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Case Report

B-lymphoblastic lymphoma with renal lesions as first symptom in a child: a case report and review of literature

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Abstract: Lymphoblastic lymphoma (LBL) is a type of non Hodgkin's lymphoma. It is highly malignant and aggressive. Most patients have poor prognosis. Extramedullary involvement of B-LBL is very common, and the most vulnerable tissues are skin, bone, and soft tissues. Primary renal B-LBL is rarely reported. In this article, we report an 8-year-old boy who was admitted to hospital due to abdominal pain and vomiting. He was diagnosed with B lymphoblastoma by CT guided renal biopsy and bone marrow puncture. We review the clinical characteristics and diagnosis and treatment process of this case.

Keywords: Non-Hodgkin's lymphoma, lymphoblastic lymphoma, kidney

Introduction

Lymphoblastic lymphoma (LBL) is a rare and highly malignant tumor, which usually develops rapidly and has a high mortality rate. In the latest classification of the World Health Organization (WHO), LBL is divided into two categories: T-lymphoblastic lymphoma (T-LBL) and B-lymphoblastic lymphoma (B-LBL) [1]. About 90% of the precursor lymphomas are T cell phenotypes, mainly occurring in male adolescents. Clinical manifestations are mediastinal mass, lymphadenopathy, bone marrow and central nervous system involvement [2]. Compared to T-LBL, B-LBL mainly occurrs in children, extramedullary involvement is common, and it mainly involves lymph nodes or extralymph nodal tissues, such as skin, bone, and soft tissues. [2, 3]. However, renal involvement has not been reported. We now describe an 8-year-old boy with bilateral kidney space occupying lesions. He was diagnosed with B-LBL by biopsy and bone marrow puncture.

Case report

An 8-year-old boy was admitted to the hospital after abdominal pain and vomiting for a week. The vomit was stomach contents, 4-5 times a day, which had nothing to do with body position and diet. In addition, there was no related history and family history of malignant tumor. Physical examination: there was slight tenderness in the right middle and upper abdomen, and a right middle and upper abdomen mass could be palpated, accompanied by percussion pain in bilateral kidneys. Emergency ultrasound examination showed that the right kidney was abnormal in shape, about 11.2 cm × 7.8 cm × 6.3 cm in size, with uneven thickness and echogenicicty of renal parenchyma, weakened echogenicicty of renal vertebral body, irregular liquid dark area reflection in the kidney. CDFI showed the color blood flow signal of the right kidney was sparse. This suggests that the right kidney had malignant lesions and the right ureter was involved; and the echo of the left renal parenchyma was irregular (**Figure 1**). On the second day after admission, enhanced CT showed that the right kidney area occupied a large space, and the boundary was fair. The enhanced CT showed uneven enhancement, and there was a liquid non-enhanced area in it, indicating a malignant tumor (possibly right nephroblastoma. This

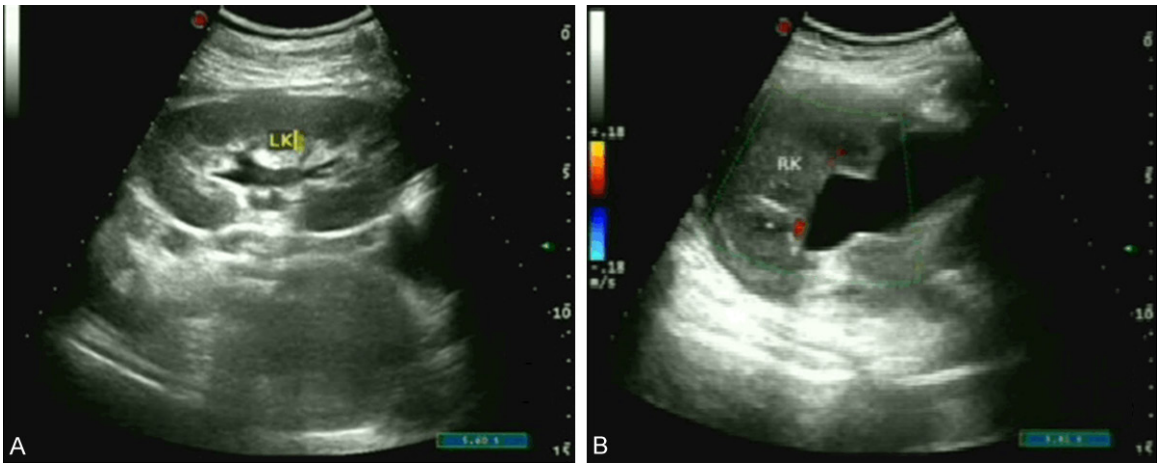

Figure 1. Ultrasound showed bilateral renal morphologic abnormalities, Echogenicicty was less homogeneous, and fluid necrosis was visible on the right.

