Case Report

Primary Hepatic Diffuse Large B Cell Lymphoma: A Case Report

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Abstract

Non-Hodgkin’s lymphomas presenting exclusively in the liver are rather uncommon in adults and extremely rare in children. We describe a seven-year-old white boy with abdominal pain, nausea, vomiting and fever of two weeks’ duration and he denied night sweats or weight loss. Physical examination disclosed asthenia, abdominal swelling, and large hepatomegaly. Lactate dehydrogenase and liver function tests were significantly elevated. Bone marrow aspiration, cerebrospinal fluid, chest x-ray, renal function tests, and uric acid were normal. Abdominal ultrasound showed that the liver was extremely enlarged, with 2 solid hypo echogenic nodules, confluent and well delineated in relation to the parenchyma, distributed in right lobes. A laparoscopic hepatic biopsy revealed Diffuse Large B Cell Lymphoma, identifying lymphoma cells CD20+, CD43+, CD10−, BCL-6+, BCL-2+, cyclin D1 −, EBER−, KI-67 90%, CD99, CK7−. The child showed an excellent response to chemotherapy based on the LMB-96 protocol for B cell non-Hodgkin’s lymphomas. The patient had his therapy discontinued in June 2017 and remains in first complete remission as of May 20th, 2017.

Keywords: diffuse large b cell lymphoma, primary hepatic lymphoma, acute liver failure

Introduction

Lymphoma is a malignant condition of the blood with an annual incidence of 15 cases per 1 million children in the USA, representing the 3rd most common cancers in pediatric age [1]. Lymphomas are divided in 2 main categories: Hodgkin (HL) and non-Hodgkin lymphomas (NHL), with specific clinical manifestations and treatment. In children, NHL comprises 4 wide categories: lymphoblastic lymphoma, Burkitt lymphoma (BL), diffuse large B-cell lymphoma (DLBCL), and anaplastic large cell lymphoma. Even though most of the children present with the novo NHL, some of these cases may be secondary to other etiologies, such as: inherited or acquired immune deficiencies, viruses, or are included in the spectrum of genetic syndromes [1]. Depending on ethnicity, lymphomas are much more frequent in Black Africans along with leukemia and central nervous system cancers in comparison with other ethnic groups, where leukemia and central nervous system were the most common types of malignancies [2]. For example, in Africa, the incidence of BL is approximately 50-fold higher than that encountered in the USA, [3] therefore being named endemic BL. Besides, endemic BL, there are also defined another 2 types of BL, sporadic and immunodefi cient. The
clinical appearance of HHL in children depends in all cases on sites of involvement and the pathologic subtype. Therefore, lymphoblastic lymphoma presents most commonly as an intrathoracic or mediastinal mass and own a predilection for metastasizing in the bone marrow or central nervous system. Likewise, BL can also spread to those 2 sites, but it usually manifests and an abdominal mass in case of sporadic type, or head and neck in case of endemic type. On the other hand, DLBCL rarely metastasizes to the bone marrow or central nervous system, but it can manifest as both abdominal or mediastinal mass. Last, but not least, anaplastic large cell lymphoma is a particular type, which can present as a primary cutaneous tumor or a systemic disease, and usually spreads to liver, lungs, spleen, and mediastinum, rarely in bone marrow or central nervous system [1]. Most common manifestations related to the tumor site are: fast lymph node enlargement without associated pain, cough, or dyspnea in case of intrathoracic masses, even superior mediastinal syndrome; ascites and increase of the abdominal perimeter or bowel obstruction in case of abdominal masses; while in case of Waldeyer ring involvement, nasal congestion, earache, hearing loss, or tonsils enlargement are the most frequent symptoms; and bone pain in case of bone metastases [1]. In particular cases, NHL can also manifest as a life threatening oncolgic condition requiring intensive supportive care, like: superior mediastinal syndrome, acute paraplegias (spinal cord tumors), renal failure, or cardiac impairment due to tumor lysis syndrome, especially in BL, which can lead to hyperuricemia, hyperphosphatemia, hyperkalemia, and hypocalcemia [1]. The treatment for children diagnosed with NHL includes multi agent systemic chemotherapy with intrathecal administration, surgical intervention is used mainly for diagnosing the tumors, while radiation therapy is only for central nervous system involvement, superior mediastinal syndrome, or paraplegias [1]. We present this case of abdominal lymphomas with the aim of underlining the variability of diagnostic and prognostic particularities encountered in children diagnosed with NHL. The informed consent was obtained from the patients’ mothers (legal guardians) for the publication of this cases.

Case Report

Presenting concerns

We present the case of a seven-year-old white boy was admitted at the National Institute of Oncology and Radiobiology, Havana in April 2017. His past and family history was unremarkable. He was asymptomatic until 20 days before admission when he developed progressive abdominal pain, nausea, vomiting and fever. During this period, he denied night sweats or weight loss.

Clinical findings

On physical examination, he 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.

Laboratory evaluation

Laboratory tests revealed complete blood count, renal tests, urinalysis, serum electrolytes, partial thromboplastin, and prothrombin times, bilirubin, alkaline phosphatase, and serum α-fetoprotein were normal. Viral markers including Hepatitis B surface antigen and anti-hepatitis C antibodies were all negative. Human immunodeficiency virus enzyme-linked immune sorbent assay was non-reactive. Serology for Epstein–Barr virus was negative. Lactate dehydrogenase and liver function tests was elevated.

