Acute lymphoblastic leukemia with pancreas involvement in an adult patient mimicking pancreatic tumor

A case report

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Abstract

Rationale: Acute lymphoblastic leukemia (ALL) is a malignant disease originating from abnormal proliferation of B or T lymphocytes in bone marrow (BM). Invasion of the pancreas is extremely rare in adults.

Patient concerns: In this article, we report a case presenting that ALL invades the pancreas, as well as liver, kidney, and duodenum detected by magnetic resonance image. The patient was misdiagnosed as pancreatic tumor at initial since hemogram was unremarkable.

Diagnoses: The diagnosis of ALL was established based on the endoscopic ultrasonography-guided fine-needle aspiration and bone marrow examination, showing BCR/ABL gene positive.

Interventions: The patient was actively treated with chemotherapy. Hematological remission was obtained and the lesions in the pancreas disappeared.

Outcomes: The patient finally died of complication from fungal pneumonia and central nervous system involvement 12 months after diagnosis.

Lessons: Under the context of infection, persistent or intermittent fever and complete blood count are not significant prognoses of pancreatic involvement for adult with ALL. We hope that this case will help hepatobiliary and pancreatic surgeon to be aware of this kind of disease as pancreatic carcinoma and pancreas involvement by ALL have totally different treatment strategy.

Abbreviations: ALL = acute lymphoblastic leukaemia, allo-PBSCT = allogeneic peripheral blood stem cell transplantation, Ara-C = cytosine arabinoside, BM = bone marrow, CBC = complete blood count, CNS = central nervous system, CR = complete remission, CSF = cerebrospinal fluid, CT = computed tomography, EUS-FNA = endoscopic ultrasonography-guided fine-needle aspiration, MRI = magnetic resonance image, MTX = methotrexate, VDP = vinorelbine, idarubicin, prednisone, VP = vinorelbine, prednisone, WBC = white blood count.

Keywords: acute lymphoblastic leukemia, diagnosis, pancreas

1. Introduction

Acute lymphoblastic leukemia (ALL) could involve several extramedullary sites [central nervous system (CNS), testis, mediastinum, kidney, liver, etc], with peak prevalence between the ages of 2 and 5 years.\textsuperscript{[1]} Presentation with pancreatic involvement in an adult patient with ALL was very rare. Only a few cases have been reported.\textsuperscript{[2-4]} In most situation, patients with leukemic-cell infiltration of the pancreas would present with abdominal pain, jaundice, cholestasis, or pancreatitis. Pancreatic enlargement might be detected by imaging studies. Hematological disease could be easily taken into consideration based on abnormal laboratory test (pancytopenia) and more common clinical manifestations of pallor and fatigue (caused by anemia). However, in unusual cases, early diagnosis is challenging due to nonspecific symptoms, insignificant blood examinations, and rarity of the disease.

In this article, we report an adult patient with pancreas involvement by common B-cell ALL. Due to absence of typical symptoms and abnormal hemogram, our patient was initially misdiagnosed as pancreatic tumor. Final diagnosis was established by endoscopic ultrasonography-guided fine-needle
aspiration (EUS–FNA) and bone marrow (BM) aspiration. In spite of the aggressive treatment, the patient died 1 year after diagnosis.

2. Case report

A 39-year-old female patient, being found with multiple lesions in the pancreas for 5 days, was hospitalized in June 2016 in Department of Hepatobiliary and Pancreatic Surgery of our hospital. The patient had recurrent fever for nearly 1 month, and was once diagnosed for pneumonia 2 weeks ago. She received antibiotics treatment, and the fever was well controlled. Her past medical history was unremarkable, and she denied smoking and alcohol intake. Her physical examination was nonsignificant.

Initial laboratory tests after admission showed moderate anemia and slightly elevated CA125 (40.4 IU/mL, reference range <35 IU/mL). The white blood count (WBC), the percentage of neutrophile and lymphocyte, prothrombin time, hepatic and renal function tests, and other tumor markers were all in normal range. Computed tomography (CT) of the abdomen identified multiple hypoattenuating mass lesions in the pancreas (Fig. 1A). Magnetic resonance image (MRI) scan confirmed multiple lesions in the pancreas (Fig. 1B), as well as in kidney (Fig. 1C), liver, and thoracic and lumbar vertebrae (Fig. 1D). EUS–FNA for the pancreatic lesions was performed and atypical cells were detected on cytology examination, which might originate from lymphohematopoietic system. During EUS examination, abnormal cell infiltration in duodenum mucosa was identified (Fig. 2). Biopsy

![Image](image1)

Figure 1. (A) CT scan of portal phase displaying hypoattenuating mass lesions (arrowhead) in the head of pancreas before treatment. (B) MRI scan of T2 phase showing more lesions (arrowhead) in the pancreas than ones of CT before treatment. (C) MRI DWI showing multiple pancreatic masses and involvement of kidney (arrowhead) before treatment. (D) MRI demonstrating involvement of vertebral body (arrowhead) before treatment. (E) MRI scan of T2 phase and (F) MRI DWI confirming no lesions after treatment. CT = computed tomography, DWI = diffusion weighted imaging, MRI = magnetic resonance image.

![Image](image2)

Figure 2. (A) EUS scan image showing uneven echo (arrowhead). Duodenum morphology demonstrating erosions: (B) fish scale like or (C) volcanic vent like. EUS = endoscopic ultrasonography.
was also conducted, and the pathological diagnosis indicated ALL (immunopositive for CD10 and PAX-5 but negative for CD5, CD21, and CD23).

