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Case Report

Obstructive Jaundice due to a Pancreatic Mass: A Rare Presentation of Acute Lymphoblastic Leukaemia in children

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Abstract

Introduction: Acute lymphoblastic leukaemia (ALL) is the most common type of cancer in children. Cholestatic jaundice is an unusual presentation of ALL. It is even rarer to be caused by involvement of the pancreas resulting in obstructive jaundice. Purpose: Describing obstructive jaundice secondary to a pancreatic involvement in childhood mature B cell ALL.

Objective: A four years old girl who had been diagnosed as mature B cell ALL in Paediatric oncology department, Viet Nam National Cancer Hospital. Method: Describing a clinical case.

Result: Pancreatic involvement in ALL is rare and obstructive jaundice secondary to a pancreatic mass as a primary presentation of ALL has not been reported in the literature, only in some case reports. Primary result of treatment by FAB LMB 96 protocol is excellent

Conclusion: This is a rare clinical case of mature B cell ALL in children with very severe conditions. Exact diagnosis results in successful treatment.

Keywords: Jaundice; Pancreatic Mass; Acute Lymphoblastic Leukaemia

Introduction

Leukemia is the most common malignant disease in children. In 2017, in America, approximately 4.970 children, adolescent and young adult under 20 year old have been diagnosed as leukemia in that acute lymphoblastic leukemia (ALL) is the most common type, approximately two third in all leukemia [1,2]. Recently, thank to advances in making diagnosis, treatment and supportive care, survival rate is being increasing more and more. From 2006 to 2012, 5 years overall survival rate off ALL is 92,3% for children under 15 years old and 94,1% for children under 5 years [1,2].

Cholestatic jaundice is an unusual presentation of acute lymphoblastic leukaemia. It is even rarer to be caused by involvement of the pancreas resulting in obstructive jaundice. We report a case of B cell acute lymphoblastic leukaemia presenting as a pancreatic mass and obstructive jaundice.

Purpose of Study

Case study a child with cholestatic jaundice as an unusual presentation of acute lymphoblastic leukaemia.

Patient and Method

Patient: 4-year-old female patient with B cell ALL, treated in Pediatric Oncology Department, Viet Nam National Cancer Hospital.

Content of study: Content of study: Clinical, paraclinical symptoms help making the definitive diagnosis, treatment result of the patient.

Method of study: Case presentation.

Case Report

Administration

- Name of the patient: Mai Thị Đan L Sex: F Age: 4 years old.
- Home address: Tan Le Village, Đong Tan Commune, Thanh Hoa City.
- Number of medical profiles: 16307388, Code of patient: 163053287.
- Date to hospital: 07, July 2016, Date of discharge:20, Feb ruary 2017.
- Reason to hospital: Cholestatic jaundice.

Past medical history

Operated congenital heart, horsehoe kidney.

Medical history

The patient presented with 10 days ascending jaundice, yellow scissors, no fiver, no pain, generalized weakness, anorexia, tiredness, pale stools, darkened urine→Province Hospital: Abdominal ultrasound showed an abdominal mass→ Viet Nam National Pediatric Hospital: abdominal CT scans presented many abdominal tumors, tumors in the liver→ Viet Nam National Cancer Hospital.

Clinical examination on the day of hospitalization

- Lethargy, fatigue, weakness, mild shortness of breath, T^0 38^0C.
- Severe jaundice, yellow scissors, Pale, no edema
- Clay-coloured stools. Darkened urine.
- Chest like chicken breasts, surgical scar, Heartbeat: 90/m, clear T1 T2.
- Lung: no alveoli whispering in the left. Normal in the right.
- Soft belly, no distention, no ascite, hepatomegaly, many tumors in abdomen, size of tumor 60 x 50 mm, no spleenomegaly.