Diagnostic procedures

His abdominal ultrasonography (USG) report showed that the liver was extremely enlarged, with 2 solid hypoechoic nodules, this confluent and well delineated in relation to the parenchyma, distributed in right lobes. Abdominal computed tomography (CT) scan with contrast confirm that the liver was extremely enlarged. Showed with
2 solid hypodense nodules, well defined, variable density, 26 to 65 HU, measuring 123 x 75 mm, in the right lobe of the liver (Figure 1).

![Figure 1: A mesentery lymphadenopathy measuring 12 mm.](image)

A laparoscopic hepatic biopsy revealed Diffuse Large B Cell Lymphoma, identifying lymphoma cells CD20+, CD43+, CD10−, BCL-6+, BCL-2+, cyclin D1−, EBER−, KI-67 90%, CD99, CK7. For staging work up CT scan of neck, thorax, bone marrow aspiration and biopsy, cerebrospinal fluid cytology were done, which were normal.

**Hospital course**

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 (HD MTX)] 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.

**Follow-up and outcome**

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 residual lesion measuring 1 cm. The quart evaluation was performed after second CYM with CT image showing complete response rate without any residual lesion. Patient is under regular follow up for any recurrence of the disease.

**Discussions**

The incidence of lymphomas varies worldwide, 60% being classified as NHL, accounting for 8% of all pediatric malignant conditions [4–6]. In approximately 70% of patients diagnosed with NHL, the onset of the disease involves extranodal involvement, such as bone marrow and central nervous system impairment, being labeled as stage III or IV tumors [1]. Sporadic BL is the most common subtype in the USA and Western Europe, where the incidence is of approximately 2.2 cases per 1 million [7]. The most common onset age reported in the literature for BL is between 5 and 9 years of age [8–10]. Most frequently, BL affects males, [8,9] but it can also appear in females [10]. The onset age for BL differs depending on the subtypes, therefore usually endemic BL appears at younger ages, 5 to 6 years of age in comparison to sporadic BL, 8 to 9 years of age [11,12]. Also, according to the study performed by Stefan and Lutchman,[13] white population tends to follow the sporadic pattern of BL. Even though our patients belong to the Caucasian population and therefore presented with sporadic BL, only 1 of 3 diagnosed with this type of malignancy had the age of 8 years, the other 2 tended to follow the endemic pattern of BL due to the younger age of onset, approximately 5 years. It is well-known that the gastrointestinal tract is one of the most common sites for NHL, and that up to 90% of the primary gastrointestinal lymphomas are of B-cell origin [14,15]. B-cell NHL comprises BL and DLCBL. These types
of malignancies affecting the gastrointestinal tract can manifest with different symptoms, such as abdominal pain, anorexia, weight loss, diarrhea, and ileus [16]. Our patient presented abdominal pain, nausea, vomiting and fever. In rare cases, DLBCL can also lead to bowel intussusception [14,17]. In addition to intussusception, presenting symptoms of both BL and DLBCL can also mimic appendicitis. It is well-documented that sporadic or no endemic BL has, in most of the cases (91%), an abdominal presentation affecting the distal ileum, the stomach, the cecum and/or mesentery, the kidneys, testis/ovary (6%), but it can also involve the breast, bone marrow (20%), and/or central nervous system (14%) [18]. The literature also reported that BL can rarely involve the pancreas [19,20]. In addition, bone marrow involvement is encountered in under 10% of the cases at onset but is more frequent in case of recurrence or with treatment resistance [21]. In our cases diagnosed with BL none presented bone marrow involvement. The diagnosis of NHL is suspected based on ultrasound or CT scans, but it is only confirmed by the histopathological exam. Nevertheless, a careful ultrasound exam performed by an experimented individual will guide the diagnosis very well [22]. CT scan is a useful diagnostic tool in case of patients with abdominal masses that can guide properly the surgical intervention, but it also establishes the exact stage of the tumor or the mediastinal adenopathy’s, and pleural, pericardial, renal, muscle, and peritoneal metastases [23]. Even though CT scans are very important for the diagnosis of abdominal tumors, in one of our cases this exam was not relevant, and therefore, we were forced to perform an exploratory laparotomy in order to identify the exact cause of the patient’s symptoms. The prognosis of children diagnosed with NHL is reported as very good, even in those with advanced disease. Due to the advances in the management of these cases, the prognosis children diagnosed with this type of tumor improved very much in the last decades. According to the studies performed on children below the age of 15 years, the survival rate at the ages of 5 and 10 years increased from 76.6% and 73%, respectively, between 1990 and 1994 to 87.7% and 86.9%, respectively, between 2000 and 2004. Even better, the survival rate at the age of 10 years in case of children diagnosed between 2005 and 2009 improved to 90.6% [24]. Many studies tried to identify the factors that influence the prognosis, and some of them underlined that high levels of LDH maybe a negative prognostic factor for these patients [25].

**Conclusion**

Primary hepatic lymphoma should be considered in the differential diagnosis in a patient with space-occupying liver lesions and normal levels of alpha-fetoprotein and CEA. If the clinical picture is suspicious for primary hepatic lymphoma, a liver biopsy should be obtained, because the disease is treated with chemotherapy. The prognosis of these tumors is not mandatory influenced by the tumor stage because the survival rate can be high even in cases of advanced stages at onset.

**Conflict of Interest**

No potential conflict of interest exists.

**References**