Relapse of acute lymphoblastic leukemia in the pancreas after bone marrow transplant

Guang-Xian Wang, Jun-Lin Liao, Dong Zhang, Li Wen
Chongqing, China

Background: **Relapse of acute lymphoblastic leukemia (ALL) in the pancreas is rare. We report a case of a 12-year-old boy who experienced a relapse of ALL in the pancreas after a bone marrow transplant.**

Methods: **Clinical data, including course of illness, laboratory results, and imaging studies are included. The patient presented with acute pancreatitis, suspected to be secondary to gallstones, with ampullary obstruction. Ultrasound and magnetic resonance imaging demonstrated a distended gallbladder and intra- and extra-hepatic biliary dilatation with a cutoff at the pancreatic head, but with no evidence of gallstones.**

Results: **Ultrasound-guided biopsy of the pancreas revealed ALL in the pancreas. Systematic chemotherapy was recommended, but was declined by the parents. The patient died one week later.**

Conclusion: **Relapse of ALL in the pancreas is rare, but when a history of ALL is present, it should be considered in patients with pancreatic enlargement, obstructive jaundice, and pancreatitis.**

World J Pediatr 2015;11(4):389-391

Key words: **acute lymphoblastic leukemia;**
leukemic infiltration;
pancreas;
relapse

Author Affiliations: Department of Radiology, Xinqiao Hospital, Third Military Medical University, Chongqing 400037, China (Wang GX, Zhang D, Wen L); Department of Surgery, Carver College of Medicine, University of Iowa, 200 Hawkins Drive, 1422 JCP Iowa City, IA 52242, USA (Liao JL)

Corresponding Author: Li Wen, Department of Radiology, Xinqiao Hospital, Third Military Medical University, Chongqing 400037, China (Tel: 86-23-68774676; Email: cqzdwl@163.com)

doi: 10.1007/s12519-014-0489-6
Online First June 2014

Introduction

Extramedullary involvement in childhood acute lymphoblastic leukemia (ALL) most often occurs in the brain or testes. Pancreatic ALL may be characterized by biliary obstruction,[1] cholestatic hepatitis,[2] and pancreatitis.[3,4] We report a patient with a history of bone marrow transplant (BMT) performed 2 years previously, who developed a relapse of his precursor B-cell ALL in the pancreas. This patient presented with obstructive jaundice and pancreatitis, without bone marrow involvement or other diseases.

Case report

A 12-year-old boy with lethargy was admitted to our institute due to lethagy. Laboratory investigations indicated a hemoglobin level of 9.3 g/dL, a white cell count of 35×10^9/L, and a platelet count of 42×10^9/L. Bone marrow biopsy showed 84% of original and young lymphocytes, and cytometric studies revealed the cells were positive for CD79a, CD10, CD19, CD22, and terminal deoxynucleotidyl transferase (TdT), and negative for CD3, CD5, CD20, and CD34. The boy was diagnosed with precursor B-cell ALL (L3). He was subjected to daunorubicin, vincristine, l-asparaginase and prednisone (DVLP) chemotherapy after bone marrow biopsy showed 54% of original and young lymphocytes. Subsequently, he underwent mitoxantrone, vincristine, l-asparaginase and prednisone (MVLP) chemotherapy, and achieved the first complete remission (CR1). Eight months later, however, the patient relapsed, and was treated with vincristine, tetrahydropyran adriamycin (THP-ADM), l-asparaginase and prednisone (VTLP) chemotherapy, and achieved CR2. Three months later (11 months from CR1), the patient relapsed again, and underwent l-asparaginase, vincristine, dexamethasone (LVD) chemotherapy and reached CR3. The patient relapsed twice during the first year after CR1, and the interval was increasingly shorter. Therefore, he was considered for stem cell transplantation. HLA match including HLA-A, HLA-B, HLA-DR loci was identical between the patient and the unrelated donor from the Chinese Marrow Donor Program. Before

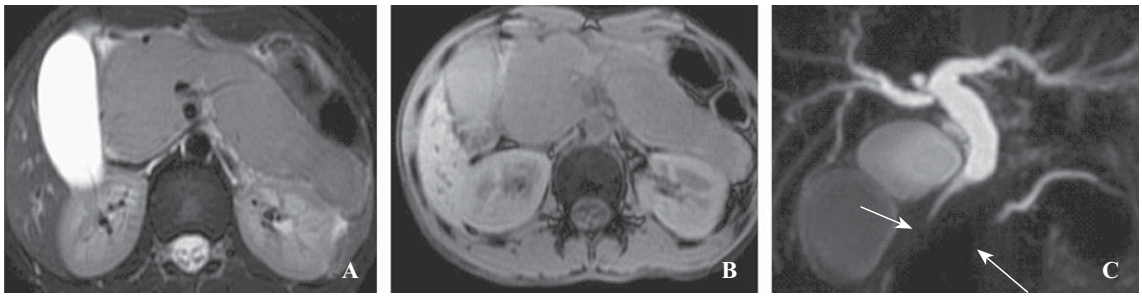

Fig. 1. Plain MRI with abdominal axial T_2 (**A**) and T_1 (**B**) weighted images showing diffuse enlargement of the pancreas and homogeneous long T1 and long T_2 weighted signal intensities; **C**: Magnetic resonance cholangiopancreatography demonstrating intra- and extra-hepatic biliary dilatation to the level of the enlarged pancreatic head (white arrow) and a distended gallbladder.