Laboratory tests on the day of hospitalization

- CBC: Hb 68 g/L, WBC 6,16 G/L (Neut 3,43 G/L), Platelet 83 G/L.
- Biochemistry: Ure 3,1 mmol/l. Creatinin 45 µmol/L, GOT/GPT 219,4/101,4 U/L, total serum bilirubin/direct bili 238,3/134,0 µmol/L, A.Uric 58,1 g/L, LDH 1868 U/L
- Serum Amylase 433 U/L, Protein 57,1 g/L-Albumin 33,6 g/L, Electrolytes: normal.
- Coagulation: PT 16'', APTT 63'', fibrinogen 1,8 g/L, INR 2,3.
- CSF: No malignant cells.
- Chest CT scans: Left lung: pleural effusion, many tissular density tumors in pleural cavity 43 x 62 mm, total lung's atelectasia.
- CT scans Abdomen 32 rows with contrast: Hepatomegaly, uneven liver parenchyma, many hypodensity lesions, light enhancement post IV contrast injection. Many abdominal solid tumors, tumor in front the left kidney 20 x 30 mm, tumour in the lower right flank 50 x 60 mmm, many tumors in bilateral pelvic and pelvic area. Pancreatic involvement. Thrombosis in the below vena cava and hepatic vein. Horseshoe kidney.
- Hematomyelogram (bilateral aspiration): Bone marrow cell count 81, 970 G/L. Lymphoblast 81%. Conclusion: ALL L2.
- Immunokaryotype: Mature B cell lympho.

Myelo marker		B cell		T cell		No specification	
MPO	-	CD10	+	CD99	-	CD34	-
CD33	-	CD19	++	CD2		HLA-DR	
CD13	-	CD20	++	CD5	-	Other markers	
CD14	-	cCD22	-	CD7	-	CD45	++
CD15		cCD79a	-	cCD3	-	CD38	+++
GLyA		Cµ		CD3	-	CD123	-
CD41a		Kappa	-/+	CD4	-	TdT	-
CD117	-	Lamda	-/+	CD8	-	CD56	-
Populations of cell				%/total			
CD10/CD19/CD20				80%			

Table: Population of blast: approximately 80%, with B cell markers. Conclusion: Mature B cell ALL.

Confirmed diagnosis

- B cell lymphoblastic leukemia
- Risk stratification: High risk.
- Acute liver failure: Diagnostic criteria: elevation of trans aminases, INR > 2. Poor prognosis by: < 10 years old, jaundice > 1 week, not caused by A, B, C virus or halothane [3].
- Acute pancreatitis: poor prognosis: jaundice, Thrombo sis in the below vena cava and hepatic vein, Very highly elevated serum amylase-GOT/GPT-LDH [4].
- Previously operated congenital heart. Concomitant dis ease: Horseshoe kidney.

Different diagnosis

Non-Hodgkin's lymphoma stage IV, B cell. We strongly agreed the diagnosis as mature B cell ALL because there is no histopathology of biopsy specimen and there are 81% of lymphoblasts in bone marrow.

Treatment

Apply FAB LBM 96 protocol for group C (high risk)

- **Criteria of C group**: There CNS involvement and/or > 70% blast in bone marrow.

- **Very poor prognosis:** High risk ALL + Acute liver failure + severe acute pancreatitis Past medical history: operated congenital heart, very young, cachexia, horseshoe kidney.
- She was commenced on chemotherapy according to the FAB LMB 96 acute lymphoblastic leukaemia protocol, she was intensively taken care with intermittent packed red blood cells and platelet transfusions, more nutrition providing: nutrient rich diet, Glucose 10%, acid Amin.
- Separate patient room, antibiotics. After prophase, the patient reached clear remission (50%), after initial prepare, the patient was done with induction chemotherapy (Induction COPADM1). A repeat bone marrow assessment showed complete remission with no residual disease by flow cytometry. Side effects induction phase: neutropenia grade 4, thrombocytopenia grade 2. There is no non hematological side effects.
- **Supportive care:** Packed red blood cells and platelet transfusions, nutrition providing; prophylactic antibiotics, separated room.
- Toxicities during the whole treatment: Tolerable haematology toxicities. Induction phase: neutropenia grade 4, thrombocytopenia grade 2, but by good supportive care→the patient was recovered quickly.
- **Nonhematological toxicities:** mild vomiting, alopecia, diarrhoea, mucositis. There was only one time, the patient has mouth mucositis grade III in a week after induction phase COPADM1 (HD Methotrexate infusion).

Discharge

The patient has reached complete response according to WHO 2000 criteria (Complete response: no evidence of residual lesions, partial response: at least remission 50% of all lesions. Aggressive disease: Increasing at least 25% of lesions size). Our patient was discharged on 20, February 2017.