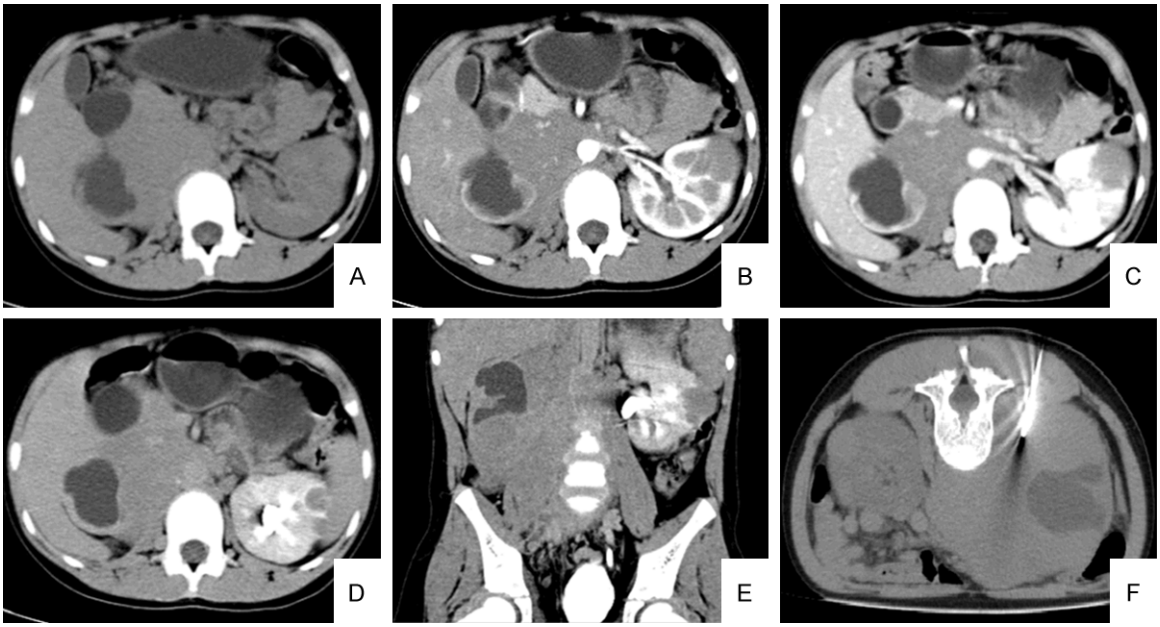

Figure 2. A-E: Enhanced CT scanning showed a large irregular mass in the right kidney and multiple nodules in the left kidney. The plain scan showed a soft tissue mass with flaky necrosis. In the cortical, medullary, and delayed phases, the solid portion of the lesion was slightly strengthened. F: CT-guided percutaneous biopsy to obtain pathologic specimens.

may invade the retroperitoneal lesions, and the left kidney had multiple nodules and masses, so the possibility of metastasis was considered (**Figure 2**). The results of tumor markers showed an abnormal increase of NSE, at 60.2 ug/l.

With the consent of patients and their families, CT guided percutaneous renal tumor biopsy was carried out. The pathologic results showed that under the microscope, there were many naked nuclear small cells in fibrous tissue and striated muscle tissue. Immunohistochemistry results showed TDT (+), CD99 (+), CD79a (+), CK (-), CD5 (-), CD3 (-), CD20 (-), CD21 (-), WT-1 (-), syn (-), CGA (-), Ki-67 (+, about 90%) (**Figure 3**). The results of bone marrow puncture showed that the proliferation of bone marrow was active, and immature lymphocytes accounted for 1%, supporting B cell lympho-

blastic lymphoma. One month after chemotherapy with Hyper-CVAD regimen, the patient was in stable condition.

