CASE REPORT

HISTIOCYTE RICH PSEUDOTUMOUR OF SPLEEN/SPLENIC LYMPH NODE AFTER CHEMOTHERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA – A CASE REPORT

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ABSTRACT

Post chemotherapy histiocyte-rich pseudotumour of spleen and lymph node are a rare occurrence and can be seen in patients after chemotherapy of haematological malignancies. We report the case of a two years old child, a diagnosed case of Acute Lymphoblastic Leukemia under going chemotherapy. He presented to the paediatric oncology department of Combined Military Hospital, Rawalpindi for follow up examination. Clinical examination and ultrasound abdomen revealed splenomegaly. Haematological investigations revealed worsening of blood counts. Splenectomy was planned in order to improve hypersplenism and to evaluate leukemic infiltration of spleen. Spleen and a perihilar lymph node were removed surgically and the specimens were sent to the histopathology department of Armed Forces Institute Pathology, Rawalpindi. Histologically, spleen and lymph node showed sinus dilatation and infiltration by numerous macrophages, which were positive for histiocytic immunohistochemical markers. On the basis of histopathological and immunohistochemical features, the diagnosis of post chemotherapy histiocyte-rich pseudotumour of spleen and lymph node was made.

Keywords: Histiocytic Pseudotumour, Lymph node, Post chemotherapy and Spleen.

INTRODUCTION

'Post chemotherapy histiocyte rich pseudotumour' or 'Xanthomatous tumour' is an unusual, benign condition. This term has been suggested for post chemotherapy massforming lesions composed of lipid-laden histiocytes and tumor necrosis. It has been reported previously in patients who presented with residual masses persisting after chemotherapy in organs like spleen, breast and intestine where it may be considered as a persistent or a recurrent lesion. After effective chemotherapy, there is regression of tumour masses due to necrosis. However, in a group of patients, necrotic tumour may persist as a mass, where it raises the suspicion of residual or recurrent disease. In such cases, the diagnosis and exclusion of pseudotumour is clinically important. Cases of post chemotherapy pseudotumours have already been reported in patients with Hodgkin's and Non Hodgkin's lymphoma, but this phenomenon has not been reported earlier in patients with acute lympholastic leukemia.

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CASE REPORT

A two years old male patient presented to the paediatric oncology department of Combined Military Hospital, Rawalpindi with six months history of progressive pallor, on and off fever and abdominal distention. On examination, he was found to have pallor and splenomegaly. Heamatological investigations including blood complete picture, bone marrow aspiration and were carried out. Blood complete picture showed hemoglobin of 11.2 g/d*l*, total leucocyte count of $6.5x10^9/l$ and platelet count of $78x10^9/l$. Bone marrow aspiration revealed infiltration by 45% blast cells. Immunophenotyping was then performed, and the diagnosis of precursor B-cell acute lymphoblastic leukemia was made. The patient was started on multi agent chemotherapy. Upon follow-up investigations, the blast count had reduced indicating heamatological remission, but hemoglobin and platelet count further declined. The splenomegaly also persisted. Splenectomy was planned in order to improve hypersplenism and to evaluate the possibility of residual disease within spleen. The spleen along with a perihilar splenic lymph node were removed surgically and the specimens were sent

to Armed Forces Institute of Pathology, Rawalpindi for histopathological examination.

On gross examination, the spleen measured 15.5x10x5 cm and weighed 322 grams. The external surface was smooth and regular. On serial slicing, the cut surface was homogenously reddish brown (Figure-1 A and B). The splenic hilar lymph node measured 1.6x0.8x0.5 cm. On bisecting, the cut surface was homogenously light brown. Multiple representative sections were prepared from the spleen and lymph node.

On microscopic examination, the sections from the spleen revealed partial effacement of the architecture, dilatation of the sinuses and infiltration by sheets of foamy macrophages having abundant, pale, eosinophilic nuclei with inconspicuous nucleoli (Figure-2 A, B). The sections of the lymph node also revealed hyperplasia of the lymphoid follicles with prominent germinal centres, dilatation of the sinuses and infiltration by sheets of foamy macrophages. On the basis of pseudotumour, Langerhan cell histiocytosis, storage disorder and infections like tuberculosis or mycosis.

