Primary Hepatic Burkitt Lymphoma: A Bizarre Site and Triumph Tale

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Primary hepatic Burkitt lymphoma (PHBL) is an extremely rare form extra nodal lymphoma and till now only 11 case reports have been found in the literature. We are reporting an adult female with primary hepatic Burkitt's lymphoma, who achieved complete remission after 5 months of combination chemotherapy containing vincristine, cyclophosphamide, doxorubicin, methotrexate, prednisolone and intrathecal chemotherapy. She is under regular follow up at our institute. (J CLIN EXP HEPATOL 2015;5:159–162)

Gastrointestinal (GI) tract is the most common extra nodal site involved by lymphoma accounting for 5–20% of all cases and is usually secondary to the widespread nodal diseases. However, primary gastrointestinal lymphoma is very rare, constituting only about 1–4% of all gastrointestinal malignancies. Primary hepatic Burkitt's lymphoma is a very condition with only 11 case reports reported in the literature till date [Table 1]. As rarity of its occurrence, accurate epidemiology and etiology is not established for PHBL. Burkitt's lymphoma is an undifferentiated malignant lymphoma of B lymphocytes. PHL is defined as an extra nodal lymphoma restricted to the liver, accounting for only 0.4% of all the extra nodal lymphomas.^{1,2}

CASE VIGNETTE

Twenty one years old female presented with abdominal discomfort, nausea, reduced appetite, and malaise for 15 days duration. Her past and family history was unremarkable. Her performance score was 1 and had no B symptoms (fever, significant weight loss or drenching perspiration). On physical examination, she was conscious, oriented, and his vitals were stable. There was no icterus, cyanosis or lymphadenopathy. Per abdominal examination revealed hepatomegaly, liver was firm, tender and was palpable 4 cm

below the costal margin. Viral markers including Hepatitis B surface antigen and anti-hepatitis C antibodies were all negative. Human immunodeficiency virus enzyme-linked immuno sorbent assay was non-reactive. Serology for Epstein-Barr virus was negative.

Her abdominal ultra sonography (USG) report revealed multiple hypo echoic lesions in both lobes of the liver and she was advised to undergo computed tomography (CT) scan abdomen and pelvis. It revealed multiple hypo dense lesions suggestive of infiltration of the lymphoma. [Figure 1] Mass showed intense enhancement on arterial and venous phase and delayed phase shows early washout, rest of the study was normal. There was no abnormal lymphadenopathy in any part of body or ascites or splenomegaly was clinically evident.

USG guided true cut biopsy from liver mass was taken without any complication. Histopathological examination showed features of non-Hodgkin's lymphoma of Burkitt type. Cytological smears showed cellular smears comprising of mature B cells arranged in sheets, round in shape, pleomorphic nuclei, medium to large in size with prominent nucleoli, with fine chromatin and moderate cytoplasm with many mitotic figures. Numerous apoptotic bodies were also seen, which are engulfed by the macrophages imparting the characteristic "starry sky" appearance. Immunohistochemistry revealed positivity for, CD20 [Figure 2], CD10 [Figure 3], and BCL-6; immunonegativity for CD3 and BCL-2. Mib-1 labeling index was close to 99% [Figure 4]. Fluorescence In Situ Hybridization (FISH) for C-MYC (8q24) gene amplification assay was done from the peripheral blood with interphase nuclei and found to be positive for the C-MYC (8q24) gene amplification (Figure 5). For staging work up CT scan of neck, thorax, bone marrow aspiration and biopsy, cerebrospinal fluid cytology were done, which were normal. Complete blood counts revealed hemoglobin of 11.5 gm/dl, leukocyte count of 4700/cu mm, and platelet count of 4.75

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Abbreviations: CEA: carcino embryonic antigen; DLBCL: diffuse large cell lymphoma; LDH: lactate dehydrogenase; PHBL: primary hepatic Burkitt lymphoma

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Table 1 Shows Previous Scattered Case Reports and Available Literature on PHBL.