Discussion

Cholestatic jaundice as an initial presentation of acute lymphoblastic leukemia (ALL) is exceedingly rare. It is even rarer to be caused by involvement of the pancreas resulting in obstructive jaundice. Maria S Felice., *et al*. (2000) report a 7 - year/old white girl who was admitted because of acute severe hepatic failure. Her complete blood count revealed pancytopenia and a bone marrow aspiration was consistent with acute lymphoblastic leukemia (ALL). Blasts cells were positive for cytoplasmic CD3 and cell surface T-associated markers. Viral, metabolic, immune and toxic causes for hepatic failure were ruled out. Treatment prephase with prednisone was started and liver function tests clearly improved after one-week therapy. However, due to her hepatic insufficiency, daily etoposide was administered orally for 15 days. On day 33 complete remission was achieved and hepatic function was normal, except for an increase in the bilirubin level which normalized on day 72. She received our current treatment for intermediate risk ALL and is still receiving continuation phase therapy, currently, with normal liver function and good tolerance to chemotherapy + 8 months after achieving complete remission [5]. Salihcesur., *et al*. (2004) reported a 15-year-old boy presented at our clinic with a 2 weeks history of anorexia, malaise and jaundice in the sclera of the eye and skin, with darkened urine. The history revealed that one of his siblings had neurofibromatosis, the patient had not taken any toxic drug and no jaundice case was present in his family. The patient was generally well, alert and not confused. His temperature was 37.9°C and pulse 88/min. There was a marked icterus in the sclera and the skin. He had no splenomegaly or hepatomegaly. Laboratory investigations showed that the leukocyte count was 2500/mm3, Hb 14.1g/dl, platelet 80,000/mm^3 and erythrocyte sedimentation rate 10 mm/h. Biochemical analysis demonstrated that total bilirubin was 18.9 g/dl, direct bilirubin 10.3 g/dl, AST 350 U/L, ALT 1140 U/L and LDH 1789 U/L. Other biochemical tests were normal. The hepatitis markers anti-HBs and anti-HAVIgG were positive but HBsAg, anti-HCV and anti-HAVIgM were negative. Polymerase chain reaction showed that HBVDNA and HCV-RNA were negative. Other viral markers including EBVIgM, CMVIgM, HSV-I and II IgM and HPVB19 were negative but, EBVIgG, CMVIgG and HSV-I and II IgG were positive. Peripheral blood film showed atypical lymphocytes, blast cells and neutropenia (Figure 1-3).


BỆNH VIỆN NHI TRUNG ƯƠNG

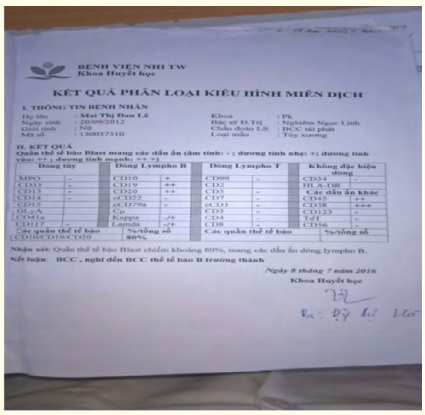
PHIẾU KẾT QUẢ CTSCAN

MÔ TẢ CHI TIẾT

KẾT LUẬN

ĐỀ NGHỊ

Figure 1: Preoperative abdominal CT scans.


BỆNH VIỆN NHI TW
Khoa Huyết học

KẾT QUẢ PHÂN LOẠI KIỂU HÌNH MIỄN DỊCH

I. THÔNG TIN BỆNH NHÂN

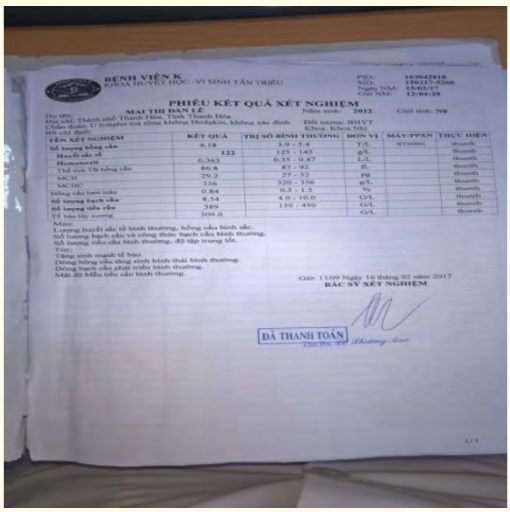
II. KẾT QUẢ

Dòng tủy		Dòng Lympho B		Dòng Lympho T		Không đặc hiệu dòng	
MPO	-	CD10	+	CD99	-	CD34	-
CD33	-	CD19	++	CD2	-	HLA-DR	-
CD13	-	CD20	++	CD5	-	Các dấu ấn khác	
CD14	-	cCD22	-	CD7	-	CD45	++
CD15	-	cCD79a	+	cCD3	+	CD38	+++
CD64	-	Cy		CD3	-	CD123	-
CD15	-	Kappa	-/+	CD4	-	TdT	-
CD41	-	Lamda	-/+	CD8	-	CD56	-
Các quần thể tế bào		%/tổng số		Các quần thể tế bào		%/tổng số	
CD10/CD19/CD20		86%					

Nhận xét: Quần thể tế bào Blast chiếm khoảng 80%, mang các dấu ấn dòng lympho B.
Kết luận: BCC , nghĩ đến BCC thể tế bào B trưởng thành

Ngày 8 tháng 7 năm 2016
Khoa Huyết học

Figure 2: Immunokaryotype.


