Isolated Extramedullary Relapse in the Gastrointestinal Mucosa of a Patient with T cell Lymphoblastic Lymphoma

Rajan Yadav, Sonia Parikh**, Harsha Panchal***, Apurva Patel***

Abstract

An unusual case of extramedullary relapse in a known case of T cell lymphoblastic lymphoma is presented here. The patient is a 24-year-old girl diagnosed with T cell lymphoblastic lymphoma in June 2020. The patient showed extramedullary relapse in the gastrointestinal mucosa without bone marrow recurrence whilst on the 6th month of BFM (Berlin Frankfurt Munster) -90 maintenance. Isolated gastrointestinal infiltrate is unusual at presentation or relapse of T cell lymphoblastic lymphoma. While on BFM-90 maintenance, she presented with multiple vomiting and abdominal pain episodes. Upper gastrointestinal scopy revealed multiple gastric ulcers, with morphology and immune-phenotyping identical to her initial T cell lymphoblastic lymphoma. We could not find evidence of leukaemic activity in the blood, cerebrospinal fluid or bone marrow. Several types of leukemic infiltrates have been recognised at post-mortem examination; the fact that makes our case is unique is T cell lymphoblastic lymphoma presenting as an isolated malignant ulcer, which to the best of our knowledge, has not been reported. We conclude that relapsed T cell lymphoblastic lymphoma may present with gastrointestinal infiltration. Further investigations are warranted to establish the same.

Keywords : BFM-90, Isolated gastrointestinal relapse, Lymphoblastic leukaemia/lymphoma

Case Report:

We report an unusual case of T cell lymphoblastic lymphoma, in which the patient showed isolated extramedullary relapse in gastric mucosa. A 24-year-old girl diagnosed with T cell lymphoblastic lymphoma had completed delayed intensification and was on 6th month of maintenance therapy of treatment. She presented with epigastric pain of 1 month's duration.

A year back, she had presented in February 2020 with complaints of breathlessness and high-grade fever of ten days. X-Ray chest PA view showed mediastinum widening, prompting further evaluation. A cardiac evaluation revealed a large pericardial effusion with tamponade required tapping. On CECT (Contrast-enhanced computerised tomography) thorax, a mass 13 cm in maximum dimension was seen in the anterior mediastinum along with pericardial effusion.A CECT guided biopsy and immunohistochemistry were consistent with T cell lymphoblastic lymphoma. As seen in trephine biopsy, bone marrow at baseline was not involved by malignant cells. She was started on German protocol. The mass reduced drastically following phase 1 of induction therapy (Figure 1), there was complete resolution of the pericardial effusion. She completed BFM 90-consolidation and delayed intensification (re-induction), following which she received prophylactic cranial irradiation (18Gy in 10 fractions) and radiation to mediastinal mass (24Gy in 12 fractions). She was started in BFM-90 maintenance treatment. After a disease-free interval (DFI) of 13 months, in August 2021, while she was on the 6th month of maintenance, she presented with severe epigastric discomfort and altered bowel pattern with multiple episodes of incessant vomiting and uncontrolled diarrhoea.

Complete blood counts at that juncture showed no aberrations, and on further screening, both

* Resident,
** Professor and Head of Unit,
*** Professor and Head of Department,
Department of Medical Oncology and Haematology, Gujarat Cancer Research Institute (GCRI), B. J. Medical College, Ahmedabad, Gujarat, India
Correspondence : Dr. Sonia Parikh
E-mail : doctorsoniaparikh@gmail.com

cerebrospinal fluid and bone marrow examination showed no evidence of involvement by leukaemia. Upper gastrointestinal scopy revealed flat crescentic elevated ulcers with central umbilication in the lesser curvature of the gastric body (Figure 2); samples for histopathological examination were taken. Histopathologic and immunohistochemistry study revealed infiltration by high-grade lymphoblastic lymphoma, Tdt– Positive, CD2-Positive,CD3 – Positive & MIB1 - 70 % (High) (Figure 4).Tissue was also negative for CD20,AE1 & CD79a.In pursuit of disease elsewhere, a whole-body-FDG-PET-CT scan was done; it showed gastric and colonic mucosa (Figure 3).

