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Case Report

Plasmablastic lymphoma of the colon in HIV negative patient; a case report with literature review

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ABSTRACT

Introduction: Plasmablastic lymphoma (PBL) is a rare and aggressive variant of diffuse large B cell lymphoma characterized by weak or absent expression of conventional B cell markers and strong expression of plasma cell markers. Very few cases of PBL of the colon have been reported in HIV negative patients.

Case presentation: A 57 years female with HIV negative serology, a known case of hypertension under medication presented with right lower abdominal pain associated with vomiting and significant weight loss. On abdominal examination, soft, tender, and globular lump was palpable. Contrast enhanced computed tomography of abdomen and pelvis revealed asymmetrical enhancing mass like wall thickening involving ileocaecal region, caecum, and ascending colon, which on colonoscopy was found to be ulceroproliferative in nature. Open right hemicolectomy was performed and postoperative histopathology and immunohistochemistry results confirmed plasmablastic lymphoma as the final diagnosis. She was treated with nine cycles of chemotherapy.

Clinical discussion: Although PBL is commonly found in the oral cavity, and HIV positive patients, it can rarely occur in extra-oral sites, and HIV negative patients. Due to its rarity, no optimal therapeutic approach has yet been defined for the treatment of PBL. It has a poor prognosis, and the overall survival rate has been correlated with international prognostic index score and achievement of complete remission.

Conclusion: As plasmablastic lymphoma is rare and highly aggressive, its delayed diagnosis will lead to poor outcome. Thus, awareness about its clinical presentation, histopathological features, and immunophenotype is essential.

1. Introduction

Plasmablastic lymphoma (PBL) is a rare and aggressive variant of diffuse large B cell lymphoma (DLBCL) with characteristic plasmacytic differentiation [1]. It was initially described by Delecluse et al., in 1997 in 16 cases as a distinct entity, exclusively found in the oral cavity, strongly associated with Human immunodeficiency virus (HIV), and characterized by weak or absent expression of conventional B cell markers and strong expression of plasma cell markers [2]. In the last ten years, an increasing number of cases have been found in extra-oral sites (gastrointestinal tract, lymph nodes, skin, bone, and other regions), in HIV negative patients immunocompromised by other conditions such as post-transplantation as well as in immune-competent patients [3].

Very few cases of PBL of the colon have been reported in HIV negative patients [4–9]. We describe a case of PBL of the caecum and ascending colon in an HIV negative patient along with the review of literature of rare cases of HIV negative PBL of the colon. This case has been reported in line with the SCARE 2020 criteria and includes a brief literature review [10].

2. Case presentation

A 57 years old female, a known case of hypertension for two years under medication with no relevant family and personal history presented to our hospital outpatient department with progressive right lower abdominal pain for three months. It was associated with vomiting and significant weight loss. There was no history of per rectal bleeding, hematemesis or melena, burning micturition, and vaginal bleeding. She

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had no history of diabetes, organ transplantation, intake of immunosuppressive therapy, or any past surgical interventions.

On abdominal examination, soft, tender, globular lump of size 10 cm × 10 cm, free from the skin was palpable in the right lower quadrant. Digital rectal examination revealed no impacted stool or any palpable mass. Rest of the systemic examination was normal. Laboratory investigations including complete blood count, electrolytes, serum calcium, liver function test, renal function test, and lactate dehydrogenase were within the normal range at the time of initial presentation. Serum protein electrophoresis showed no monoclonal protein and was normal. Abdominal ultrasonography (USG) revealed circumferential mass like hypoechoic wall thickening of the terminal ileum, ileocaecal junction, and proximal ascending colon. Contrast enhanced computed tomography (CECT) of abdomen and pelvis revealed asymmetrical enhancing mass like wall thickening involving ileocaecal region, caecum and proximal part of ascending colon with multiple pericolic lymph nodes. With these findings, carcinoma of colon, ileocaecal tuberculosis, and gastrointestinal lymphoma were kept as differential diagnoses. For further confirmation, colonoscopy was done. Easily bleeding friable ulceroproliferative lesion was noted on colonoscopy and biopsy could not done for histopathological examination (Fig. 1).

With the view of most likely diagnosis of carcinoma of the colon, after preoperative optimization, open right hemicolectomy was performed. The intraoperative findings revealed a large 10 cm × 8 cm mass involving caecum to ascending colon with large multiple paracolic lymph nodes and no liver or peritoneal metastases. The postoperative period was uneventful.