transplant, a combination of TBI (a total dose of 8 Gy), CTX (cyclophosphamide, 4 g), HD-Ara-c (188 mg), lobaplatin (50 g) and ATG (700 mg) was given as pretreatment. After treatment for 8 days, at rest for 1 day, the patient received a successful input of $CD34^+$ (4.5×10^6/kg) and MNC (7.5×10^8/kg). After allogeneic BMT, the patient was treated with antibiotics, antianaphylaxis and antiviral agents as early as possible to prevent complications caused by infection, methotrexate and cyclosporin A were used to prevent graft versus host disease (GvHD). However, after BMT for 13 days, the patient had frequent micturition, dysuria, endless urinary urges, itchy sensation near the entrance to the urethra and unresponsive to anti-infection. Acute GvHD was considered and methylprednisolone pulse therapy was effective. Viral complications were negative. Chimerism was 80% at 39 days after transplantation. The patient was given intrathecal injection every two months and bone marrow biopsy was negative.

Twenty-five months after allogeneic BMT, at the age of 15 years, the patient presented with a 20-day history of intermittent upper abdominal pain, lethargy, scleral icterus, and a weight loss of 3 kg. On physical examination, he was tender in the upper abdomen and profoundly jaundiced. There was no peripheral lymphadenopathy. Laboratory investigations (reference ranges in parentheses) indicated a hemoglobin level of 12.2 g/dL (reference range:12-17 g/dL), a total white cell count of 4.81×10^9/L (reference range: 100-300×10^9/L), a bilirubin level of 104.7 μmol/L (reference range: 1.7-20 μmol/L), an alanine transaminase level of 124 IU/L (reference range: 0-50 IU/L), an aspartate aminotransferase level of 71 IU/L (reference range: 0-50 IU/L), an alkaline phosphatase level of 444 IU/L (reference range: 40-150 IU/L), a lipase level of 517 IU/L (reference range: 0-190 IU/L), a hemodiastase level of 361 IU/L (reference range: 0-96 IU/L), and a urinary amylase level of 948 IU/L (reference range: 0-96 IU/L).

Acute gallstone pancreatitis was suspected. Abdominal ultrasound (US) demonstrated a distended gallbladder, intra- and extra-hepatic biliary dilation, and pancreatic enlargement, without evidence of gallstones. MRI confirmed the US findings, with axial images demonstrating a diffusely enlarged pancreas (head 4.3 cm, and body 3.6 cm), with homogeneous T_1 and T_2 weighted signal intensities and intra- and extrahepatic biliary dilatation to the level of the enlarged pancreatic head on magnetic resonance cholangiopancreatography (Fig. 1). No masses were identified.

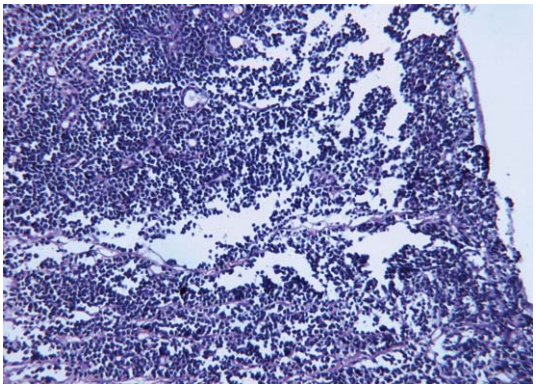

Fig. 2. Ultrasound-guided biopsy showing diffuse lymphoid cell infiltration of pancreas tissue (hematoxylin-eosin staining, original magnification × 200).

Bone marrow biopsy on hospital day 7 showed something normocellular without leukemic blasts. The patient was subjected to the treatment of acute pancreatitis, although his symptoms worsened initially with increased jaundice and pruritus. On day 10, a common bile duct stent was placed under endoscopic retrograde cholangiopancreatography. Three days later, US-guided pancreas biopsy revealed diffuse lymphoid cell infiltration of the pancreas (Fig. 2), with immunohistochemical staining positive for CD10, CD19, CD22, CD79α, TdT, and Ki-67, and negative for CD3, CD5, CD20, and CD34, which indicate a precursor B-cell phenotype consistent with a relapse of ALL in the pancreas.