BỆNH VIỆN K
KHOA HUYẾT HỌC -VI SINH TÂN TRIỀU

PHIẾU KẾT QUẢ XÉT NGHIỆM

TÊN XÉT NGHIỆM	KẾT QUẢ	TRỊ SỐ BÌNH THƯỜNG	ĐƠN VỊ	MÁY/PPXN	THỰC HIỆN
Số lượng hồng cầu	4.18	3.9 - 5.4	T/L		thanh
Huyết sắc tố	122	125 - 145	g/L		thanh
Hematocrit	0.363	0.35 - 0.47	L/L		thanh
Thể tích TB hồng cầu	86.8	83 - 92	fL		thanh
MCH	29.2	27 - 32	Pg		thanh
MCHC	336	320 - 356	g/L		thanh
Hồng cầu lưới máu	0.84	0.5 - 1.5	%		thanh
Số lượng bạch cầu	8.34	4.0 - 10.0	G/L		thanh
Số lượng tiểu cầu	389	150 - 450	G/L		thanh
Tỉ lệ hồ sơng	309.0				

Giờ: 1109 Ngày 16 tháng 02 năm 2017
BÁC SỸ XÉT NGHIỆM

ĐÃ THANH TOÁN

Figure 3: Hemomyelogram after treatment.

Because his body temperature exceeded 38.3°C, an empiric double antibiotic combination consisting of cefepime and amikacin were initiated to treat him according to the febrile neutropenia protocol. To establish the etiology of the pancytopenia, the patient was referred to the department of haematology. The examinations of peripheral blood and bone marrow aspiration revealed a leukemic infiltration. Escherichia coli was isolated in peripheral blood and bone marrow cultures. Jaundice was considered to be secondary to leukemic liver infiltration since other causes of hepatitis (i.e. viral hepatitis, toxic hepatitis, and metabolic liver disease) were ruled out. The patient's abdominal ultrasonographic imaging showed parenchymal echogenicity, granulation patterns without mass and hepatic steatosis. At this time, we planned to perform a liver biopsy to clarify the cause of hepatic dysfunction. However, it was not performed due to the low level of platelets and coagulopathy. In addition, his family did not give permission for this procedure. The patient was definitely diagnosed with aberrant myeloid marker bearing pre-B ALL consequent to flow cytometry and immunohistochemical investigations. Cytogenetic analyses detected hypodiploidy and clonal deletion of chromosome 22. Remission induction chemotherapy for ALL was not initiated in the patient because of the risk of inducing massive liver necrosis and a worse outcome. Approximately 1 week later, his clinical and laboratory parameters such as fever, complete blood count, liver function tests and peripheral blood smear started to improve with supportive care and empirical ant biotherapy and he became almost normal. At this time, to clarify the unexpected improvement, it was decided to repeat the bone marrow examination, but his family did not give permission for this repeat procedure. Because of this improvement in the clinical and laboratory picture, we decided to follow the patient without therapy. After several days, the fever rose together with severe jaundice in the patient. The laboratory parameters including liver function tests and complete blood count rapidly deteriorated. We observed leukemic cells in the peripheral blood smear again. Within several days, the clinical picture rapidly progressed to hepatic failure and encephalopathy. Finally, he died of multiorgan failure. No post-mortem examination was performed since informed consent from the patient's family could not be obtained for autopsy [6]. Litten JB., *et al*. (2006) reported a previously healthy 4 - year-old boy was admitted because of acute liver failure. He was icteric, lethargic, had elevated ammonia and abnormal liver function tests. Serology was negative for viral hepatitis. There was no history of hepatotoxic drugs. Family history was unremarkable. The child was taken to the operating room for a living-related hepatic transplant. Frozen section showed massive hepatic leukemic infiltration and hepatocellular necrosis. Bone marrow aspiration confirmed the diagnosis of acute lymphoblastic leukemia (ALL). Transplant was withheld, and chemotherapy was attempted. He died the following day due to systemic leukemic infiltration, cerebral edema, and severe anoxic ischemic encephalopathy [7]. Chang LS., *et al*. (2011) reported a 15-year-old boy presenting with severe jaundice and hyperferritinemia, whose bone marrow smear showed B-lineage precursor ALL. We treated him with intravenous immunoglobulin, steroid, and etoposide; then his condition improved. ALL should be considered as a possible diagnosis in severely jaundiced children. Steroid and etoposide can be used as first aid when many chemotherapeutic drugs are contraindicated [8].

