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Primary Hepatic Precursor B Lymphoblastic Lymphoma in a Toddler

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Non-Hodgkin lymphoma (NHL) of childhood is a group of lymphomas that comprises all of the malignant lymphomas except for Hodgkin lymphoma (HL). The incidence of NHL in childhood differs by age and alters significantly in different world regions. The NHLs are extremely rare in children younger than 5 years. Pediatric NHL mostly involves the abdomen, neck, or mediastinum as an extranodal disease. Even though abdominal involvement is the most common presentation and lymphoma commonly spreads to the liver, primary hepatic lymphoma (PHL) is extremely uncommon at any age.[1,2]

Although Burkitt Lymphoma is the most common subtype of pediatric NHLs, only 7 cases of primary hepatic Burkitt Lymphoma (PHBL) have been reported in the literature. Precursor B-lymphoblastic lymphoma is only 3% of all pediatric NHLs. Although the liver has lymphoid tissue, individual factors make it as a poor environment for the development of lymphoma. Primary hepatic lymphoma has described the involvement of the liver at presentation without a predominant lymph nodal or splenic involvement in other subtypes of NHL.[3-6]

Herein, we report a toddler with primary hepatic precursor B lymphoblastic lymphoma (PBLL). He is the first reported case of PBLL involving the liver. Also, we explain the child's response to intensive chemotherapy.

A 3-year-old previously healthy boy presented to the emergency room (ER) with nausea, vomiting, and abdominal pain for 3 weeks. His parents did not describe fever, night sweats, and weight loss. The patient had no history of allergy, disease, or surgery in his previous medical history. He was found to have pallor, petechial rash, a hard-tender liver 6 cm below the right costal margin, and an enlarged spleen 4 cm below the left costal margin upon physical examination. No peripheral lymph nodes were palpable and there was no pathological finding in other system examinations. Complete blood count showed hemoglobin 9.4 g/dL, leukocyte 6140/μL with an absolute neutrophil count 2120/μL, and platelets 40 000/μL. A peripheral blood smear revealed the absence of atypical lymphocytes. Serum biochemistry showed elevated lactate dehydrogenase 585 U/L, uric acid 7.1 mg/dL, alanine transaminase 81 U/L, and aspartate transaminase 95 U/L. Serum total protein, albumin, urea, bilirubin, creatinine, and electrolyte levels were within normal limits.

Bone marrow aspiration was performed to examine erythroid, myeloid, and megakaryocytic morphology and look for other atypical cells like blasts. There were normocellular, heterogeneous, and sufficient numbers of precursor cells in the smear. There was no blastic clan.

In the conventional computed tomography (CT), hepatomegaly (155 mm) with normal density and homogeneity of parenchyma and splenomegaly (100 mm) were reported. No mediastinal or abdominal lymphadenopathy was found in the CT. After 5 mCi F-18 FDG injection, positive emission computed tomography (PET/CT) scan was performed. On maximum intensity projection (MIP) (A) and fused (B) F-18 FDG PET/CT images, the liver was quite large, and diffusely increased fluoro-deoxy-glucose (FDG) uptake was observed (with SUMmax 8.5). There was slightly increased activity uptake in the bone marrow. There was no finding to suggest lymph node involvement (Figure 1A and 1B).

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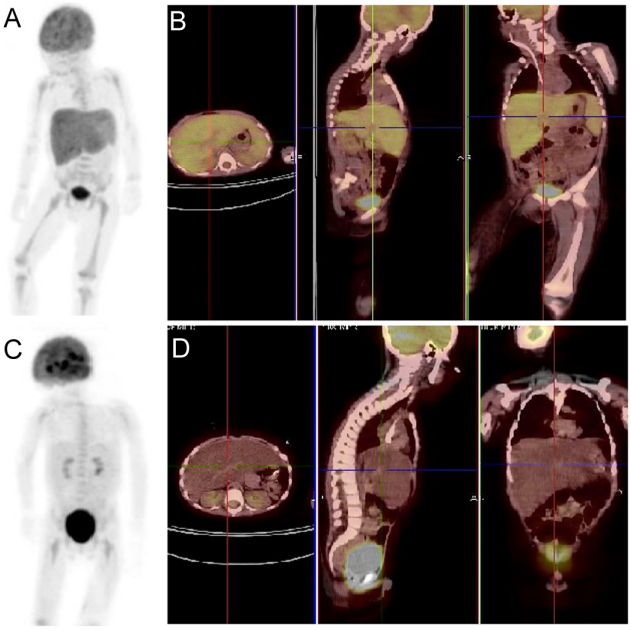