Discussion

Lymphoblastic lymphoma (LBL) is a type of non-Hodgkin's lymphoma, that is highly invasive and is derived from immature precursor T cells or B cells, accounting for about 2% of all lymphomas [2, 4]. LBL is similar to acute lymphoblastic leukemia (ALL) in terms of cell morphology, immunophenotype, genotype, cytogenetics, and clinical manifestations. Therefore, the latest WHO classification has classified LBL and ALL as different phases of the same disease: LBL is diagnosed when there is no tumor or only slight blood and bone marrow involvement (the ratio of immature lymphocytes in bone marrow is less than 25%), and ALL is diagnosed when there is extensive bone marrow and blood involvement (the rate of immature lymphocytes in bone marrow is more than 25%) [5]. According to the different immunophenotypes, it can be divided into T-LBL and B-LBL, in which B-LBL accounts for about 10% of all LBL, and the incidence in males is slightly higher than that of females [6, 7].

Unlike T-LBL, mediastinal masses and marrow involvement are rare in B-LBL, and it often involves lymph nodes and external tissues (such as skin, bone, soft tissues, etc.) [2, 3]. There are also some rare cases reported in the testis, gallbladder, rectum and other organs [8-10]. The onset of B-LBL originating in the kidney is covert and may be misdiagnosed. In this case, the first symptoms were abdominal pain and vomiting, and the clinical manifestations were non-specific. We later studied CT images in an attempt to explain the cause of vomiting, namely, the mass compressed the descending and horizontal segments of the duodenum. While it was not particularly helpful for diagnosis, physical examination revealed abdominal mass. Ultrasound and CT showed bilateral kidney involvement. The initial diagnosis was nephroblastoma, which was confirmed after further pathologic examination.

In most cases, the histologic characteristics of B-LBL and T-LBL need to be distinguished by immunohistochemistry [11]. Histopathologically, B-LBL consists of small and medium round blue cells with a high mitotic rate. Intracellular basophilic cytoplasm is small, nucleoli are not obvious, and chromatin is fine. Other features are that in a background of mature small lymphocytes and plasma cells, focal or diffuse starry patterns, necrotic lesions, linear arrangement and sclerosis of tumor cells can be seen. In B-LBL, tumor cells were always positive for CD19, CD79a, and CD22. In addition, they are usually positive for the acute lymphoblastic leukemia antigens CD10 (CALLA), CD24, Pax-5 and terminal deoxytransferase (TdT), while the expression of CD20 and CD34 is variable, and CD45 may be negative [2, 7, 16]. PAX-5 is generally considered to be the most sensitive and specific marker of B lymphocyte strains, and the expression of TDT is the best marker to judge the origin of lymphomas' immature cells, and it can also increase the detection of CD79a and CD99 to help determine the differentiation of mother cells. Immunohistochemistry of this patient showed TdT (+), CD99 (+), CD79a (+), CK (-), CD5 (-), CD3 (-), CD20 (-), CD21 (-), WT-1 (-), SYN (-), CgA (-), KI-67 (+, about 90%) (**Figure 3**). Bone marrow aspiration showed that the proportion of immature lymphocytes accounted for 1%, which met the diagnostic criterion of B-LBL. In addition, it is worth noting that NSE was significantly increased in this case. Previous studies have reported that NSE can be expressed at specific differentiation stages of normal lymphocytes. After malignant changes in lymphoid tissues, dysregulation of gene regulation in tumor cells leads to accelerated cell proliferation and increased oxygen consumption, including enzymes involved in glycolysis, including NSE. The synthesis of serotonin also is increased. Through the mechanism of cell damage and energy metabolism disorder, the release of NSE in tumor cells is increased, and the serum NSE concentration increases accordingly, but this increase is not related to the pathologic type and immune phenotype of lymphoma [12-14].

For the treatment of B-LBL, there is still no standard treatment. LBL treatment methods include conventional NHL regimens, intensive chemotherapy regimens designed for high-grade NHL, and regimens for ALL. In addition, stem cell transplant (SCT) is used to varying degrees in treatment regimens, and most are autologous SCT (ASCT) [2, 7, 15]. Conventional NHL