Our patient was intensively tankan care and treated with chemotherapeutic FAB LMB 96 protocol for group C (high risk). The FAB/LMB96 study was an open randomized trial that investigated the reduction of treatment. It was a cooperative international study with the collaboration of SFOP (France and some centers in Belgium and The Netherlands), Children's Cancer Group (CCG of the United States, Canada, and Australia), and the United Kingdom Children's Cancer Study Group (UKCCSG). It was a planned 5-year study that opened in May 1996 and closed in June 2001. It included patients in 161 pediatric cancer centres from the 3 national groups. Parents or patients over 18 years of age signed an informed consent form before randomization, in accordance with the Declaration of Helsinki. The protocol was approved by each participating institution's institutional review board. Each national group was responsible for the scientific, ethical, and administrative approvals, the randomization, and the data collection in a national database. These data were transferred every 6 months to the international database held at Institute- Gustave-Roussy for the SFOP. SFOP was responsible for interim and final analysis of group B. Every 6 -month reports and interim analyses were reviewed by an international, independent Data and Safety Monitoring Committee (DSMC) including 3 pediatric oncologists and one statistician.

Our patient has many poor prognostic factors but reached very good primary treatment result. She reached complete response, was discharged. Mitchell S Cairo., *et al*. (2006), reported 4 years event free survival rate by FAB/LMB 96 protocol in B cell ALL CNS negative ≥ 90% [9]. Catherine Patte., *et al* (2007) reported 4 years event free survival rate by FAB/LMB 96 protocol in 23 children with B cell non-Hodgkin's lymphoma stage IV and ALL L3 CNS positive and/or bone marrow involvement > 70% is 85,6% [10]. Theo Eun Sil Park., *et al*. (2011) compared the outcomes of patients with Burkitt lymphoma and French-American-British (FAB) L3 acute lymphoblastic leukemia treated using Lymphoma Malignancy B (LMB) or other treatment protocols. Thirty - eight patients diagnosed between July 1996 and December 2007 were treated using LMB 96, and 22 patients diagnosed between January 1991 and May 1998 (defined as the early period) were treated using the DCOMP or CCG-106B protocols. Were retrospectively reviewed their medical records and analysed cumulative survival according to the treatment period by using Kaplan-Meier analysis. There were no intergroup differences in the distribution of age, disease stage, or risk group. The median follow-up period of the 33 live patients in the LMB group was 72 months (range, 36 - 170 months). Overall survival (OS) and event-free survival (EFS) of patients treated using LMB 96 were 86.8% ± 5.5% and 81.6% ± 6.3%, respectively, whereas OS and EFS of patients treated in the early period were 72.7% ± 9.6% and 68.2% ± 9.9%, respectively. In the LMB 96 group, OS of cases showing non-complete response (N = 8) was 62.5% ± 17.1%, and OS of relapsed or primary refractory cases (N = 6).

Was 33.3% ± 19.3%. Central nervous system (CNS) disease, high lactated hydrogenase levels at diagnosis, and treatment response were significant prognostic factors [11].

Conclusions

Acute lymphoblastic leukemia should be one of the differential diagnoses that should be considered when initial work-up for jaundice is inconclusive. Some cases of acute lymphoblastic leukemia have been reported in both adults and children to have presented with the initial manifestation of jaundice, but only a few had no radiographic evidence of biliary obstruction. Such presentation can pose a serious diagnostic dilemma for clinicians. This manuscript attempts to highlight it. Moreover, we believe that if acute lymphoblastic leukemia presentations similar to this case continue to be reported in adults or children, a specific immunophenotypic expression and cytogenetic abnormality may be found to be associated with hepatic infiltration by leukemia. This may substantially contribute to the further understanding of the pathophysiology of this hematologic disease. The randomized international FAB/LMB 96 trial for dose-re- during treatment of early responding patients (tumor response > 20% at day 7) showed that dose-reducing treatment was possible without jeopardizing survival. This protocol is very effective and has tolerable toxicities in ALL and B cell non-Hodgkin's lymphoma.

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