The Turkish Journal of Pediatrics
Volume 27, No. 4, October - December 1985

ISOLATED SPLENOMEGALY DURING REMISSION IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA*

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Key words : acute lymphoblastic leukemia, isolated splenomegaly, portal hypertension.

Splenomegaly is a common clinical finding in acute childhood leukemia (ALL), which regresses with the induction of remission. Crist et al[1] and Lister et al[2] have reported it as an isolated finding in patients with ALL during remission, but its significance was emphasized by Manoharan et al[3]. We would like to report two cases of leukemia where splenomegaly during remission was related to portal hypertension of undetermined origin.

Case Report

Case 1

A 10-year-old boy who had been followed and treated for ALL since March 20, 1978. His original moderate splenomegaly regressed in four weeks following induction of remission with vincristine sulfate and corticosteroid. The spleen again became palpable during an acute febrile illness which occurred in the seventh month of remission while he was on maintenance treatment with 6-mercaptopurine and methotrexate. At that time cervical lymphadenopathy and skin eruptions were also observed without any hematological evidence of relapse. In the fifteenth month of remission he was readmitted because of convulsions and marked splenomegaly. Serum calcium, skull X-ray, electrolytes and cerebrospinal fluid examinations revealed no cause for the convulsions. Toxoplasma dye, brucella agglutination, liver function tests and peripheral blood findings were also non-contributory. However, he was given reinduction treatment of vincristine sulfate and cytoxan for two weeks because of splenomegaly. No change occurred

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in the size of the spleen and repeated bone marrow examinations indicated that the patient was in complete remission. Maintenance treatment was therefore discontinued as of January 1982. The results of liver function tests stayed within normal limits, and HB_s Ag and anti HB_s were negative in each of several studies. Splenic needle aspiration material did not show any blasts, and liver and spleen scanning by 99m Tc sulfurcolloid indicated splenomegaly. Intraveous pyelography disclosed no cause for this condition, and a liver biopsy obtained in May 1982 revealed neither fibrosis nor infiltration. Splenoportography revealed an enlarged spleen with left coronary varices (Figure 1). Splenic pulp pressure was markedly elevated (410 mm/H_2O).

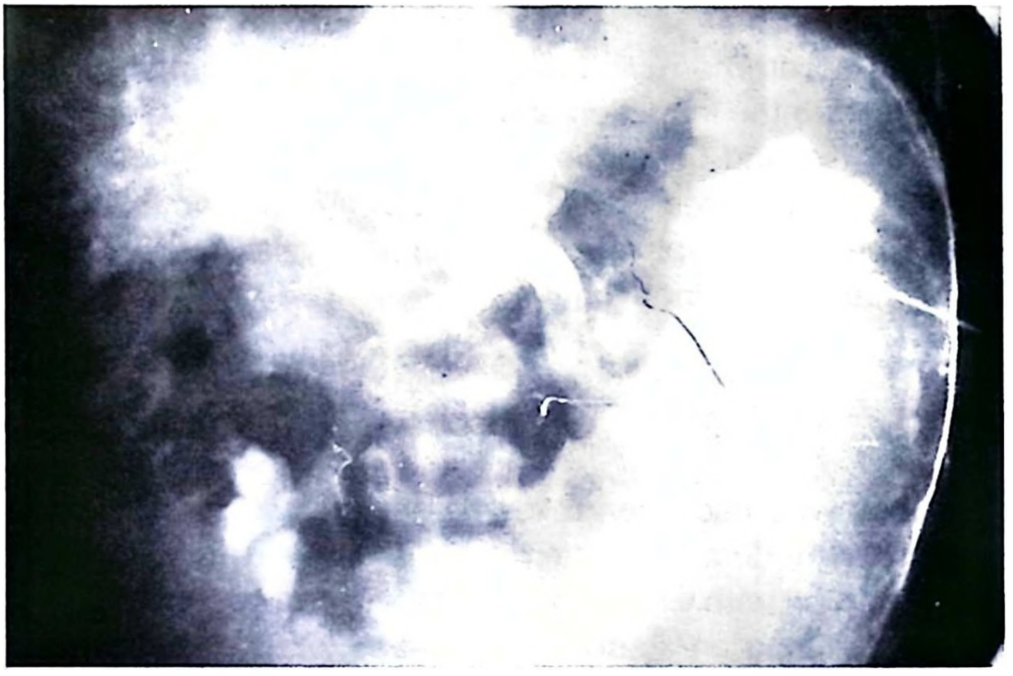

Figure 1

Splenoportography of Case 1 visualized enlarged spleen with left coronary varices