Microscopic examination of the specimen revealed diffuse proliferation of atypical lymphoid cells infiltrating up to the serosa. Individual cells were large, with high nucleocytoplasmic ratio, round nuclei, regular nuclear membrane, coarse to hyperchromatic chromatin, inconspicuous to prominent nucleoli, and a moderate amount of pale eosinophilic cytoplasm. Most of these cells had eccentrically placed nuclei with a plasmacytoid appearance. Multinucleated and binucleated tumor cells were present along with frequent atypical mitotic figures (Fig. 2). On immunohistochemistry, the tumor cells were positive for CD 138, CD 10, EMA, MUM 1, and CD45 (weak), and negative for CD 20, CD79a, CD30, and PAX 5, with a ki-67 score of 80–90% (Fig. 3). Based on these features, plasmablastic lymphoma was confirmed.

Our patient was treated with six cycles of EPOCH (etoposide 200 mg/m^2, prednisolone 600 mg/m^2, vincristine 1.6 mg/m^2, cyclophosphamide 750 mg/m^2, and doxorubicin 40 mg/m^2 in each cycle, repeated at the interval of 21 days) with intrathecal methotrexate 3 mg/cycle from cycle 3 to cycle 6, however relapse occurred, and she was planned for hematopoietic stem cell transplantation. Due to financial constraints, she denied it, and then was given two cycles of ICE (ifosfamide 1500 mg/m^2 infused over 2 hours daily on day 1–3, carboplatin AUC 5 i.v. on day 1, and etoposide 100 mg/m^2 i.v. daily on days 1–3 in each cycle, repeated at the interval of 21 days) regimen. Along with this regimen, the patient also received inj. pegfilgastrim 6 mg sc stat on day 5 as a primary prophylaxis to prevent chemotherapy induced neutropenia. The patient developed pancytopenia, and subsequently single agent ifosfamide was given on third cycle. She is alive at 13 months of diagnosis with resolution of the obstructive symptoms of the tumor and normal blood parameters.

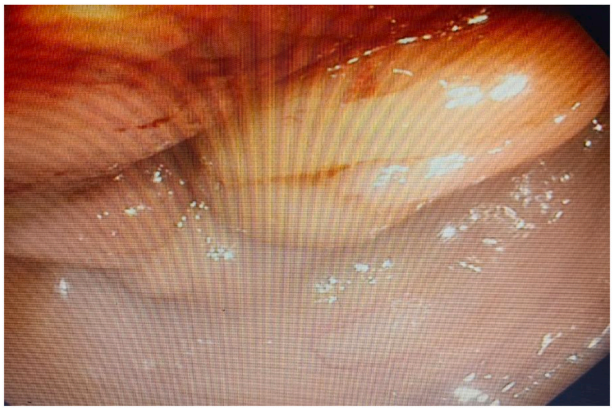

Fig. 1. Colonoscopy: Ulceroproliferative lesion in ascending colon.

3. Discussion

Plasmablastic lymphoma was identified as a distinct entity in 1997 in the study done in 16 cases. In all of these cases, the lesion was confined to the oral cavity. 15 out of 16 cases were HIV positive [2]. However, PBL is equally prevalent in HIV negative patients who are often post-transplant recipients. In HIV negative/non transplanted patients, older age and past medical history of autoimmune or chronic systemic diseases are the contributing factors. Extranodal site is much more common compared to nodal sites, and in extranodal presentation, the most common site is the mouth followed by the gastrointestinal tract, skin, nose, and pharynx [11,12].

PBL cells show characteristic immunophenotype showing positivity for plasma cell markers (CD38, CD138, MUM1, Blimp1), variable expression for CD45, CD79a, EMA, and CD30, and weak/absent expression of B cell markers (CD20 and PAX5) [13]. CD138 and MUM1 are found to be positive in 88% and 96%of the cases respectively with 10% of the cases showing weak positivity for CD20 [12]. In HIV negative patients with PBL, the expression of Ki67 is universally high which indicates their aggressive behavior [14]. Ki67 score is 80–90% in our case, thus indicating aggressiveness of the disease.

Gastrointestinal PBL is twice as common in males compared to females, and almost all female patients are HIV negative as in our case. In HIV negative patients, the most common site of gastrointestinal PBL is the stomach followed by the small bowel and colon [15]. To the best of our knowledge, only eight cases of colon PBL have been reported in HIV negative patients before. The demographic and clinical characteristics of these patients and our case are compared in Table 1. Immunophenotypic variation and Epstein Barr Virus (EBV) data of these cases are compared in Table 2.

