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Case Report

Pathology Section

Aggressive Lymphoma in a 14 Year Old Indian Boy, Diagnosed on Fine Needle Aspiration Cytology

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ABSTRACT

Burkitt's lymphoma(BL) is a highly aggressive B -cell Lymphoma of childhood with a doubling time of 24 to 48 h. Depending upon the clinical and epidemiological factors it is classified as Epidemic, Sporadic and Immunodeficiency associated Burkitt's lymphoma. Sporadic Burkitt's lymphoma has its own characteristics with few differences pertaining to specific geographical location. Here, we present a case of 14-year-old boy who presented with advanced stage disease. On examination he had cervical lymphadenopathy and CNS involvement in the form of nerve palsy.USG revealed multiple well defined solid lesions in liver, both kidneys and pancreas. However, PBS did not show the presence of lymphomatous cells. Fine needle aspiration cytology (FNAC) of cervical lymph node and liver lesion showed features suggestive of Burkitt's lymphoma, which was further confirmed on Histopathological and immunohistochemical examination.

Keywords: Burkitt's, FNAC, Lymphoma, Lymphadenopathy, Sporadic

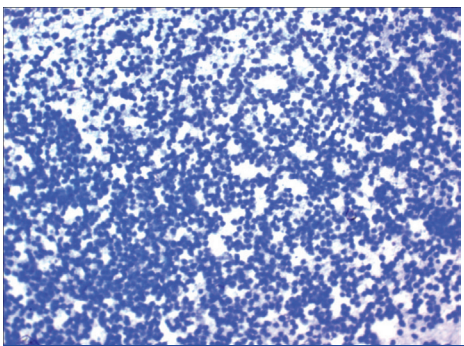
CASE REPORT

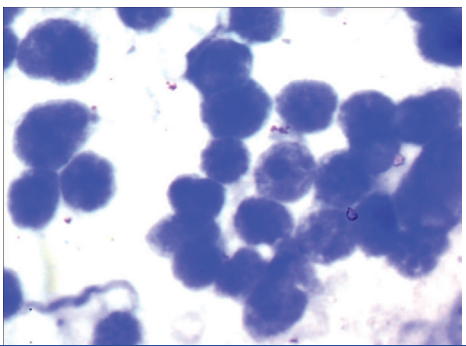
A 14-year-old boy presented to surgery OPD of DM Wayanad Institute of Medical Sciences, Naseera Nagar, Meppadi, with abdominal pain and vomiting since 10 d. He had painless swelling on left side of neck since two months. History of weight loss was present. On examination patient was dehydrated and emaciated. He had foul smelling breath and had slurred speech. Multiple discrete upper cervical lymph nodes were palpable, the largest being 2 X 2 cm, irregular firm and non-tender. Other lymph nodes were smaller in size. Few small axillary and inguinal lymph nodes were also palpable. Per abdomen, liver was enlarged extending up to umbilicus. On neurological examination he had bilateral lower motor neuron (LMN) palsy of 7th and 12th nerve. Hematological and biochemical investigations revealed, Haemoglobin 12.2gm%, TLC 5700/µl, DLC was within normal limits, ESR 43mm at the end of one hour, routine urine examination was within normal limits, Random Blood sugar level was 72mg/dl, blood urea 45mg/dl, serum creatinine 0.65 mg/dl, coagulation profile within normal limits. Chest X-ray did not show any mediastinal lymphadenopathy, CT brain was normal with no organic lesion. Ultrasonography of abdomen revealed lymphomatous infiltrates in liver, kidneys and pancreas. FNAC cervical lymph node showed cellular smears with a uniform population of intermediate sized cells [Table/Fig-1] having round nuclei, coarse chromatin with few showing prominent nucleoli [Table/Fig-2]. Mild increase in mitotic activity and few tingible body macrophages were also seen. Reid Sternberg cells were not seen and hence the diagnosis of high grade Non-Hodgkin's Lymphoma, possibly Burkitt's was offered. Biopsy was advised for confirmation and further studies.

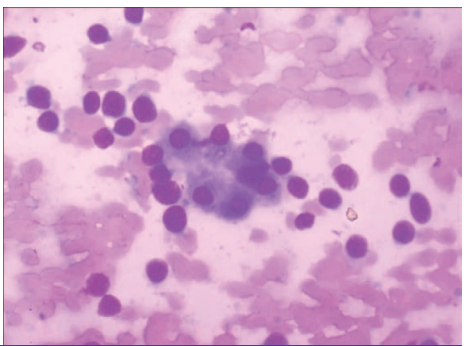
FNAC from liver lesion was performed which showed moderately cellular smears with few clusters and sheets of normal hepatocytes intermixed with monotonous population of intermediate sized lymphocytes [Table/Fig-3], confirming the presence of lymphoma infiltrates in liver.