Figure 1. On MIP (A) and fused (B) F-18 FDG PET/CT images, the liver was quite large, and diffusely increased FDG uptake was observed. FDG uptakes of liver and bone marrow were normal in the post-treatment MIP (C) and fused (D) FDG PET/CT images. PET/CT, positive emission computed tomography.

Ultrasound-guided core-needle biopsy of the liver was planned when the patient was evaluated in all aspects. Histopathology showed lymphoid infiltration of the portal areas and sinusoids in the liver. At low power magnification, all portal areas and sinusoids were enlarged due to neoplastic lymphoid cells. The sinusoidal architecture of hepatocytes was distorted. There was bile duct proliferation in portal areas (Figure 2). Neoplastic lymphoid cells had narrow cytoplasm and small- to medium-size-notched hyperchromatic nuclei with no nucleoli. There were only reactive changes in hepatocytes (Figure 3).

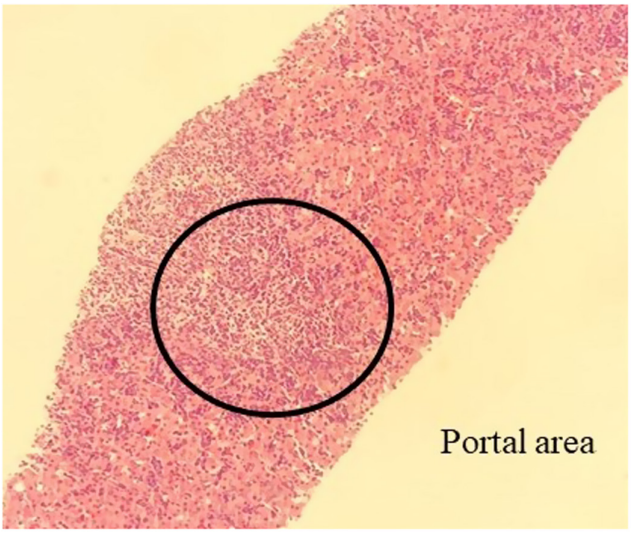

Figure 2. Lymphoid infiltration of the portal areas and sinusoids in the liver (Hematoxylin & eosin staining, ×100).

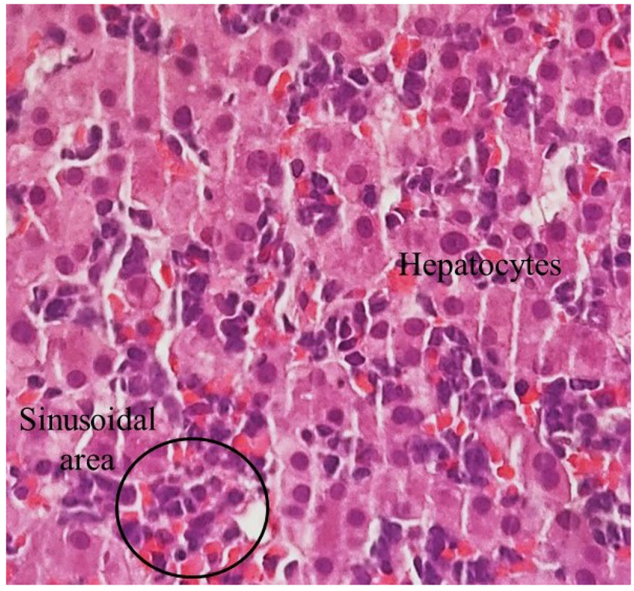

Figure 3. Hyperchromatic neoplastic lymphoid cells with narrow cytoplasm and small-medium size notched nuclei, infiltrate the sinusoidal areas.