The most challenging differential diagnoses of PBL are plasmablastic plasma cell myeloma, primary effusion lymphoma, and ALK positive large B cell lymphoma as their morphologic and immunophenotypical features closely resemble that of PBL. The features that favor a diagnosis of PBL are the presence of a high ki-67 score, frequent EBV positivity in neoplastic cells and association with human herpes virus 8, and absence of renal dysfunction, significant paraprotein, osteolytic lesions, hypercalcemia, bone marrow involvement, and ALK in neoplastic cells in IHC [16]. Normal renal function test, serum calcium level, and serum protein electrophoresis with no bone marrow involvement, and typical histopathology, as well as immunophenotype of our case, confirmed the diagnosis of PBL.

No optimal therapeutic approach has yet been identified for the treatment of PBL. Different chemotherapy regimens for its treatment are CHOP and more intensive regimens such as infusional EPOCH, hyper-CVAD, and CODOX-M/IVAC. CHOP is the most commonly used regimen [3]. Although more intensive regimens are recommended over CHOP [17], they have not shown significant benefit in overall survival [12]. Bortezomib-based regimen CyBorD (bortezomib, cyclophosphamide orally and dexamethasone orally) and lenalidomide-based regimen (lenalidomide and dexamethasone) have also been used for refractory cases [18].

In patients treated with chemotherapy, low or low intermediate International Prognostic Index (IPI) score, absence of bone marrow involvement, absence of CD30 expression, and HIV positive status are associated with the achievement of complete response (CR). The overall survival rate has been correlated with IPI score and achievement of CR [12].

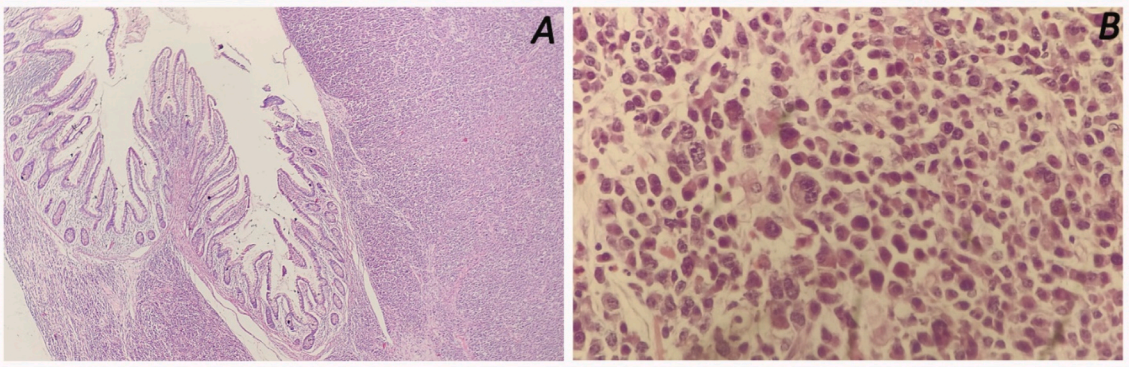

Fig. 2. Photomicrograph A: Low power image shows replacement of submucosa of colon by diffuse proliferation of cells with plasmacytic differentiation (40X, H and E). **Photomicrograph B:** High power image shows diffuse and cohesive proliferation of cells with plasmacytic differentiation. Many of the tumor cells are large, with round nuclei, and variably prominent nucleoli and coarse chromatin. Binucleated forms are also seen. Smaller cells with plasmacytic differentiation are also present (400X, H and E).