Case 2

A 15-year-old boy was seen in this hospital for the first time in December 1978, when ALL was diagnosed. His liver and spleen were both 4 cm below the respective costal margins. With vincristine sulfate and corticosteroid treatment he went into complete remission in six weeks. Eight months later, during maintenance treatment with 6-mercaptopurine and methotrexate, his spleen became palpable 3 cm below the left costal margin. Since he was in complete remission, HB_s Ag, anti HB_s, a toxoplasma dye test and liver function tests were repeated and results were normal. His spleen became nonpalpable within a month but became enlarged again 18 months later, although the patient was still in remission.

In June 1982, six months after discontinuation of treatment splenoportography and splenic needle aspiration were carried out. With the exception of elevated splenic pulp pressure (210 mm/H_2O) the findings were normal. Repeated liver function tests and liver needle biopsy did not disclose any abnormality or infiltration.

Discussion

Isolated splenomegaly during remission in patients with ALL has been reported in children[1,3,4] as well as in adults[2,5]. Because of these reports splenectomy was postponed in our first patient and the pathogenesis of the splenomegaly was sought in both patients. Although liver fibrosis due to leukemia or its treatment is postulated, the pathogenesis of this finding was shown in only two of the nine patients in whom microscopic examination of the liver was carried out[3,4]. Portal hypertension due to hepatic fibrosis with esophageal varices and hypersplenism has also been reported previously in acute lymphocytic leukemia treated with antimetabolities for long periods of time, which might be better differentiated from the above cases of isolated splenomegaly during remission[6].

Associated chronic cytomegalovirus infections were considered as the cause of isolated splenomegaly during remission in two patients with ALL by Hardisty and Chessells[4]. Although details for these two patients were not given, to our understanding they were different clinically from the non-cirrhotic portal hypertension cases, with fibrocongestive splenomegaly and prominent gastric and esophageal varices with focal subendothelial fibrosis of the small and medium sized vein radicals and within the parenchyma of the liver, which generally are related to cytomegalovirus infections[7,8].

To our knowledge, portal hypertension in isolated splenomegaly without liver involvement, during remission of ALL, has not previously been documented; however, its occurrence without cirrhosis or fibrosis of the liver in several hematological conditions is known. Though thrombosis of the portal, splenic or hepatic veins may occur, in myeloproliferative syndromes, alternative explanations include increased portal flow secondary to splenomegaly "forward flow" and increased hepatic resistance due to infiltrative lesions in the portal tracts and sinusoids[9]. When the portal vein is patent and the liver appears normal in light microscope studies, sinusoidal portal hypertension with marked hypertrophy of Kupffer's cells with narrowing of the sinusoidal lumina should be considered[10].

In some patients with portal hypertension, the morphologic appearance of the liver may be completely normal. These patients are grouped under the heading of idiopathic portal hypertension, which is the second most frequent cause of this syndrome, following childhood cirrhosis, in Turkey[11].

Because of the relatively early appearance of splenomegaly and absence of hepatic fibrosis in our patients, portal hypertension could hardly be related to antimetabolite usage[6]. Extrahepatic portal obstruction in these patients was ruled out by the splenoportographic examination. Though the spleen of our first patient became palpable following a febrile episode with skin eruption and lymphadenopathy, suggesting a viral illness retrospectively, we have no laboratory evidence of it. It should also be considered that chronic isolated splenomegaly in virus infections in children with ALL is a rare occurrence[12]. Such an episode was not described by our second patient.

Considering the normal morphology of the liver in our patients, we are inclined to favor forward flow as the cause of their portal hypertension.

We believe that in addition to liver biopsy, splenoportographic examination and splenic blood flow determination should be carried out in patients with isolated splenomegaly during remission in acute childhood leukemia, if the cause of splenomegaly cannot be found otherwise.

Summary

Persistent splenomegaly was observed in two boys, aged 10 and 15 years, with acute lymphoblastic leukemia, beginning seven and eight months after induction of complete remission. Portal hypertension (410 mm/H_2O and 210 mm/H_2O) was documented in both during splenoportography. No evidence of liver disease or infiltration was shown by liver biopsy or liver function tests, and the splenic needle biopsy examination did not disclose any infiltrative disease four years after leukemia was diagnosed. We believe splenoportography and portal blood flow determinations should be carried out in patients with isolated splenomegaly during remission from acute lymphoblastic leukemia, if no other cause can be found.

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