Chemotherapy with vincristine, aclacinomycin, prednisone was promptly started and his cholestasis and pancreatitis quickly improved. By day 17 of

chemotherapy, there was a significant drop in serum amylase and lipase (187 IU/L and 106 IU/L, respectively), urinary amylase (546 IU/L), bilirubin (47.6 μmol/L), alanine transaminase (59 IU/L), aspartate aminotransferase (11 IU/L), alkaline phosphatase (138 IU/L), hemoglobin (10.2 g/dL), and white cell count (2.82×10^9/L). Follow-up US 3 days later showed no signs of improvement in pancreatic swelling. These results were discussed with the patient's parents, who decided to terminate medical treatment against medical advice. The patient died at home one week later.

Discussion

The meninges and testes are the most common sites for ALL relapse and the less common sites include the bones, orbit, gingival, mediastinum, heart, breast, abdominal lymph nodes, and kidney.[5] The pancreas is one of the rarest sites for extramedullary infiltration of leukemic cells.

ALL relapse in the pancreas may present with nonspecific symptoms such as pain, weight loss, fatigue, and those specific to the pancreas (obstructive jaundice, acute pancreatitis). Occasionally, such patients may be asymptomatic.[6] ALL relapse in the pancreas is typically associated with cholestasis or pancreatitis.[2-4] In this case, intra- and extra-hepatic biliary dilatation to the level of the enlarged pancreatic head required biliary stenting for the management of cholestasis. The rapid improvement of pancreatitis after chemotherapy indicated that pancreatitis was a complication of pancreatic infiltration with leukemic cells.

ALL relapse in the pancreas is difficult to diagnose if pancreatitis is the only symptom and only the pancreas is involved. In adults, imaging results may vary from diffuse pancreatic infiltration to solid nodular lesions,[7] while in children diffuse infiltration only,[2-4,6] as in our case. Definitive diagnosis is confirmed pathologically by US-guided fine needle aspiration (FNA) of the pancreas as in our patient. In our experience, FNA has the potential to diagnose diffuse invasion of malignant cells in the pancreas.

BMT is now considered one of the effective treatments for patients with refractory and relapsed ALL. The frequency of extramedullary relapse of ALL after BMT varies from 30% to 50%.[5] When ALL relapses after BMT, it is often more resistant to treatment and has a poor prognosis.[5] However, pancreatic lesions before BMT tend to respond to chemotherapy,[1,3,4] combined with surgical excision or radiotherapy which is potentially effective to the improvement of the prognosis.[5] In this case, surgery was not attempted because of the diffuse enlargement of the pancreas without a discrete resectable mass.

In conclusion, we demonstrated a low frequency of extramedullary relapse of ALL after BMT, which should be considered as a potential cause of pancreatic enlargement, obstructive jaundice, and pancreatitis. There is no defined treatment for patients with this presentation; however, intensive chemotherapy with subsequent BMT (if only the procedure is possible) is strongly recommended in the case of ALL relapse after BMT, even if it is only isolated in an extramedullary manner. In obstructive jaundice, extra-hepatic bile duct stenting can expedite resolution of cholestasis, potentially contributing to the recovery and survival.

Acknowledgements

We thank Mr. Paul Casella, faculty consultant of the Carver College of Medicine, the University of Iowa for editing the manuscript.

Funding: None.
Ethical approval: Not needed.
Competing interest: None declared.
Contributors: Wang GX wrote the first draft of this paper. All authors contributed to the intellectual content and approved the final version. Wen L is the guarantor.

References

1 Daniel SV, Vani DH, Smith AM, Hill QA, Menon KV. Obstructive jaundice due to a pancreatic mass: a rare presentation of acute lymphoblastic leukaemia in an adult. JOP 2010;11:72-74.
2 Rausch DR, Norton KI, Glass RB, Kogan D. Infantile leukemia presenting with cholestasis secondary to massive pancreatic infiltration. Pediatr Radiol 2002;32:360-361.
3 Ikawa Y, Saikawa Y, Horisawa T, Kuroda R. Pancreatic and renal involvement in pediatric acute lymphoblastic leukemia/lymphoma. J Clin Oncol 2007;25:451-453.
4 Malbora B, Avci Z, Alioglu B, Tutar NU, Ozbek N. A case with mature B-cell acute lymphoblastic leukemia and pancreatic involvement at the time of diagnosis. J Pediatr Hematol Oncol 2008;30:87-89.
5 Lee KH, Lee JH, Choi SJ, Lee JH, Kim S, Seol M, et al. Bone marrow *vs*. extramedullary relapse of acute leukemia after allogeneic hematopoietic cell transplantation: risk factors and clinical course. Bone Marrow Transplant 2003;32:835-842.
6 Collado L, Dardanelli E, Sierre S, Moguillansky S, Lipsich J. Asymptomatic leukemic-cell infiltration of the pancreas: US findings. Pediatr Radiol 2011;41:779-780.
7 Choi EK, Byun JH, Lee SJ, Jung SE, Park MS, Park SH, et al. Imaging findings of leukemic involvement of the pancreaticobiliary system in adults. AJR Am J Roentgenol 2007;188:1589-1595.

Accepted after revision March 16, 2014