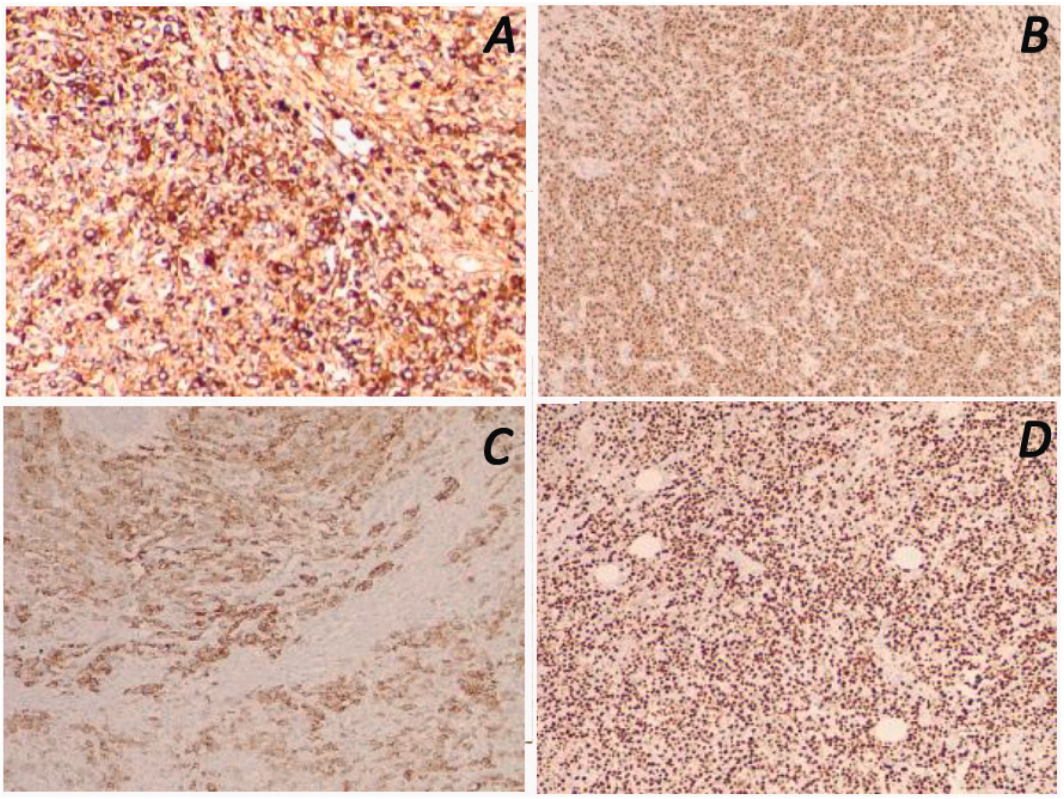

Fig. 3. Immunohistochemistry: Plasmablastic lymphoma cells are strongly positive for CD138 (**A**), MUM 1 (**B**), and EMA (**C**). Ki-67 is positive for 80–90% of cells (**D**).

Early diagnosis of PBL was done in our patient after postoperative histopathological examination and comprehensive immunophenotyping, thereby leading to early administration of chemotherapy which is the strength of our case. Most of the cases of PBL (70%) are associated with EBV infection which has prognostic importance [19]. As it is very expensive considering the economic background of our patient, the test for detecting EBV encoded RNA was not done which is the limitation of our case.

Plasmablastic lymphoma is to be considered as a differential diagnosis when a patient presents with features of bowel obstruction to avoid unnecessary surgery, post-surgical morbidity, and delay in standard treatment. Dose adjusted EPOCH with low toxicity and easier to infuse compared to the standard CODOX-M/IVAC regimen might be a reasonable option to consider in resource limited setting. Single agent ifosfamide as our patient is receiving, and tolerating well might be a reasonable option as a palliative treatment modality.

4. Conclusion

Given the rarity of plasmablastic lymphoma of the colon, a high index of suspicion is required for its diagnosis. As it is very aggressive with a dismal prognosis, the delayed diagnosis will lead to poor outcome. Therefore, awareness among clinicians, surgeons, and pathologists about the occurrence of PBL even in immunocompetent patients, and its clinical presentation, histopathological features and immunophenotype are essential for early identification, diagnosis and

Table 1
Literature review and case study summary of demographic, clinical presentation, treatment and outcome of plasmablastic lymphoma of colon in HIV negative patients.