A diagnosis of T cell lymphoblastic lymphoma with isolated relapse in the gastrointestinal (GI) mucosa was thus established.

Fig. 1: CECT post phase 1 induction

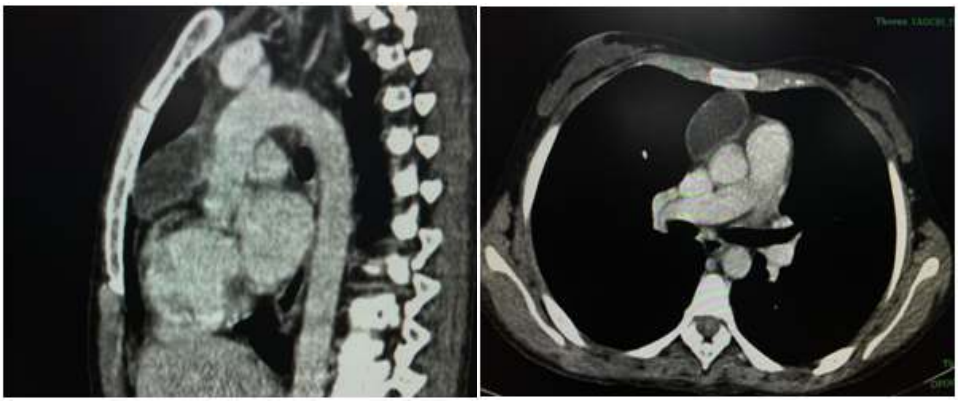


Fig. 2: Upper GI tract Scopy: Crescentic ulcers with central umbilication

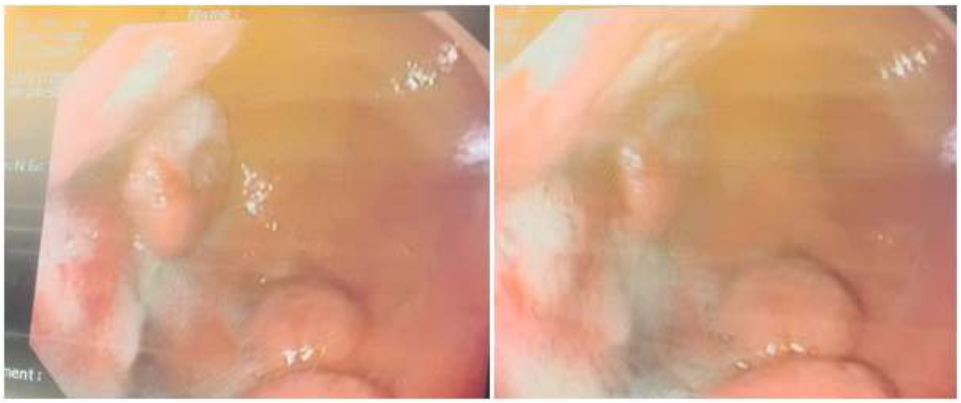
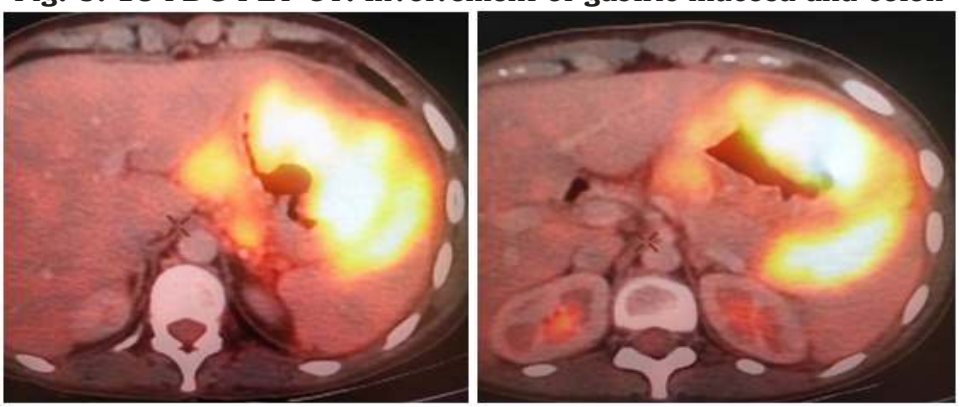


