**TITLE OF CASE**

**A series of atypical clinical presentations of Plasmablastic lymphoma involving gastrointestinal**

**tract in immunocompromised patients.**

**RUNNING TITLE**

Plasmablastic lymphoma of GIT.

**AUTHORS DETAILS**

**Sarbjit Mohapatra(1); Badareesh Lakshminarayana(2,\*); 3. Vidya Monappa 4. Chethana Babu Udupa**

1. Resident 2. Associate Professor & Unit Head 3 & 4. Associate Professor

 1 & 2. Department of General Surgery, Kastuba Medical College, Manipal, Karnataka- 576104.

 3 & 4. Department of Pathology, Kastuba Medical College, Manipal, Karnataka- 576104

**\* Corresponding author**

Badareesh Lakshminarayana

Associate Professor & Unit Head

Department of General Surgery, Kasturba Medical College, Manipal, Karnataka. India- 576104 Telephone Number- +91 9844774035.

Email id- drbadareesh.l@gmail.com

**ABSTRACT:**

Plasmablastic lymphoma, a subtype of diffuse, large B-cell lymphoma, is rare but aggressive malignancy commonly associated with immunocompromised individuals. In our case series, we present three patients presenting with atypical presentation involving lower gastrointestinal tract. Two male patients were diagnosed to have HIV while the other female patient was suffering from Hepatitis B. One patient had features of perianal abscess while other two presented with acute intestinal obstruction who were operated. These patients were started on EPOCH regimen. First patient had rapid progession of disease and died within 2months of diagnois while other two patients are on follow up following chemotherapy. Plasmablastic lymphoma have a poor prognosis and due to low reported cases, clincopathogenesis and treatment has not been clearely defined. To contribute to further understanding of this rare entity we have discussed the varied presentation in our patients.

**KEY WORDS:**

Plasmablastic lymphoma, gastrointestinal tract, B-cell lympoma

**INTRODUCTION:**

Plasmablastic lymphoma (PBL) is a subtype of diffuse, large, B-cell lymphoma with morphologic and immunophenotypic characteristics overlapping with B-cell lymphoma and plasma cell neoplasm. It is highly aggressive and possesses a diagnostic difficulty cause of rarity and lack of expression of markers[1].Although the spectrum of disease is increasing with more reporting of cases, but still, there has no clear etiopathogenesis of plasmablastic lymphoma. Since PBL is very rare with a high mortality rate, there are no established guidelines on the chemotherapy regimen[2].

**CASE PRESENTATION:**

Here we describe 3 cases of unusual presentation of PBL found in the GI tract of patients who presented to our institution for evaluation and treatment.

CASE REPORT 1

A 51years old male, a diagnosed case of HIV positive on treatment, presented with bleeding per rectum associated with constipation and pain in the perianal region. He denied any episodes of fever but gives a history of weight loss over the last two months. On digital examination, a bulge was palpable at the right lateral wall of the rectum, no active bleed and no signs of hemorrhoides. The laboratory investigations indicated anaemia with low leukocyte count. MR pelvis reported a large exophytic lesion arising from the right lateral wall with involving anorectal junction and lower portion of the rectum. In colonoscopy, a 3cm growth visualized at the verge of the anal canal from which tissue sent for biopsy. The immunohistopathology study confirmed the diagnosis of plasmablastic lymphoma. Nuclear molecular imaging revealed active disease in the large soft tissue lesion involving anorectal region with local extension. Bone marrow aspirate and bone marrow biopsy reports were normal.. He was started on EPOCH regimen. After a month of chemotherapy, cycle patient developed invasive aspergillosis and progressed to death.

CASE REPORT 2

A 38years old male, diagnosed HIV positive not on treatment came with pain in the right lower abdomen and constipation for three days. He had no episodes of vomiting and fever. Per abdomen examination was soft, distended with tenderness and a mass palpable in the right iliac fossa. Routine blood investigation was within the normal range. A contrast study was suggestive of appendicular mass formation producing partial distal ileal obstruction along with mesenteric and omental lymphadenopathy. He was taken up for surgery and intraoperatively, a nodular growth present at the ileocaecal junction with multiple enlarged lymph nodes along SMA. Also, tumour deposits were seen over the gall bladder. Hence an extended right hemicolectomy with cholecystectomy was done. Immunohistochemistry study confirmed the diagnosis of plasmablastic lymphoma. On postoperative follow-up, the patient’s general condition improved, but due to noncompliance to treatment, chemotherapy could not be started.

CASE REPORT 3

A 51years old female presented with vomiting and constipation for 2 days. She was operated in an outside hospital a year back for retroperitoneal mass. On examination minimal diffuse tenderness present in the abdomen and hyperperistaltic bowel sounds were heard. Contrast imaging was suggestive of ileo-ileal intussusception causing obstruction. She was diagnosed to have hepatitis B. She underwent emergency laparotomy and ileal segment resection anastomosis was done. Histopathological study revealed features of plasmablastic lymphoma. Post operatively her general condition improved and was started on chemotherapy on follow up.

**DISCUSSION:**

Plasmablastic lymphoma defined by the WHO as a ‘‘diffuse proliferation of large cells, the majority of which resemble B-cells, but have a plasmacytic immunophenotype’’[3].

