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A Rare Presentation of Acute Lymphoblastic Leukaemia in a Teenage Girl: Heart Failure

HM ***Cheung,*** GCF ***Mok,*** V ***Lee,*** MMK ***Shing,*** CK ***Li***

Abstract Acute lymphoblastic leukaemia commonly presents as fever, pallor and lethargy. Lymph nodes, liver and spleen are the common organs involved. This case report describes a rare presentation of B-lineage lymphoblastic leukaemia infiltrating myocardium leading to heart failure. Leukaemia patients with unexplained heart failure should be investigated for cardiac involvement despite absence of peripheral leukaemia blast.

Key words Acute lymphoblastic leukaemia; Heart failure

Introduction

Leukaemia is a systemic disease and involves all organs and tissues of the body. Common clinical presentations include fever, pallor and lethargy. In this report, we describe a 13-year-old girl diagnosed with B-lineage acute lymphoblastic leukaemia presenting as heart failure.

Case Report

A 13-year-old girl was admitted into hospital because of progressive shortness of breath for one month. She enjoyed good past health until one month before admission. She was noticed to have itchy fine macular rash over the body and face and was treated as eczema. She was also noticed to have multiple cervical lymph nodes, the biggest one measuring 2 cm in diameter at posterior cervical region. She started to have progressive increase in dyspnoea which was associated with orthopnoea and decreased exercise tolerance. There were also anorexia, malaise and weight loss. She was afebrile all along without chest pain or palpitation. On admission, there was tachycardia with heart rate of 134 per minute, blood pressure of 118/79 mmHg, respiratory rate of 26 per minute with oxygen saturation of 97% in room air. Multiple firm, tender lymph nodes were found over bilateral cervical area and left sub-clavicular region, but there was no enlarged axillary or groin lymph nodes. Cardiovascular examination showed displaced cardiac apex at left 6th intercostal space 0.5 cm lateral to left mid-clavicular line. Heart sounds were clear and normal without murmur or pericardial rub heard. Electrocardiogram showed sinus tachycardia with axis at 60 degree. Chest examination showed decreased air entry over right posterior chest with no added sound heard. Chest X-ray revealed cardiomegaly, cardio-thoracic ratio of 0.73 and bilateral pleural effusion (Figure 1). Abdominal examination showed no hepatosplenomegaly.

Investigations showed haemoglobin 11.6 g/dl, white cell count 5.6 x 10^9/L (neutrophil 53%, lymphocyte 38% and no circulating atypical cells), platelet 207 x 10^9/L. Serum lactate dehydrogenase (LDH) was 5516 U/L (normal, 87-213 U/L), Creatinine kinase (CK) 412 U/L (normal 32-180 U/L), urate 0.42 mmol/L (normal 0.14-0.37 mmol/L),

Department of Paediatrics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China

HM **Cheung** (張漢明) *MBBS, MRCPCH*
GCF **Mok** (莫子楓) *FHKCPaed*
V **Lee** (李偉生) *FHKCPaed*
MMK **Shing** (成明光) *FHKCPaed*
CK **Li** (李志光) *MD, FHKCPaed*

Correspondence to: Dr HM **Cheung**

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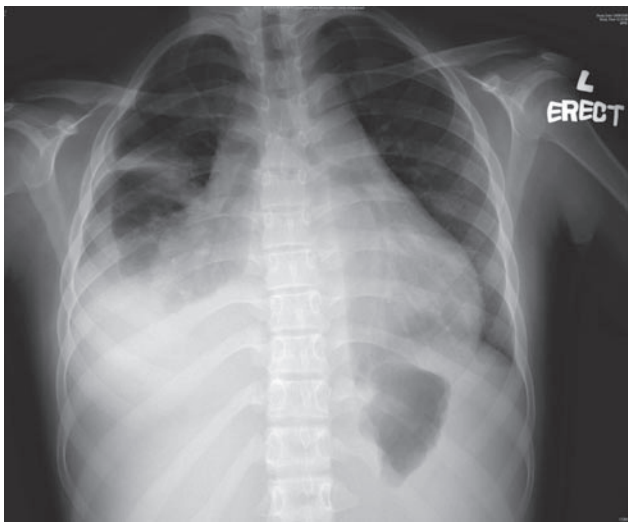

Figure 1 Right pleural effusion and cardiomegaly on initial presentation.

C-reactive protein 4.0 mg/L (normal <9.9 mg/L). Mantoux test was negative. Anti-nuclear antibody was positive with titre >320 (normal <40). Anti-neutrophil cytoplasmic antibody (ANCA), anti-DNA antibody, anti-extractable nuclear antibody was all negative. About 600 ml of straw color pleural fluid was aspirated. Pleural fluid biochemistry study showed protein of 37 g/l and lactate dehydrogenase (LDH) of 308 U/L. The pleural fluid showed the presence of atypical lymphoid cells but gram stain and acid fact bacilli stain were both negative. Pleural biopsy showed no evidence of inflammation, granulomatous change or malignancy. Echocardiogram showed thickened right ventricular wall, dilated left ventricle hypertrophy with no obstruction to left ventricle outflow tract. Ejection fraction was markedly decreased to 34% with fractional shortening of only 13%. There was no pericardial effusion or thickening.

