CASE REPORT

An adult patient with common B-cell acute lymphoblastic leukaemia who presented with pancreatic involvement, description of the second adult case and review of paediatric cases

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SUMMARY

Pancreatic involvement in acute lymphoblastic leukaemia (ALL) may go unrecognised. There are only a few paediatric cases; nevertheless, presentation with pancreatic involvement in an adult patient with ALL has been reported rarely. Our 52-year-old male patient came to us with abdominal pain, nausea and vomiting; he had pancreatic enlargement on CT. He was diagnosed with common B-cell ALL with pancreatic involvement. The patient obtained haematological remission and the pancreatic enlargement regressed after chemotherapy, but later he had central nervous system and liver relapses. He died 6 months after diagnosis because of progressive pneumonia and chemotherapy-resistant ALL with multiple extramedullary relapses.

BACKGROUND

Acute lymphoblastic leukaemia (ALL) might involve different extramedullary sites either at diagnosis or during the disease course. The most frequently involved organ is the central nervous system.¹ Pancreatic involvement in ALL is limited to a few paediatric case reports,^{2–6} and presentation with pancreatic involvement in an adult patient with ALL was reported only once.⁷

In this paper, we present our adult patient with common B-cell ALL who had pancreatic involvement causing acute pancreatitis at initial presentation. In spite of the clearance of leukaemic cells from the bone marrow and pancreas, the patient had relapses from other extramedullary sites and died 6 months after diagnosis.

CASE PRESENTATION

A 52-year-old male patient was hospitalised in July 2003 in the department of gastroenterology of our hospital with abdominal pain, nausea and vomiting for the past 2 weeks. His medical history was non-significant. He denied smoking and alcohol intake. On physical examination he had abdominal tenderness on palpation and his spleen was palpable 3 cm below the left costal margin.

INVESTIGATIONS

Laboratory data were as follows: haemoglobin, 11.6 g/dL; haematocrit, 35.1%; leucocytes, 18 000/mm³; platelets, 64 000/mm³; glucose, 170 mg/dL; alanine transaminase, 117 U/L; aspartate aminotransferase, 172 U/L; alkaline phosphatase (ALP), 474 U/L;

γ-glutamyl transferase (GGT), 404 U/L; total protein, 4.9 g/dL; albumin, 1.8 g/dL; lactate dehydrogenase, 2617 U/L (N<192); erythrocyte sedimentation rate, 119 mm/h; and C reactive protein CRP, 7.9 mg/dL (N<0.8). Urea, creatinine, uric acid, sodium, potassium, calcium, phosphorus and bilirubin levels were normal. Serum amylase was 262 U/L (N: 25–125) and lipase was 796 U/L (N: 8–78). His anti-EBV IgM, anti-CMV IgM, HBsAg, anti-HBc IgM, anti-HAV IgM, anti-HCV and anti-HIV serologies were negative.

Abdominal ultrasonography demonstrated splenomegaly; there was also diffuse pancreatic enlargement which was most prominent in the head region, and the pancreas had a heterogeneous appearance with some small anechoic cysts. Abdominal tomography confirmed findings on the abdominal sonography (figure 1).

After detection of 80% lymphoblasts on peripheral blood smear, the patient was transferred to the department of haematology. Bone marrow aspiration showed 92% lymphoblasts. Flow cytometry of the bone marrow showed that the malignant cells were positive for CD45, HLADR, cytoplasmic CD79a, CD19, CD22, CD10 and TdT; and they were negative for CD2, CD3, CD4, CD7, CD13, CD14, CD33, CD34 and CD56. The microscopic

Figure 1 Abdominal tomography showing splenomegaly, and diffuse enlargement of the pancreas with some small cysts.

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and flow cytometric examinations of cytocentrifuged samples of cerebrospinal fluid showed no lymphoblasts. Fluorescent in situ hybridisation studies of bone marrow with probes specific for BCR-ABL and MLL fusion genes were negative.

TREATMENT

Being diagnosed with standard-risk common B-cell ALL with pancreatic involvement, the patient was administered standard-risk GMALL (05/93) protocol.⁸ GMALL contains vincristine, methotrexate, daunorubicine, etoposide, cytosine arabinoside, 6-mercaptopurine and prednisolone. The protocol also includes intrathecal methotrexate prophylaxis.