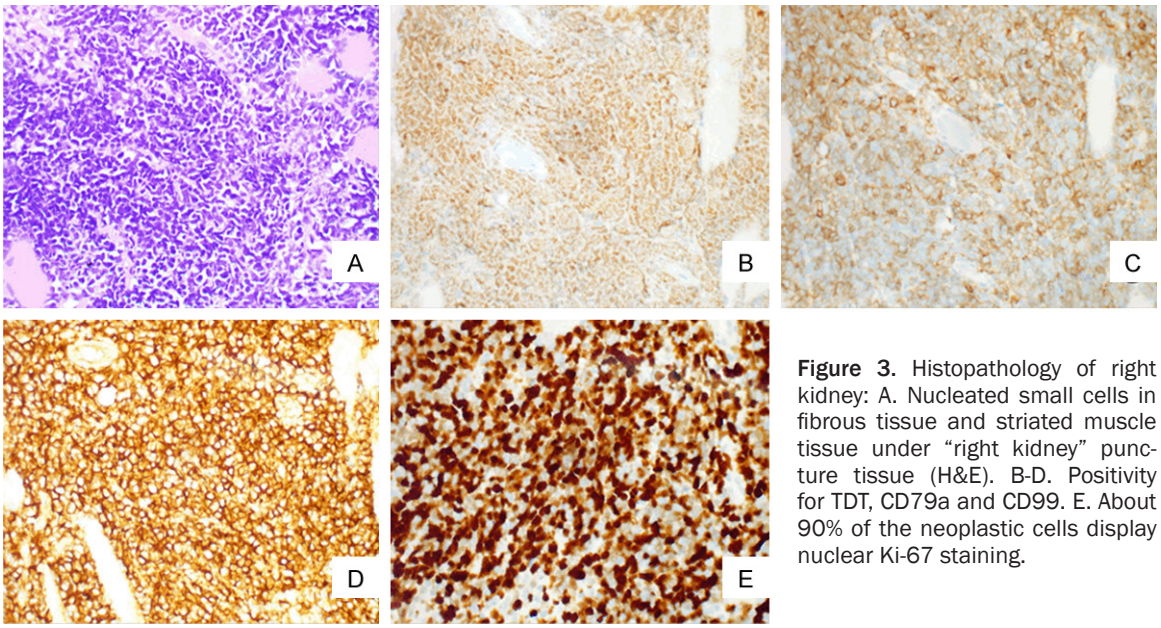

Figure 3. Histopathology of right kidney: A. Nucleated small cells in fibrous tissue and striated muscle tissue under "right kidney" puncture tissue (H&E). B-D. Positivity for TDT, CD79a and CD99. E. About 90% of the neoplastic cells display nuclear Ki-67 staining.

treatments are not effective for LBL, especially in high-risk patients, with disease progression or relapse, who are difficult to treat and have a poor prognosis. Most patients relapse and eventually die of unresponsive progressive disease [16, 17]. The use of intensive chemotherapy and ALL treatment can improve CR and DFS of LBL to a certain extent. In a retrospective cohort study, Oliveira et al. used an intensive chemotherapy regimen based on ALL for 27 patients with LBL, and the results confirmed that an intensive chemotherapy regimen using ALL therapy gave a good prognosis for children with LBL [18]. Research by Termuhlen et al. also showed that LBL treated with a 2-year ALL intensive chemotherapy regimen (COG A5971) had excellent results [19]. The initial central nervous system involvement of LBL is relatively low (3-9%) [20]. However, without central nervous system precautions, the central nervous system is a site of frequent recurrence [21]. In a study of single intrathecal chemotherapy prevention, the recurrence rate in the central nervous system was between 3% and 42%. In the study of combined use of head radiotherapy and intrathecal treatment, the recurrence rate is between 3% and 15%. In the study of no central nervous system treatment (NHL type scheme), the recurrence rate was between 42% and 100%, which suggests that central nervous system prophylaxis is important [21]. In addition, Bersvendsen pointed out that the early use of ALL-type induction consolidation chemotherapy, followed by auto-SCT on patients, and local radiotherapy for patients with initial mediastinal masses, bone marrow lesions, or testis lesions can achieve higher cure rates [22]. Although the study had few subjects, it also pointed the way for the treatment of LBL. Hyper-CVAD A/B regimen was given in this case: regimen A (cyclophosphamide + vincristine + epirubicin + dexamethasone) and regimen B (high-dose methotrexate + cytarabine) to induce chemotherapy, and triple intrathecal injection. The chemotherapy process was smooth without infection, and there was no obvious bone marrow suppression. After reexamination, the number of neutrophils and platelets was normal, hemoglobin was not significantly reduced, and liver and kidney functions were normal. The effect of early chemotherapy is ideal. However, due to the low incidence of B-LBL, its prognosis is unknown.

In general, B-LBL is a highly malignant and aggressive hematologic malignancy. Because of its rare occurrence in the kidney, lack of specificity in clinical symptoms, and difficulty in early diagnosis, diangosis is delayed. The chemotherapy effect of LBL in children is good. If the diagnosis is confirmed, timely systemic chemotherapy can give a good prognosis, and treatment should not stop too early.

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Disclosure of conflict of interest

None.

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