Author	Year/region	Age/sex	Comments
Y. L. Wan et al	1988	Pediatric	–
Kuroda J et al	2001/Japan	75/M	Patient was HCV positive.
Jacobs SL et al	2006/USA	40/F	Patient was HIV positive; Hyper vascular enhancement was unique in this case.
Lee SH et al	2008/Korea	19/M	Patient was positive for Hbsag, HbeAg. He was treated with the combination of chemotherapy.
Mantadakis E et al	2008/Greece	8.5/M	Diagnosis was achieved after laparotomy and incisional biopsy. The patient received short, intensive multiagent chemotherapy.
Mattar WE et al	2010/USA	–	Presenting as acute liver failure. Author concluded that patient may respond well to emergent chemotherapy even in the setting of acute liver failure.
Saffar H et al	2011/Iran	–	–
EC Citak et al	2011/Turkey	CHILDHOOD	–
Sunita Singh et al	2013/India	28/M	–
Sekiguchi Y et al	2013/Japan	30/M	Burkitt lymphoma was diagnosed on surgical specimen; then further treated with multiagent chemotherapy.
S paydas et al	2013/Turkey	31/F	–

lakhs/cumm. Erythrocyte sedimentation rate (ESR) was of 50 mm at 1st hour. Liver function tests bilirubin of 0.7 mg/dl, albumin 3.1 gm/dl, SGOT of 27 IU/L, SGPT of 30 IU/L, alkaline phosphatase level of 112 IU/L and INR of 1.1. Renal function tests like urea 18 mg/dl and creatinine of 1.1 mg/dl. Tumor lysis profile including serum creatinine, calcium, potassium, phosphorus, and uric acid was within normal limits. Serum LDH (lactate dehydrogenase) level was 995 IU/L (Normal range 105–333 IU/L).

According to the Ann Arbor staging system, involvement liver constitutes Stage IV disease. Our patient was classified as Stage IV PHBL, because of diffuse liver involve-

ment. Appropriate counseling regarding the disease, cost and side effects of chemotherapy were explained to patient. Patient was managed with supportive care for tumor lysis syndrome prevention and LMB-96 protocol for intermediate risk BL with COP [cyclophosphamide, oncovin (vincristine) and prednisolone] as reduction or prophase, COPADM [cyclophosphamide, oncovin (vincristine), prednisolone, doxorubicin and high dose methotrexate (HDMTX)] 1 & 2 as induction chemotherapy and CYM (cytarabine, HDMTX) 1 & 2 as consolidation chemotherapy courses with intrathecal (IT) chemotherapy prophylaxis during all phases of the therapy. COP → COPADM1 → COPADM2 → CYM1 → CYM2. The first evaluation was performed after COP at day 7 with a response rate of more than 20%. The second evaluation was performed after first COPADM with a response rate of more than 50% decrease in the size of mass. The third evaluation was performed after first CYM with CT image showing complete response rate without any residual lesion. Patient is under regular follow up for any recurrence of the disease.

DISCUSSION

Secondary involvement of liver in myriad lymphomas is universal findings but occurrence of primary hepatic lymphoma (PHL) is infrequent. PHL is defined as an extra nodal lymphoma restricted to the liver, accounting for only 0.4% of all the extra nodal lymphomas.¹ Diffuse large cell lymphoma (DLBCL) is the most common histology type among PHL. As a subtype of PHL, primary hepatic

Figure 1 Computed tomography of the image shows multiple hypodense lesions suggestive of infiltration of the lymphoma.

Figure 2 IHC image showing positivity for CD20.

Figure 4 IHC image showing positivity for MIB1.