OUTCOME AND FOLLOW-UP

The patient obtained complete haematologic remission 4 weeks after onset of chemotherapy; his abdominopelvic tomography 1 month after the initial one revealed regression of the pancreatic enlargement. Seven weeks after diagnosis the patient had symptoms of headache, nausea and vomiting. He had right VI cranial nerve paralysis, and a cranial MR revealed an extra-axial tumoral mass arising from the cranial bone. The microscopic and flow cytometric examinations of cerebrospinal fluid showed CD19, CD10, CD45 positive lymphoblasts. The patient was in haematological remission. As he had central nervous system involvement of ALL, the regimen was switched to high-risk GMALL (05/93) chemotherapy. In November 2003—4 months after diagnosis—the patient was in haematological remission, there was no pancreatic enlargement on abdominal tomography and the cerebrospinal fluid was clear of lymphoblasts. In December 2003—5 months after diagnosis—the patient had an episode of febrile neutropenia, and was diagnosed to have a pneumonic consolidation on thorax CT. His fever was continuous in spite of being administered imipenem, amikasin and liposomal amphotericin B. In the meanwhile, his total bilirubin was 12.3 mg/dL; direct bilirubin, 7.8 mg/dL; alkaline phosphatase, 181 U/L (N<126 U/L); GGT, 89 U/L; total protein, 4.2 g/dL; albumin, 1.2 g/dL; and prothrombin time was 17.4 s. Abdominal ultrasonography revealed multiple masses in the liver. The patient died in January 2004—6 months after diagnosis—and the histopathological examination of the postmortem liver biopsy showed leukaemic infiltration.

DISCUSSION

Clinical pancreatic involvement in ALL has been reported in only five paediatric case reports. The first was a 10-month-old infant who presented with cholestasis secondary to massive pancreatic infiltration. She died in the early stages of chemotherapy.² The second was a 5-year-old boy who had acute renal failure due to leukaemic infiltration of the kidneys, and who later had multiple extramedullary relapses including that of the pancreas.³ Ikawa *et al* reported on an 11-year-old girl who had bilateral renal and pancreatic involment at diagnosis. She had regression of renal and pancreatic involvement after chemotherapy.⁴ Recently, Malbora *et al* presented a 4-year-old boy who had pancreatic involvement at the time of diagnosis. The patient was in remission nearly 1 year after chemotherapy.⁵ The most recently published case is that of a 3-month-old baby who had asymptomatic pancreatic involvement by ALL detected by ultrasonography.⁶ In four of the above-reported cases, including our case, patients had multiple extramedullary organ involvements and the prognoses were poor in most of them.^{2–4 6}

Nagasawa *et al*⁹ said that CXCR4 and its ligand stromal cell-derived factor (SDF-1) might have important roles in the extravasation and trafficking of normal lymphocytes. Crazzolar

*et al*¹⁰ found that the high expression of the chemokine receptor CXCR4 predicted extramedullary organ infiltration in childhood ALL. There has been no report on an adult patient with ALL presenting

with acute pancreatitis caused by infiltration of the pancreas with ALL cells. Nevertheless, an autopsy study performed many years ago found that the most frequently involved organs by ALL were the testes, leptomeninges, dura mater, uterus, large bowel and pancreas.¹¹ This means that some patients with ALL who have no pancreatic enlargement or symptoms of pancreatitis might have microscopic infiltration of the pancreas with leukaemic blasts. Our patient had pancreatic involvement causing diffuse pancreatic enlargement and symptoms of acute pancreatitis at initial diagnosis.

He obtained haematologic remission and regression of pancreatic involvement. Later, he had central nervous system involvement for which remission was obtained after chemotherapy. Nevertheless he died because of progressive pneumonia and liver infiltration.

Pancreatic involvement causing acute pancreatitis has been reported in only one adult patient with ALL. In our case and in the reported case, pancreatic involvement by ALL could not be verified histopathologically. However, in their autopsy series Barcos *et al*¹¹ reported that pancreatic involvement was 8%. Some of the patients in this ALL series were adults and, probably, pancreatic involvement was more frequent in adult patients with ALL. There is also a report on one patient with ALL who presented with pancreatitis.¹² It is highly likely that pancreatic involvement in ALL goes unrecognised without causing any clinical symptoms.

Our patient was administered GMALL (05/93) chemotherapy protocol as suggested in the literature.⁸ This protocol includes L-asparaginase. It is known that L-asparaginase is toxic to the pancreas. Nevertheless, our patient had pancreatic enlargement before using L-asparaginase. Our current knowledge is not sufficient to comment on whether it might be a poor prognostic factor. Patients with multiple extramedullary organ involvements, including that of the pancreas, might initially need to be treated with more aggressive chemotherapy protocols.

Learning points

- ▶ The involvement of various extramedullary sites might occur in acute lymphoblastic leukaemia (ALL) and it infers poorer prognosis.
- ▶ The involvement of the pancreas has been reported in five paediatric patients with ALL; it rarely becomes symptomatic in adult patients with ALL.
- ▶ Abdominal imaging should be undertaken in patients with ALL having gastrointestinal system symptoms.
- ▶ Patients with ALL having extramedullary involvement should be treated with more aggressive chemotherapy regimens.

Contributors GEP was involved in literature search, wrote the manuscript and gave consent for the final form of the paper. UT read the manuscript, made suggestions and wrote some parts of it and gave consent for the final form of the paper. SA interpreted the radiologic investigations, wrote some parts of the manuscript and gave consent for the final form of the paper. HU commented on the patient's gastrointestinal symptoms, interpreted the patient's CT with the radiologist and gave consent for the final form of the paper.

Competing interests None.

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