Biopsy of cervical lymph node was received in histopathology section, in the form of single tissue bit, firm in consistency. Cut section showed multiple grey white lymph nodes [Table/Fig-4], largest measuring 2X1 cm. Multiple sections studied through these lymph nodes showed effaced architecture replaced by sheets of intermediate sized cells having high nuclear-cytoplasmic ratio, open chromatin, few nucleoli and increased mitotic activity and areas of apoptosis with a characteristic starry sky appearance [Table/Fig-5&6]. With these features diagnosis of Burkitt's lymphoma was confirmed and patient was immediately referred to Regional Cancer Center (RCC), Trivandrum for Immunohistochemistry (IHC) and further management.

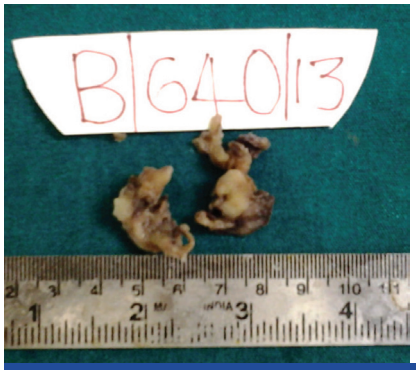
IHC performed at RCC revealed very high growth fraction in the form of positive staining for Ki-67 in more than 95% of neoplastic cells[Table/Fig-7]. Cells were also positive for CD20 [Table/Fig-8]

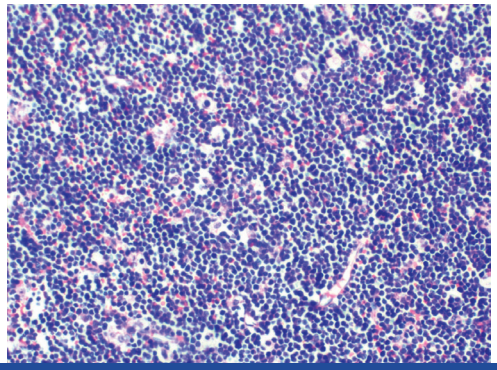


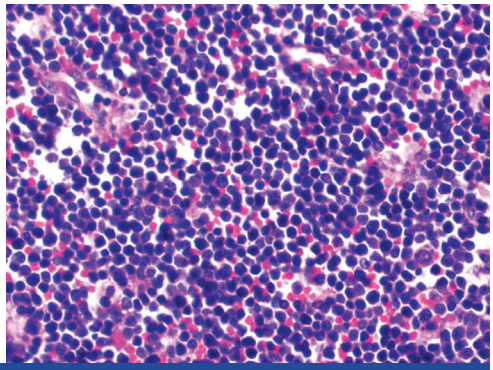




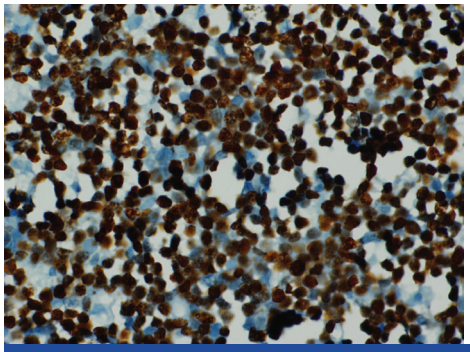
[Table/Fig-1]: FNAC Cervical Lymph Node - Smear showing uniform population of intermediate sized cells (10 x 10; Leishmann stain) **[Table/Fig-2]:** FNAC Cervical Lymph Node - Smear showing coarse chromatin and prominent nucleoli (10 x100; Leishmann stain) **[Table/Fig-3]:** FNAC Liver lesion - Smear showing monotonous population of lymphocytes intermixed with normal hepatocytes (10 x 40; Leishmann stain)