S. N.	Study	Age	Sex	Primary site	Symptoms/sign	Chemotherapy	Outcome
1	Mansoor et al.	77	F	Ascending colon and caecum	Abdominal pain Vomiting Abdominal mass	High dose steroids (too unwell to give chemotherapy)	Died at 3 weeks of diagnosis
2	Hatanaka et al.	75	M	Caecum	Abdominal pain Fever	NR	NR
3	Teruya- Feldstein et al.	56	M	Sigmoid colon	NR	CODOX-M/IVAC	Died at 3 months
4	Teruya- Feldstein et al.	29	M	Colon	NR	COPP/BLAM x 2 cycles CHOP x 4 cycles	Alive at 15 months
5	Haramura et al.	86	F	Sigmoid Colon	Bloody stool	Refused by patient	Died at 2 months after surgery
6	Luria et al.	65	M	Terminal ileum and caecum	Acute bowel obstruction	Hyper-CVAD + Rituximab	Died at 25 months of diagnosis
7	Komaranchath et al.	13	M	Ileocaecal junction	Right iliac fossa pain and distension	Auto HSCT Not given (Supportive care)	Died at 2 weeks of presentation
8	Komaranchath et al.	45	F	Ascending colon	Abdominal pain	CHOP-R	Died within 6 months of diagnosis
9	Our case	57	F	Caecum Ascending colon	Abdominal pain Vomiting Weight loss	EPOCH x 6 cycles ICE x 2 cycles	Alive at 13 months of diagnosis

M: Male; F: Female; NR: Not reported; CHOP: Cyclophosphamide, hydroxydaunorubicin, oncovin, prednisone; CHOP-R: Cyclophosphamide, doxorubicin, vincristine, prednisone-rituximab; EPOCH: Etoposide, vincristine, doxorubicin, cyclophosphamide, and prednisone; Hyper- CVAD: Fractionated cyclophosphamide, vincristine, doxorubicin and dexamethasone; ICE: Ifosfamide, carboplatin and etoposide, CODOX-M/IVAC: Cyclophosphamide, doxorubicin, vincristine and methotrexate alternating with ifosfamide, etoposide and cytarabine; COPP/BLAM: cyclophosphamide, vincristine, procarbazine, prednisone, bleomycin, adriamycin; HSCT: Hematopoietic stem cell transplantation.

Table 2
Literature review and case study summary of immunophenotypic variation and Epstein Barr Virus (EBV) data of plasmablastic lymphoma of colon in HIV negative patients.

S.N.	Study	CD45	CD20	CD79a	PAX5	CD90	CD138	MUM-1	Ki67	EBV
1	Mansoor et al.	+(w)	–	+(w)	NR	NR	+	NR	90%	NR
2	Hatanaka et al.	–	–	–	NR	–	+	NR	90%	–
3	Teruya- Feldstein et al.	–	–	–	NR	NR	+	NR	NR 90%	–
4	Teruya- Feldstein et al.	+/-	–	–	NR	NR	+	NR	75–90%	+
5	Haramura et al.	–	–	–	NR	NR	+	NR	NR	+
6	Luria et al.	NR	–	+	–	NR	+	NR	100%	NR
7	Komaranchath et al.	+	–	–	NR	–	+	+	95%	NR
8	Komaranchath et al.	–	+	–	NR	–	+	+	90%	NR
9	Our case	+(w)	–	–	–	NR	+	+	80–90%	NR

NR: Not Reported; +: Positive; -: Negative; (w): Weak; EBV: Epstein Barr Virus.

treatment of the disease.

Sources of funding

Since we are medical students under supervision, we don't have any financial support for our research.

Ethical approval

Ethical approval is not required for case report.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of written consent is available for review by the editor-in-chief of this journal on request. We also ensure, none of the identifying characteristics are included in the case report.

Author contribution

Ved Prakash Pant: literature review, follow-up the patient, writing the manuscript, and final approval of the manuscript. Nishanta Dallakoti: literature review, follow-up the patient, writing the manuscript, and final approval of the manuscript. Priyanka KC: literature review, data collection, and final approval of the manuscript. Akshat Mishra: literature review, data collection, and final approval of the manuscript. Sandip Pokharel: literature review, and writing the manuscript. Purbesh Adhikari: pathologist, data collection, and final approval of the manuscript. Soniya Dulal: treating medical oncologist, follow-up the patient, and final approval of the manuscript.

Provenance and peer review

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Author contribution

Ved Prakash Pant, Nishanta Dallakoti: literature review, follow-up the patient, writing the manuscript, and final approval of the manuscript. Priyanka Kc, Akshat Mishra: literature review, data collection, and final approval of the manuscript. Sandip Pokharel: literature review, and writing the manuscript. Purbesh Adhikari: pathologist, data collection, and final approval of the manuscript. Soniya Dulal: treating medical oncologist, follow-up the patient, and final approval of the manuscript.

Registration of research studies

Not applicable.

Guarantor

Ved Prakash Pant.

Declaration of competing interest

There are no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103750.

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