Immunohistochemical staining revealed that the neoplastic lymphoid cells were CD20, CD19, CD79a, PAX5, BCL2, CD10, CD99, HLADR, and TdT diffuse positive and were CD3, CD5, CD4, CD7, CD8, CD15, CD56, CD33, CD38, CD117, CD34, CD13, CD163, CD61, BCL6, CMYC, MUM1, and EBV negative. The Ki-67 proliferation index was over 90% (Figure 4A-F). These features were consistent with the primary hepatic precursor B lymphoblastic lymphoma. Bone marrow biopsy was identified as a neoplastic precursor B cell infiltration similar to the liver. Cerebrospinal fluid was unremarkable. The characteristic chromosomal translocations were normal and were studied in biopsy materials of both liver and bone marrow.

Primary hepatic lymphoma may involve the liver with 2 patterns: nodular or diffuse. Our case presented with the diffuse involvement pattern of an enlarged liver with the absence of pathologically hypermetabolic foci in any other nodes or organs in the PET/CT. Therefore, the liver biopsy led us to identify PHL

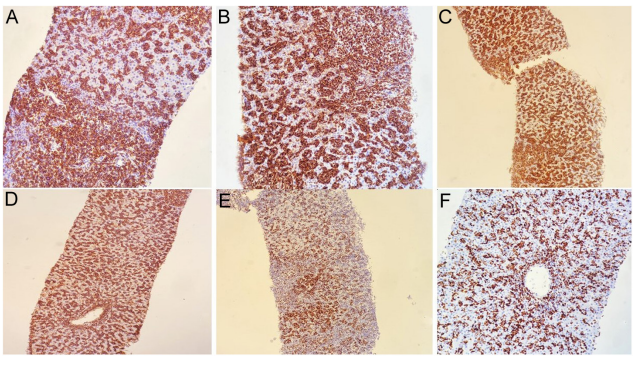

Figure 4. Immunohistochemical (IHC) staining with the neoplastic lymphoid cells; (A) CD20, (B) Bcl2, (C) CD10, (D) CD99, (E) TdT, and (F) Ki-67 (IHC staining, ×200).

as a final diagnosis. The patient was evaluated with a stage 4 disease according to Non-Hodgkin Lymphoma - Berlin Franfurt Münster (NHL-BFM) Registry 2012. The liver shrank rapidly with chemotherapy. The PET-CT scan on the 33rd day of the induction phase and completion of the reinduction phase showed that FDG uptakes of liver and bone marrow were normal in the post-treatment MIP (C) and fused (D) FDG PET/CT images (Figure 1C and 1D). Disease-free survival has been achieved during ongoing maintenance therapy.

Precursor B cell neoplasms generally appear as childhood leukemia. Precursor B lymphoblastic lymphomas create a very small part of childhood NHL. Bone, lymph nodes, soft tissues, and skin involvement is observed more prevalent in childhood PBLLs. Visceral disease (i.e., liver, gastrointestinal tract, and kidney) is exceptionally rare, only having been reported a few cases in the literature until to date.[7,8]

The diagnosis of PHL has difficulties to define due to its rarity and can be confused with other diseases.[4] The most common subtype of PHL is Burkitt Lymphoma and 7 cases have been reported in the literature.[5] The youngest patient was reported by Al-Tonbary et al[9] a 2.5-year-old boy who presented with jaundice and irritability. Despite difficulties in diagnosis, remission was achieved with the chemotherapy. Similar to our case, abdominal distension and pain were the most common symptoms and the vast majority achieved remission with chemotherapy.[5]

Precursor B lymphoblastic lymphoma has mostly been detected involving the skin during childhood. Song et al[10] summarized the primary cutaneous B cell lymphoblastic lymphomas in the literature and there were 37 published cases. The article underlined that the similarity to dermatologic conditions such as rash, eczema, or hypersensitivity reactions complicate the identification of the lymphoma diagnosis. Also, PBLLs can present with the involvement of the oral cavity and the mandible similar to Endemic Burkitt's Lymphoma.[11,12] To the authors' knowledge, this is the first reported patient of childhood precursor B lymphoblastic lymphoma primarily involving the liver.