Immunohistochemistry and special stains were applied on the sections from spleen and lymph node. The immunohistochemical markers for histiocytes. i.e., CD68 and S100 were stronglypositive in the histiocytes while CD1a was negative, excluding the possibility of Langerhan cell histiocytosis (Figure-2 C). The Periodic Acid Schiff and Ziehl Neilsen stains were negative ruling out storage disease and the infectious causes respectively. The histomorphology and immunohistochemical stains were suggestive of histiocyte rich pseudotumour of Spleen and Lymph node. No evidence of residual disease was found in the spleen or lymph node.

DISCUSSION

Post chemotherapy histiocyte-rich pseudotumour also referred to as xanthomatous pseudotumour[1] is a rare, benign, treatment-related sequel of tumour cell lysis and phagocytosis of lipid-membranous debris by histiocytes[2]. The presence of post chemotherapy residual masses at nodal and extranodal sites and within the medistinum[3,4] have been reported in cases of testicular carcinoma[5] Hodgkin's and Non Hodgkin's lymphoma[3] including Burkitt's Lymphoma[2] and breast carcinoma[1]. Although, induction of necrosis is a well documented

Figure-1: Gross appearance of spleen.

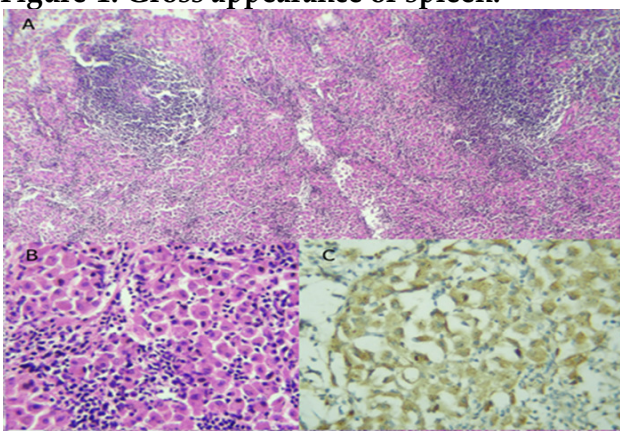

Figure-2: Photomicrograph of histiocyte rich pseudotumour of spleen, showing infiltration by sheets histiocytes with scattered preserved lymphoid follicles (Hematoxylin-Eosin, original magnifications 10x [A] and 40x [B]) and CD 68 (original magnification x10) [C].

consequence of chemotherapeutic drugs; the mechanism of persistance of residual masses is largely unknown. It may be due to the possibility that the chemotherapeutic drugs selectively

destroy tumour cells while the stromal component of the tumour remains unaffected. On the other hand, inflammation and fibrosis can occur in response to destruction of tumour cells[6]. A proposed mechanism is that as a result of necrosis, antigens are taken up, processed, and presented to T lymphocytes. In response to immune stimulus, various cytokines (notably interferon gamma, tumor necrosis factor-α, IL-1, IL-6, IL-12 and IL-23)[3] and macrophage activating factors are produced leading ultimately to the proliferation of macrophages.

Pre and post-chemotherapy suspicious masses detected by imaging techniques are important while evaluating responsiveness to chemotherapy and radiotherapy. The Dana-Farber Cancer Institute (DFCI) series suggested that CT scan appearance of the masses and the magnitude of change during therapy cannot exclude the possibility of residual carcinoma[7]. This can result in inaccurate measure of efficacy of a particular treatment. In such cases, the differential diagnosis rests between residual tumour and necrotic tumour and definite diagnosis is confirmed histopathologically[8,9]. Hodgkin's Lymphoma most commonly presents with tumour masses. In the studies conducted by Radford etal[10], it has been observed that in cases of Hodgkin's Lymphoma, residual masses in the mediastinum may not represent residual disease. In the present case, persistent splenomegaly also raised suspicion of residual disease. Therefore splenectomy was done for histological confirmation.

The phenomenon of post chemotherapy Histiocytic Pseudotumour involving the spleen has been reported earlier in patients treated for Diffuse Large B cell Lymphoma[11]. However, our patient was a case of acute lymphoblastic leukemia. Microscopically, the spleen and lymph node did not reveal primary disease and were infiltrated by abundant sheets of foamy macrophages, that were positive for the histiocytic markers, i.e., CD 68 and S100. Similar findings were also observed in earlier studies[1].

To summarize, the purpose of reporting this case is to highlight the fact that suspicious lesions persisting after chemotherapy might not represent residual tumour. In such cases, histiocyte rich pseudotumours should be kept in mind and considered in the differential diagnosis.

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