In order to establish the diagnosis, excision biopsy of left sub-clavicular nodule was performed under local anesthesia. Histology examination showed dense atypical lymphoid cell infiltration of small to moderate size, fine chromatin, indistinct to small nucleoli and scanty indistinct cytoplasm. Mitotic figures were frequently seen. Immunohistochemical study showed the atypical lymphoid cells with diffuse strong positivity for B cell marker (L26/CD20, CD10) and Tdt. The T-cell markers (CD3, CD5 and CD7) were negative. Myeloperoxidase (MPO) was also negative.

Bone marrow examination and trephine biopsy showed heavy infiltration of 72% small to medium sized blast cells. Immunophenotyping by flow cytometry showed the blasts were Tdt positive, CD10, CD19, CD22, CD20 and CD79a positive. The blast cells were negative for the T-lymphoid markers and the myeloid markers. No cytogenetic abnormality was detected. She was thus diagnosed to have acute lymphoblastic leukaemia, pre-B type. Cytogenetic study showed molecular fusion products for BCR/ABL, TEL/AML1 and MLL/AF4 were negative.

Treatment for Acute lymphoblastic leukaemia was started with prednisolone, vincristine, daunorubicin and L-asparaginase.

Echocardiogram was repeated one week after prednisolone treatment which showed marked improvement of cardiac function with normal right ventricle structure and size. Fractional shortening increased to 40% and the ejection fraction up to 77%.

Bone marrow examination on day 15 and day 33 showed remission of leukaemia. Chemotherapy was continued according to protocol and patient is now at 52 weeks after her initial presentation, and remained in remission with normal cardiac function and the subsequent echocardiograms were all normal.

Discussion

In the early era of leukaemia treatment, studies showed that cardiac leukaemic infiltration was common in children dying with leukaemia. Up to 44% of the patients had at least one focus of leukaemia infiltration in the heart.[1] However, the cardiac involvement is mostly asymptomatic and less than 5% of cases have symptomatic heart disease.[2] Leukaemic cardiac involvement ante-mortem is usually not suspected.[3] Pathological findings include leukaemic infiltrates and haemorrhage in the myocardium or the pericardium.[2]

In our patient, the initial presentation of heart failure is manifested as progressive shortness of breath, marked decrease of exercise tolerance and classical symptom of orthopnoea. The negative family and drug history made the diagnosis of familial-hereditary or toxin induced myocardial disease unlikely. Infectious myocarditis, connective tissues disease and infiltrative causes are the important differential diagnosis. The final diagnosis was made by the positive lymph node and bone marrow biopsy, and the impaired cardiac function, after having excluded other causes, was most likely due to leukaemic infiltration of myocardium. Cardiac muscle biopsy was not performed due to high risk of the procedure. The prompt response to anti-leukaemic treatment with improvement in cardiac

function supports the diagnosis of leukaemia infiltration of myocardium leading to heart failure. Although cardiac infiltration is usually associated with hyperleukocytosis and advanced disease,[1,4] the presence of a high white blood cell count is not a necessity for developing cardiac infiltration.[5] In our case, the initial white cell count was only 5.6 x 10^9/L and there was no circulating leukaemic blast found.

Symptoms of lethargy, shortness of breath and malaise in leukaemic patients are often attributed to associated anaemia.[6] Our patient had initial haemoglobin of 11.6 g/dl. The causes for these symptoms should be carefully investigated. The massive pleural effusion might explain partly for the respiratory symptoms. Cardiomegaly in leukaemia or lymphoma patients may be due to pericardial effusion, and echocardiogram should be performed to exclude these causes. The echocardiogram in our patient unexpectedly showed poor contractility and ventricular hypertrophy. Myocardium is an uncommon site of metastatic disease of cancer. Even patients with disseminated neoplastic process involving the heart, the left and right ventricular systolic function were preserved until very late in the course of the disease when the patients began to experience symptoms of heart failure.[6] A study of 20-year autopsy showed that the incidence of secondary heart tumour is only 1.23%, amongst which leukaemia constitutes only 4.0%.[7] Most of the reports of cardiac involvement in leukaemia or lymphoma are T-cell disease. T-cell leukaemia/lymphoma commonly presented as mediastinal mass. Due to close proximity to cardiac structure, this may explain the direct infiltration of leukaemic cells into myocardium.[8] Case report has shown complete regression of massive cardiac involvement associated with acute T-cell leukaemia following chemotherapy.[9] In the literature, there was no report of B-lineage leukaemia/lymphoma infiltrating myocardium.

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