Fig. 3: 18 FDG-PET-CT: Involvement of gastric mucosa and colon



Discussion:

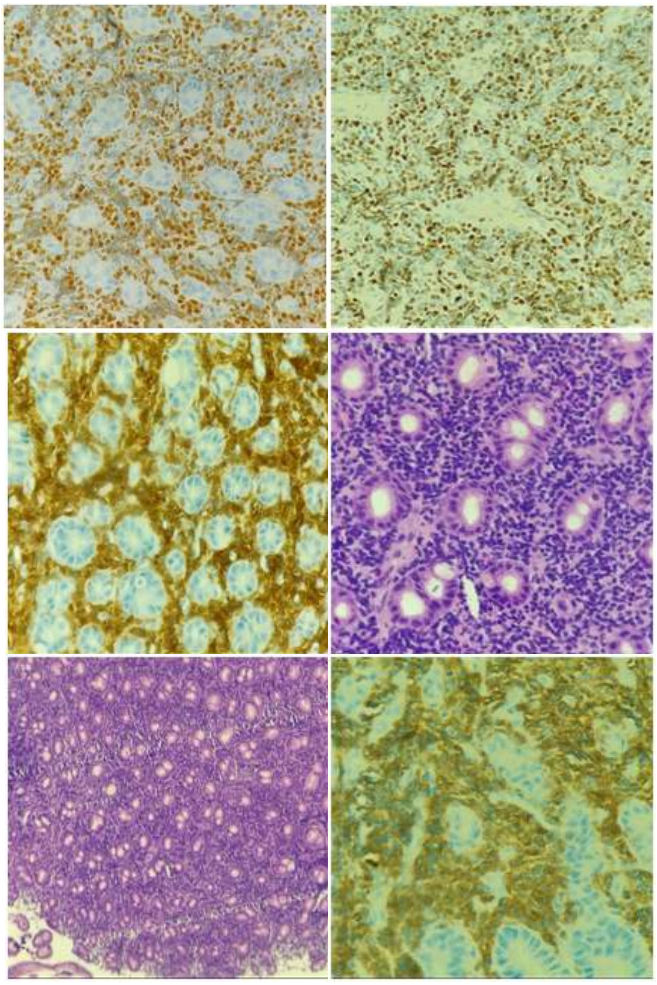
Lymphoblastic leukaemia/lymphoma (LBL) is a subset of non-Hodgkin's lymphoma (NHL) derived from B or T-lymphoid pre-cursors; it is a highly aggressive subtype.[1] As a disease, it constitutes 2%–4% of all adult NHL and is comparable to acute lymphoblastic leukaemia (ALL). In children, it's the second most common subtype of NHL.[2, 3] Due to rapid and path breaking progress in chemotherapy over the years, LBL/ALL is now considered a curable disease. Relapse still occurs in several patients, and it frequently occurs within the first two years or during therapy. The common sites of relapse are bone marrow, lymph nodes, pleural surface and CNS (Central Nervous System). Gastrointestinal (GI) relapse is rare, and isolated gastrointestinal relapse is rarer.[4]

In GI organs, lymphomatous involvement presents particular challenges. In patients on chemotherapy, GI involvement may be obscured because there is a significant overlap of the symptoms with toxicities of therapy (e.g., nausea, vomiting). Diagnostic confusion and delays are common, allowing time for tumour spread. There may be erosion and perforation of organ walls in the GI tract. Resultant bleed and complications related to perforation may at times be fatal; the precipitating cause may remain unexplained.

