L-Asparaginase Induced Pseudopancreatic Cyst: A Rare Case Report

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Abstract L-Asparaginase is a frequently used drug in hematological malignancies. Various side effects associated with its use include hypersensitivity, hyperglycemia, hypercoagulability and acute pancreatitis. We describe a rare complication of pancreatic pseudocyst in a 12 year old boy of Acute lymphoblastic leukemia (ALL) treated with MCP-841 protocol (during re-induction phase). Nearing the end of induction i.e. day 25, patient complained of a painful swelling in the epigastrium and left hypochondrium. Investigations revealed a pancreatic pseudocyst for which he underwent cystojejunostomy. Post surgical period was uneventful.

Keywords L-Asparaginase · Acute lymphoblastic leukemia · Pseudopancreatic cyst · Cystojejunostomy

Introduction

Acute lymphoblastic leukemia (ALL) is the commonest type of leukemia and constitutes 25 % of all pediatric malignancies. It is treated with combination chemotherapy which produces various side effects, both acute and chronic. The causes of acute pancreatitis in children include trauma, infections like mumps, rubella, abnormalities of pancreaticobiliary junction, metabolic disorders and drug therapy [1–3].

L-Asparaginase is an anticancer drug, derived from *E.coli* or *Erwinia* and used for treatment of ALL. Pancreatitis occurs in 2–16 % patients receiving L-Asparaginase [4]. There are many case reports of L-Asparaginase induced pancreatitis in literature, but only 8 case reports about L-Asparaginase induced pseudocyst of pancreas.

Pancreatic pseudocysts occur because of pancreatic inflammation or pancreatic duct disruption leading to collection of pancreatic secretions without having epithelial lining [5]. We report a case of pseudocyst of pancreas developed during the treatment of ALL.

Case Report

A 12 year old boy presented to us with complaints of generalized lymphadenopathy, hepatosplenomegaly and pancytopenia since 2 months. He was investigated with hemogram (including peripheral smear), biochemistry (LFT, RFT, LDH and Uric acid), bone marrow aspiration/biopsy, flowcytometry and cytogenetics and diagnosed as precursor B acute lymphoblastic leukemia. He was started on MCP 841 protocol for acute lymphoblastic leukemia. MCP 841 protocol consists of an induction phase I, Phase II, a repeat induction, consolidation and maintenance phase. He

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received Induction-phase I with (steroids, L-asparaginase, vincristine, daunorubicin and intrathecal methotrexate), following which he attained complete remission at the end of induction phase I. Then he received Induction-phase II, which was uneventful. Subsequently he was started on reinduction phase I. On day 25th of reinduction he developed epigastric discomfort. Examination of the abdomen was normal. Ultrasound abdomen revealed no abnormality. Serum amylase was normal. A possibility of steroid induced gastritis was kept and treated accordingly with antacids and proton pump inhibitors after which the pain subsided. After a week (i.e. day 32) he complained of abdominal distention and discomfort in epigastric and left hypochondrial region (by this time he had received 8 doses of L-Asparaginase during reinduction phase). Abdominal examination revealed an 8×8 cm firm, tender mass occupying epigastric, left hypochondrium and umbilical region. Abdominal ultrasound suggested an 8.9×7.2×9 cm cystic lesion in epigastric, left hypochondrium and umbilical region arising from pancreas. CT abdomen revealed a 9×8×9.8 cm well defined fluid filled thin walled lesion seen in prepancreatic aspect extending into left anterior pararenal space as in Figs. 1 and 2. Another similar smaller lesion seen in uncinete process of pancreas. His serum amylase level was 193 IU/L and serum lipase was 180 IU/L. A diagnosis of a pseudo pancreatic cyst was made on the basis of history, physical examination, imaging and laboratory parameters.

The child was managed with antibiotics, parenteral support and nasogastric suction for 13 days. However, he did not respond to the conservative approach and a surgical intervention was planned. He underwent cystojejunostomy, with postoperative period being uneventful. Serum amylase, lipase and ultrasound abdomen done after a month of surgery was normal. At present, patient has completed consolidation and is on first maintenance phase of the protocol.

Fig. 1 An axial view of CT scan abdomen non contrast study at the level of renal hila shows a well defined, thin walled 9×8×9.8 cm sized cystic lesion at the pancreatic tail region. There is another small lesion at uncinete process of the pancreas

Fig. 2 An axial view of CT scan abdomen, contrast study at the level of renal hila shows wall enhancement of the both cystic lesions as shown in the Fig. 1

Discussion

Pancreatic pseudocyst is a rare disorder in pediatric age group. Various causes have been described in literature of which trauma is implicated as a major cause [6]. Some of the drugs reported to produce pancreatic pseudocyst are L-Asparaginase, valproic acid, didanosine and azathioprine [6].

L-Asparaginase is a frequently used drug for treatment of acute lymphoblastic leukemias and we consider it to be responsible for this rare condition. Pancreatitis is one of its lethal complication. In majority of the cases it resolves with conservative management, but in a rare situation it may progress to a pseudo pancreatic cyst.

An extensive search both online and offline was done and to the best of our knowledge, only eight cases have been described in literature (Table 1). Previous reports have shown that the onset of pancreatitis ranges from few days to several weeks (maximum by 16 weeks) [11]. In our patient, pancreatitis developed on day 25th of repeat induction I. A week later he developed pseudocyst of pancreas. The approach to a patient of pancreatic pseudocyst varies from conservative management to surgical intervention. A study has shown that pseudocyst of pancreas which is present less than 6 weeks usually resolves spontaneously with conservative management in 40 % of patients, while those persisting more than 12 weeks did not resolve and required surgical intervention [12]. According to a study, the size of the pseudocyst could be a deciding factor for management. 40 % patients with size less than 6 cm and 67 % patients with a size greater than 6 cm required surgical intervention [13]. In previously reported eight cases of pseudocyst due to L-asparaginase, one was managed conservatively while seven underwent surgical intervention [11].

Table 1 Previous case reports of pseudopancreatic cyst

No	Author	Year	Course of treatment	Management
1.	Yu CH et al. [7]	1994	ALL treatment protocol- including L-asparaginase	Conservative
2	John Sadoff et al. [8]	1997	2 case reports- 3 weeks and 5 weeks after last dose	1 case-percutaneous external drainage and second case operative debridement and drainage
3	Sanjay Tomar et al. [9]	2003	MCP 841 protocol 5th maintenance- 3 weeks after 4 L-asparaginase doses	Conservative
4	R. Karabulut et al.	2005	3 months after last dose of L-asparaginase after third course of BFM-95 protocol (reinduction1)	Conservative with USG-guided percutaneous external drainage
5	Holly L Spraker et al. [10]	2009	5 case reports- 3 Total XV protocol and 2 Total XVI protocol –various duration	All 5 managed Conservatively

Our patient was symptomatic much earlier as compared to previously reported cases, developed a pseudocyst pancreas that did not respond to the conservative management. His symptoms of abdominal pain persisted and hence required surgical intervention. Because of this complication in our patient, leukemia protocol treatment was interrupted for 32-days. Surgical intervention may be associated with morbidity in 20–30 % patients and mortality in 2–6 % in reported series [14, 15]. A minimal access approach is preferred over an open approach. Post surgery complications include infection, bleeding, stomal leak and recurrence.

Our patient did not suffer from any post surgical complications and his recovery was uneventful.

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