Burkitt lymphoma (PHBL) is very rare and only 11 cases reported in world literature. Burkitt lymphoma is a highly proliferating malignant lymphoma of B lymphocytes. The term is coined from Dr Denis Parsons Burkitt, who observed this unusual type of malignancy in African children in the year 1957.³ Ordinarily Burkitt lymphoma are classified into three types: endemic (found in Africa, allied to Epstein-Barr virus infection), sporadic and immunodeficiency associated.⁴ The presentation of non endemic type is abdominal mass and involving ileocecal area or mesenteric lymph nodes.

As rarity of its occurrence, accurate epidemiology and etiology is not established for PHBL. Burkitt's lymphoma is an undifferentiated malignant lymphoma of B lymphocytes. It was first described by Denis Burkitt, who named the tumor on the African children's jaw sarcoma.³ A molecular signature of Burkitt's lymphoma is the existence of translocation between c-myc gene and IgH gene (t (8;

14)) or between c-myc gene and the gene for either the kappa or lambda light chain (t (2; 8) or t (8; 22)).^{2,5}

The clinical, laboratory, and radiographic characteristics are nonspecific, which means the diagnosis is often not suspected until histopathological examination of liver tissue. Abdominal pain or discomfort, weight loss and fever are the most frequent initial symptoms. Most cases have a solitary or multiple mass lesions in the liver, and are frequently fallaciously perceived as having a primary liver tumor or metastatic cancer. The results of liver function tests are typically abnormal. Lactate dehydrogenase (LDH) and alkaline phosphatase are usually with normal serum alfa fetoprotein and carcino embryonic antigen (CEA) levels. There is no specific imaging criteria for diagnosing PHBL but usually lymphomatous infiltration of liver lesions are hypo attenuating and hypo vascular lesions. But hyper vascular enhancement is also documented.⁶

On microscopic examination, Burkitt's lymphoma is composed of uniform population of medium sized cells

Figure 3 IHC image showing positivity for CD10.

Figure 5 Showing positive Fluorescence In Situ Hybridization (FISH) for C-MYC (8q24) gene amplification assay from the peripheral blood with interphase nuclei.

with round nuclei and multiple small basophilic nucleoli. The cytoplasm is strongly basophilic with small round cytoplasmic vacuoles best observed in air dried touch imprints. Tingible body macrophages, phagocytosing abundant apoptotic debris creating starry sky appearance is a characteristic finding, although not always present. On immunohistochemical examination, the neoplastic cells are positive for surface immunoglobulin Ig M and Ig light chains; pan B-cell antigens (CD 19, CD 20, CD 22, and CD 79) and co-expresses CD 10, BCL-6, CD 43, and p53 but not CD 5, CD23, BCL-2 and CD 138. The proliferating fraction is nearly 100%.²

Because the liver is a vital organ, involvement with lymphoma can lead to a rapidly progressive life-threatening illness. Mattar et al concluded that mortality is 85% if patient initially present as acute liver failure and also patient may respond well to emergent chemotherapy even in the setting of acute liver failure.⁷ Although primary hepatic Burkitt's lymphoma has been successfully treated with surgery followed by dose-intense chemotherapy, primary surgical resection should not routinely be considered for high grade lymphomas because of the resulting delay in the administration of chemotherapy. Usually CODOX-M IVAC is used in adult Burkitt lymphoma. We have used our pediatric experience of LMB 96 in treatment of this patient without any modification.⁸ Our patient has complete response to the LMB-96 intermediate risk protocol and is under regular follow up.

CONCLUSION

PHBL is an extremely rare lymphoma subset that often presents with diagnostic difficulties to both clinicians and pathologists. Burkitt lymphoma is an aggressive mature B-cell non-Hodgkin lymphoma, which follows a rapid clinical course and can be fatal within months if left untreated. Early assessment of the correct diagnosis is crucial for dis-

ease management. Primary hepatic lymphoma should be considered as one of the differential diagnosis of liver lesions especially in young adults.

CONFLICTS OF INTEREST

All authors have none to declare.

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