The patient started to have fever again, which was not responded well with antibiotics. WBC count elevated to 37.2 x 10^9/L, with 57% heterocyst detected (Fig. 3A). The patient was transferred to the Department of Hematology. BM aspiration (Fig. 3B) revealed 82% blasts. Flow cytometry (CD45/SSC gate) of BM showed that 79.8% heterocyst was occupied in the negative region of CD45, expressing human leukocyte antigen DR, CD10, CD19, and CD22. Part of heterocyst expressed CD33 and cCD79a, minority expressed TdT and CD38, and none expressed cytoplasmic Immunoglobulin M and secreted Immunoglobulin M, indicating common-B-ALL, the result of C-MYC gene; fluorescence in situ hybridization was negative.

Cytogenic analysis of BM aspirate indicated 48,XX,t(9;22)(q34;q11.2),+21,+der(22)t(9;22)[14]/46,XX[6]. The patient was positive for BCR/ABL (p190) fusion gene. The diagnosis of ALL was established.

3. Treatment
The patient received antiinfective therapy because of pulmonary infection. Imatinib was utilized due to positive BCR/ABL (p190) fusion gene. Chemotherapy with vinorelbine, prednisone (VP) along with imatinib protocol was administrated simultaneously with vinorelbine 40mg at day 1, 8, 15, and 22, and prednisone 10mg from day 1 to 28.

4. Outcome and follow-up
The patient obtained hematologic remission 3 weeks after onset of chemotherapy and lesions in pancreas, liver, and kidney disappeared (Fig. 1E and F). After finishing the first inductive chemotherapy, the minimal residual disease was negative and complete blood count (CBC) was normal which indicated a complete remission (CR) status. Then on August 1, 2017, the patient accepted a lumbar puncture with intrathecal injection of 50mg cytosine arabinoside (Ara-C) and 5mg dexamethasone for prevention of CNS leukemia without any CNS symptoms. So the imatinib was replaced with dasatinib, which easily crosses the blood–brain barrier. At the same time, intrathecal injection of 1.5 mg MTX, 50 mg Ara-C, and 5mg dexamethasone was given twice per week until the cerebrospinal fluid was normal.

Then the patient was prepared for allogeneic peripheral blood stem cell transplantation (allo-PBSCT) and accepted 3 cycles of MTX+VP-16+dasatinib as well as regular intrathecal injection each cycle. The patient had stable CR. Unfortunately, in August 2017, after the last VDP chemotherapy, the patient got a neutropenia and suffered a carbapenem-resistant Klebsiella sepsis. Finally, she died of severe sepsis even after trying all the accessible antibiotics.

5. Discussion
Pancreatic infiltration of ALL is a very rare manifestation and only a few cases have been reported previously in adults.[2-4] Clinical pancreatic involvement in ALL has also been reported in only 6 pediatric case reports.[5-10] Despite of the rarity, the hepatobiliary and pancreatic surgeon should be aware of this condition as accurate diagnosis is important for the following effective treatment.

Collado et al[8] reported that CBC of a 3-month-old girl showed severe anemia and WBC to be normal. The results of CBC in 3 patients previously reported revealed the blasts,[6,7,9] whereas in another 2 cases, the CBC was normal[4] and had no blasts.[10] In our patient, WBC count displayed various results, so it is difficult to distinguish and to be aware of ALL. The following elevated WBC in our patient was mainly attributed to the pulmonary infection. The hematologic disease was suspicious until appearance of atypical lymphocytes.

Classically, patients with acute leukemia presented with pancytopenia and clinical manifestations of pallor and fatigue.
caused by anemia; additionally, patients may present with unspecific symptoms, such as persistent or intermittent fever, similar to those of a viral infection. The 2 cases of adult reported previously mainly present symptom of acute pancreatitis on the onset of clinic, but our patient had no significant symptom apart from fever and waist soreness. Choi et al. reported that pancreatic leukemia shows 3 different morphologic types: a well or ill-circumscribed nodular form; a diffuse, infiltrative form; and a combination of the nodular and diffuse infiltrative forms on CT findings. However, in his report, there is only one patient with ALL (non-B-cell), and the patient had nodule on pancreas head and neck on CT. Daniel et al. also reported an adult patient with precursor B-cell ALL who had 2 masses at the head and the body of pancreas on CT. However, our adult patient with common B-cell ALL had multiple nodules from pancreatic head to tail, which was rarely reported. Interestingly, compared to CT imaging, MRI scan revealed more pathologic lesions in pancreas and extra findings of liver and retroperitoneal organs (bilateral kidney, lymph nodes, and lumbar and thoracic vertebrae) involvement, which were not well visualized on enhanced CT. This indicated that MRI has much higher sensitivity in detecting tumor cell infiltrating lesions than CT. Furthermore, on EUS, pancreatic involvement by ALL showed multiple irregular hyper-to-hypodensity lesions without clear margins. EUS-FNA of the pancreas is helpful to diagnose ALL.

In ALL, most commonly affected extra lymphoreticular sites are nervous system and testes. Our patient had multiple retroperitoneal organs and liver/duodenal involvement at the onset and CNS involvement during treatment, indicating the more aggressive biologic behavior of tumor cells. Despite good therapeutic response achieved at initial phase, the prognosis was still poor.

In conclusion, pancreatic infiltration with leukemic cells is a rare manifestation of ALL, especially for adults. Under the context of infection, persistent or intermittent fever and CBC are not significant prognostics of pancreatic involvement for adult with ALL. Leukemia of the pancreas should be considered if there are multiple or diffusing pancreatic nodules on imaging findings, and MRI possesses higher sensitivity than CT scan in identifying tumor lesions. Patients with ALL pancreas infiltration usually displayed unspecific symptoms. EUS-FNA is helpful to make the pathological diagnosis. Although long-term survival in adults is less good than children, ALL is an important diagnosis to make because it is highly chemosensitive, with majority achieving CR.

Author contributions
Conceptualization: Xuzhao Zhang, Linping Dong.
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