In conclusion, primarily visceral or cutaneous involvement of the lymphomas makes diagnosis difficult. The shortest way to diagnose these lymphomas is through doubt. Biopsy of the lesion or tissue is an acceptable, finalizer method for the diagnosis of cutaneous and visceral lymphomas. Current strategies for the treatment of lymphoblastic lymphomas have largely been obtained from successful attitudes to the treatment of childhood lymphoblastic leukemia. The presented case has put the clinicians with plenty of challenges, but the achievement of remission with the treatment provided a smile.

Informed Consent: Verbal informed consent was obtained from the patient's parents who agreed to take part in the study.

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REFERENCES

1. Sandlund JT, Downing JR, Crist WM. Non-Hodgkin's lymphoma in childhood. *N Engl J Med*. 1996;334(19):1238-1248. [CrossRef]
2. Gross TG, Perkins SL. Malignant non-Hodgkin's lymphoma in children. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 7th edn. Philadelphia: Lippincott Williams and Wilkins; 2015:664-683.
3. Sandlund JT, Martin MG. Non-Hodgkin lymphoma across the pediatric and adolescent and young adult age spectrum. *Hematology Am Soc Hematol Educ Program*. 2016;2016(1):589-597. [CrossRef]
4. Mastoraki A, Stefanou MI, Chatzoglou E, et al. Primary hepatic lymphoma: dilemmas in diagnostic approach and therapeutic management. *Indian J Hematol Blood Transfus*. 2014;30(3):150-154. [CrossRef]
5. Chamberlain G, Coltin H, Klaassen RJ, Story E, Abbott LS. Successful treatment of pediatric primary hepatic Burkitt lymphoma using rituximab: a case report. *Pediatr Blood Cancer*. 2021;68(12):e29259. [CrossRef]
6. Lohana AK, Tariq MA, Abid S. Hepatic lymphoma. In: *StatPearls* (Internet). Treasure Island (FL): StatPearls Publishing; 2021.
7. Bassan R, Maino E, Cortelazzo S. Lymphoblastic lymphoma: an updated review on biology, diagnosis, and treatment. *Eur J Haematol*. 2016;96(5):447-460. [CrossRef]
8. Burkhardt B, Hermiston ML. Lymphoblastic lymphoma in children and adolescents: review of current challenges and future opportunities. *Br J Haematol*. 2019;185(6):1158-1170. [CrossRef]
9. Al-Tonbary Y, Fouda A, El-Ashry R, Zalata K. Primary hepatic non-Hodgkin lymphoma presenting as acute hepatitis in a 2-year-old male. *Hematol Oncol Stem Cell Ther*. 2009;2(1):299-301. [CrossRef]
10. Song H, Todd P, Chiarle R, Billett AL, Gellis S. Primary cutaneous B-cell lymphoblastic lymphoma arising from a long-standing lesion in a child and review of the literature. *Pediatr Dermatol*. 2017;34(4):e182-e186. [CrossRef]
11. Sai S, Watanabe C, Okada S. A rare case of childhood precursor B-cell lymphoblastic lymphoma in the mandible. *Leuk Res*. 2012;36(1):e37-e38. [CrossRef]
12. Talreja KL, Barpande SR, Bhavthankar JD, Mandale MS. Precursor B-cell lymphoblastic lymphoma of oral cavity: a case report with its diagnostic workup. *J Oral Maxillofac Pathol*. 2016;20(1):133-136. [CrossRef]