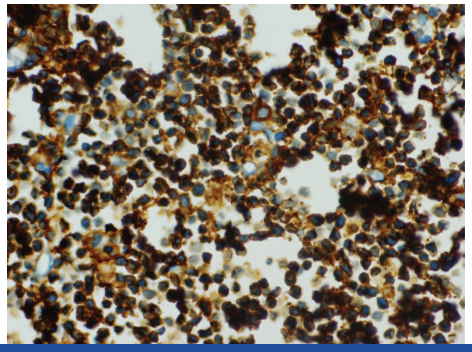


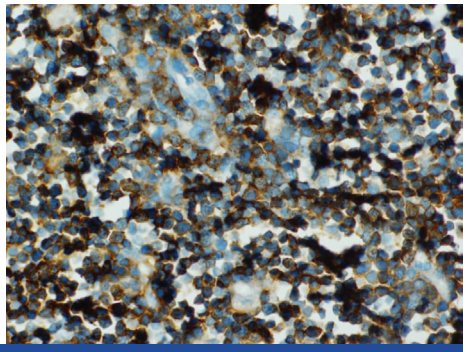




[Table/Fig-4]: Gross photograph of cervical lymph node biopsy showing grey white cut surface, **[Table/Fig-5]:** Cervical lymph node biopsy - section showing starry sky appearance (10x20; HE stained section), **[Table/Fig-6]:** Cervical lymph node biopsy - section showing tingible body macrophages and uniform population of neoplastic cells (10 x 40; HE stain)







[Table/Fig-7]: Positive immunostaining for Ki-67 **[Table/Fig-8]:** Positive immunostaining for CD-20 **[Table/Fig-9]:** Positive immunostaining for sIgM

and sIgM [Table/Fig-9] which confirmed the diagnosis of Burkitt's lymphoma. In addition bone marrow and CSF examination were performed, which showed the presence of lymphoma cells. He was put on aggressive chemotherapy and attained remission on completion of first cycle.

DISCUSSION

Burkitt's lymphoma is defined by the updated WHO classification (2008) as a B-cell lymphoma with an extremely short doubling time, that often presents in extra-nodal sites or as an acute leukaemia [1]. In western countries, it is one of the most common types of malignant tumours in children and young adults accounting for about 30% to 50% of childhood lymphomas [2]. Isolated cases of Burkitt's lymphoma are reported intermittently from all over India. However large related studies in children and young adults are very few. From the available report by Naresh KN et al., out of 2773 lymphoma cases, 50 cases i.e. 1.8% cases were of BL [2]. Pramanik et al., studied 263 cases of childhood solid tumours over a period of 10 years, out of which only 2 cases were of BL [3]. Thus in order to know the true incidence of BL in Indian children and young adults a large study needs to be undertaken.

African BL presents usually with jaw involvement, whereas sporadic BL presents as abdominal mass [1]. Clinical presentation of BL in India does not resemble either endemic or non-endemic areas. In study conducted by VP Choudhary et al., he found that BL in India presents with jaw and abdominal involvement in almost equal number and concluded this to be the third mode of clinical presentation [4].

Our patient had cervical lymphadenopathy and later developed abdominal disease. The reason for presentation with widespread disease being lack of clinical suspicion and hence the resultant delay in diagnosis. It was possible for us to give the diagnosis of high grade non- Hodgkin's lymphoma, probably Burkitt's, in the present case on the basis of FNAC of cervical lymph node. USG guided FNAC of liver nodule confirmed the presence of lymphoma infiltrate, categorizing the patient in higher stage disease. Myong NH et al., used FNAC as a primary tool in the diagnosis of abdominal BL [5]. Similarly Ogawa et al., diagnosed BL of bilateral breasts on FNAC [6]. Advanced stage disease, high LDH, and CNS or marrow involvement are associated with adverse outcomes in adults and children [7]. Our patient had bone marrow and CNS involvement, hence as per St. Jude's staging system for NHL, described by Murphy, patient was in stage IV disease [8]. He attained clinical remission after first cycle of intensive chemotherapy and is undergoing eighth cycle at present.

The closest differential diagnosis of BL is diffuse large B- cell lymphoma (DLBCL). There is no single test or marker which can differentiate between these two lymphomas. Hence, a multimodal approach is required which includes cytomorphological findings, immunocytochemistry/ biopsy with immunohistochemistry, genetic studies and clinical correlation. Intermediate sized cells with clumped chromatin, and two to three prominent nucleoli, cytoplasmic vacuolation and scattered tingible body macrophages forms characteristic cytomorphology of BL. Prototypical immunophenotype of BL includes CD 20 +, CD 10 +, BCL 6 +, BCL 2-, TdT - , and sIgM + with virtually all cells Ki-67+. Immunophenotypic analysis in present case showed neoplastic cells positive for CD 20 and sIgM. Nuclear positivity for Ki-67 was found in more than 95 % of the cells which confirmed the diagnosis of BL. Translocation involving c-myc and IgH or IgL without rearrangement involving BCL2 or BCL6 gene favours BL. However, different studies vary with respect to their results on this point and some large B cell lymphomas also express c-myc protein [7].

CONCLUSION

An early diagnosis is of paramount importance for prompt and effective management of BL. In developing countries like India, where most of the peripheral laboratories and institutions do not have advanced diagnostic facilities, FNAC forms a safe, rapid and cost effective tool towards early detection of this lymphoma.

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