma. Involvement of bone marrow suggests stage 4 disease with poor outcome. The sensitivity of bone marrow aspiration and biopsy as staging procedure for neuroblastoma carries sensitivity of 10^{-3} to 10^{-4}. Presently there are various methods of screening for bone marrow metastasis with higher sensitivity and specificity like Flow cytometry, immunocytochemistry, immunohistochemistry, molecular techniques like RQ-PCR. There are studies which have performed bone marrow aspiration and biopsy bilaterally to increase sensitivity and specificity of marrow metastasis.

Although bone marrow aspiration and biopsy is less sensitive than other modalities for screening but it is an important investigation in under resourced laboratories where advanced methodologies are not available. Franklin et al evaluated 208 cases and found that trephine biopsies were more efficient method for detecting metastasis in marrow. Rastogi P et al showed that bilateral bone marrow aspiration and biopsy is more effective in detecting metastasis and staging of disease.

CONCLUSION

In our study Adrenal medulla is the commonest site of neuroblastoma. Bone marrow aspiration with biopsy can be utilized as an important procedure for staging of neuroblastoma patients in under-resourced hospitals. In our study 53.3% of the patients showed marrow infiltration and were subsequently upstaged to 4/4S according to INSS staging. Most common pattern of infiltration was diffuse type with demonstration of rosettes. The patients with infiltration showed unilineage, bilineage or pancytopenia in peripheral blood. However significant number of patients had anaemia of chronic inflammation.

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