Small intestine leukemic tumours manifest as an obstruction as they cause concentric luminal narrowing. Whether myeloid or lymphoid, both can erode the layers of the intestinal wall, with the potential for massive blood loss or perforation.[5] Tumour masses may grow as skip lesions along the intestine or involve the entire intestine. The disease has been reported to spread to lymph nodes, mesentery, and even ascites may occur. On radiological investigations, Intestinal leukaemia appearance may be confused with lymphoma. Other differentials are inflammatory bowel disease and necrotising enterocolitis.[6,7]

Distal GI leukemic tumours in the colon and rectum commonly present as ulcers, polyps, and adenoma-like growths; rarely, transmural growth, obstruction, and

Fig. 4: Histopathologic and immunohistochemistry study revealed infiltration by T cell Lymphoma, Tdt– Positive, CD2-Positive, CD3 – Positive, CD20 – Negative&MIB1 - 70 % (High)



even perforation may occur. Reports of Isolated gastric relapse in LBL/ALL are few and far between; most of them are reported post-transplant or several years after completion of treatment. To the best of our knowledge, this is the first kind in which an LBL/ALL patient has been diagnosed with isolated GI tract relapse whilst on treatment.[8] The manifestations of GI involvement leukaemia are nonspecific, and many of the symptoms can be attributed to drug toxicity.[9,10] Afflicted patients have complained of abdominal pain, nausea, and diarrhoea in the past.

Conclusion:

Lymphoblastic lymphoma cases can present intractable GI symptoms either when on treatment or after completion. Although rare, in such instances, involvement of the GI tract needs to be ruled out. These relapses, if identified, are amenable to treatment with a good response.

References:

1. Onciu M. Acute lymphoblastic leukaemia. Hematology/Oncology Clinics of North America. 2009; 23(4):655–674.
2. Thomas DA, O'Brien S, Cortes J, et al. Outcome with the hyper-CVAD regimens in lymphoblastic lymphoma. Blood. 2004; 104(6):1624–1630.
3. Rizzardi C, Valsecchi MG, Arico M, et al. Outcome of very late relapse in children with acute lymphoblastic leukemia. Haematologica. 2004;89(4):427–434.
4. Paul S. Gaynon M.D., Roger P. Qu Ph.D., et al Survival after relapse in childhood acute lymphoblastic leukemia Impact of site and time to first relapse-the Children's Cancer Group experience ; Cancer Volume 82, Issue7 1 April 1998 Pages 1387-1395.
5. Koh FH, Chan H-L, Petersson F, et al. Thinking out of the gut: a case of obscure lower GI bleeding. Gut. 2017; 66:2068-2159.
6. Isabel Cunningham, Daniel Worthley Leukemia in gastrointestinal organs as cause of treatment failure: 378 cases analyzed; Am J Hematol. 2018; 93:1327–1336.
7. Beck TM, Day JC, Smith CE, Eddy HE. Granulocytic sarcoma treated as an acute leukemia. Report of a case. Cancer. 1984;53:1764-1766.
8. Karthik SV, Aw M, Lin TP. Extra-medullary gastric and hepatic relapse of acute lymphoblastic leukaemia in an adolescent: an unusual presentation. Dig Liver Dis. 2015; 47:e19.
9. Weisdorf D, Arthur D, Rank J, Blazar B, Gajl-Peczalska K, Snover D. Gastric recurrence of acute lymphoblastic leukaemia mimicking graft-versus-host disease. Br J Haematol 71: 559-561, 1989.
10. Kletzel M, Meitar D, El-Youssef M, Cohn SL. Gastrointestinal relapse of leukemia, mimicking acute graft vs host disease, following a stem cell transplant. Med Pediatr Oncol 34: 287-289, 2000.