Morscio et al. in 2014 have compared the clinicopathological findings of 302 cases of plasmablastic lymphoma[4]. In the reported series, PBL patients were predominantly male (77%) with a median age at diagnosis of 46 years. Extranodal presentation was most frequent (88%, of which 35% were oral, 18% gastrointestinal, 12% cutaneous). Gastrointestinal involvement being less common we take this opportunity to discuss three such cases with different presentations. Two of them were male and mean age of series was 46, which is similar to the earlier reported study. While both the males were diagnosed to have HIV, the female was suffering from Hepatitis B. It might be suggestive that age-related immunosenescence could be the cause of PBL among other immunocompromised patient.

The classical B symptoms associated with lymphoma are fever, weight loss and night sweats are not reported in gastrointestinal plasmablastic lymphoma. In the first report involving ano-rectal junction, patient presented with features typically suggestive of perianal abscess or hemorrhoides. While the other two cases came to hospital in obstruction and underwent surgery.

PBL possess an unique immunophenotypic profile and a high proliferation index. The diagnostic dilemma associated with plasmablastic lymphoma is its extensive differential diagnosis, which can be differentiated based on cell morphology and immunohistochemistry markers. A diffuse strong EBV positivity in the clinical setting of HIV infection, and lack of monoclonal paraproteinemia favour a diagnosis of plasmablastic lymphoma. DLBCL shows a weak expression of CD20 while DLBCL-NOS exhibits positivity for CD45 and CD20, while ALK-positive DLBCL expresses CD30 and ALK-1. Primary effusion lymphoma is positive for HHV-8 in almost all cases. Large cell lymphoma arising HHV8 MCD is a rare node-based disease and shows characteristic morphology. A clinical correlation is essential to differentiate cases of multiple myeloma and PBL as they display identical immunophenotype[5].

The prognosis is usually very poor, and reported survival is less than a year. However, EPOCH is regarded as the first line of treatment in HIV related PBL[6]. Some authors have described a better prognosis in HIV positive patients with PBL as compared to HIV negative patients with PBL. In HIV patient’s HAART administration and immunosurveillance, restoration correlates with better survival[7]. Although one patient had undergone retroperitoneal mass excision, a recurrence of disease due to inadequate treatment can be considered.

We would conclude that the patients with non specific lower gastrointestinal symptoms and with low CD4 counts or in immunocompromised state an early attempt should be made to rule out plasmablastic lymphoma.

These case reports are a contribution to the number of cases of gastrointestinal PBL to understand the nature of disease and facilitate the study on the biological behaviour of the disease and validate guidelines on management.

**REFERENCES**

1. Swerdlow, S.H., International Agency for Research on Cancer. & World Health Organization. WHO classification of tumours of haematopoietic and lymphoid tissues, Edn. Revised 4th. (International Agency for Research on Cancer, Lyon, France; 2017).

2. Castillo JJ, Bibas M, Miranda RN. The biology and treatment of plasmablastic lymphoma Blood. 2015 Apr 9;125(15):2323-30.

3. Vega F, Chang CC, Medeiros LJ, Udden MM, Cho-Vega JH, Lau CC, et al. Plasmablastic lymphomas and plasmablastic plasma cell myelomas have nearly identical immunophenotypic profiles. Mod Pathol. 2005; Jun;18(6):806-15.

4. Morscio J, Dierickx D, Nijs J, Verhoef G, Bittoun E, Vanoeteren X, et al. Clinicopathologic comparison of plasmablastic lymphoma in HIV-positive, immunocompetent, and posttransplant patients: Single-center series of 25 cases and meta-analysis of 277 reported cases. Am J Surg Pathol. 2014; Jul;38(7):875-86.

5. Ahn JS, Okal R, Vos JA, Smolkin M, Kanate AS, Rosado FG. Plasmablastic lymphoma versus plasmablastic myeloma: An ongoing diagnostic dilemma. J Clin Pathol. 2017; Sep;70(9):775-780.

6. Zuze T, Painschab MS, Seguin R, Kudowa E, Kaimila B, Kasonkanji E, et al. Plasmablastic lymphoma in Malawi. Infect Agent Cancer. 2018; Jun 28;13:22.

7. Guan B, Zhang X, Ma H, Zhou H, Zhou X. A meta-analysis of highly active anti-retroviral therapy for treatment of plasmablastic lymphoma. Hematol Oncol Stem Cell Ther.; 3(1):7-12 · March 2010

**LEGENDS FOR FIGURES:**

1. MRI pelvis showing large exophytic heterogeneously enhancing involving anal canal and anorectal junction which is isointense on T1 and hyperintense on T2 with few foci of blooming on FFE

1A. T2 Axial, 1B. T2 Saggital, 1C. T1 Axial post contrast

1. Nuclear Imaging scan : Increased uptake in the large soft tissue lesion involving anorectum and involving bilateral mesorectal fascia.
2. Right extended hemicolectomy specimen shows circumferential nodular growth at ileo caecal region.
3. Immunohistopathology slides:

4A: Section shows sheets of plasmablasts with increased mitosis; H&E, 200X, 4B: CD138 positive ; 200X, 4C: MUM1 diffuse positive; 200X, 4D: Ki67 high; 400X

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_