Accepted manuscripts are the articles in press that have been peer reviewed and accepted for publication by the Editorial Board of the Vojnosanitetski Pregled. They have not yet been copy edited and/or formatted in the publication house style, and the text could still be changed before final publication.

Although accepted manuscripts do not yet have all bibliographic details available, they can already be cited using the year of online publication and the DOI, as follows: article title, the author(s), publication (year), the DOI.

Please cite this article: PLASMABLASTIC LYMPHOMA AS A RARE CAUSE OF SUBOCCLUSIVE EVENTS - CASE REPORT AND REVIEW OF THE LITERATURE

ПЛАЗМАБЛАСТНИ ЛИМФОМ КАО РЕДАК УЗРОК СУБОКЛУЗИВНИХ СМЕТЊИ - ПРИКАЗ СЛУЧАЈА И ПРЕГЛЕД ЛИТЕРАТУРЕ

Authors: Snezana Lukic *,†, Sanja Dragasevic †, Sanja Zgradic †, Milena Todorovic *‡, Srdjan Djuranovic *‡, Bosko Andjelic *‡, Dragan Popovic *‡;
Vojnosanitetski pregled (2018); Online First February, 2018.

UDC:

DOI: https://doi.org/10.2298/VSP171025024L

When the final article is assigned to volumes/issues of the Journal, the Article in Press version will be removed and the final version appear in the associated published volumes/issues of the Journal. The date the article was made available online first will be carried over.
PLASMABLASTIC LYMPHOMA AS A RARE CAUSE OF SUBOCCLUSIVE EVENTS - CASE REPORT AND REVIEW OF THE LITERATURE

Плазмабластни лимфом као редак узрок субоклузивних сметњи - приказ случаја и преглед литературе

Snezana Lukic*†, Sanja Dragasevic†, Sanja Zgradic†, Milena Todorovic*‡, Srdjan Djuranovic*†, Bosko Andjelic*‡, Dragan Popovic*†

* Faculty of Medicine, University of Belgrade, Belgrade, Serbia
† Clinic for Gastroenterology and Hepatology, Clinical Center of Serbia, Belgrade, Serbia
‡ Clinic for Hematology, Clinical Center of Serbia, Belgrade, Serbia

Acknowledgments This work was supported by Ministry of Education, Science and Technological Development, Republic of Serbia (Grant No III41004).

Correspondence to: Snezana Lukic, MD, PhD, Clinic for Gastroenterology and Hepatology, Clinical Center of Serbia, Faculty of Medicine, the University of Belgrade, Koste Todorovica 2, Belgrade 11000, Serbia. lukic.snezana@gmail.com. Telephone: +381-11-3663734 Fax: +381-11-3615432
ABSTRACT

Introduction: The most common causes of subocclusive disorders are adhesion, Crohn's disease and small bowel neoplasms. Plasmablastic lymphoma (PBL) is an aggressive distinct subtype of diffuse large B-cell non–Hodgkin lymphoma initially reported in the oral cavity of HIV infected individuals.

Case report: We present a male patient with PBL of the small intestine as a rare cause of intestinal subocclusion, without HIV infection and negative serology for hepatitis C, hepatitis B, and Epstein-Barr infection. The patient underwent an ileo-colonoscopic examination with accompanying biopsy specimens. The results, based on the pathohistological and immunohistochemical pattern, confirmed a diagnosis of PBL. Following chemotherapy treatment, our patient underwent the resection of ileum. The postoperative pathohistological report confirmed PBL as the final diagnosis. Patient was treated with chemotherapy according to the CHOP protocol (cyclophosphamide, doxorubicin, vincristine, and prednisolone).

Conclusion: PBL of the small intestine is a rare and unusual cause of subocclusive events. In our patient, the crucial importance for further treatment was an accurate pathohistological verification of the detected changes in the ileum.

Key words: Plasmablastic lymphoma; Intestinal subocclusion; Crohn's disease.

АБСТРАКТ

Увод: Плазмабластни лимфом (ПБЛ) је тип агресивног дифузног крупноћелијског Б нон-Хочкин лимфома, који је први пут описан у усној дупљи код ХИВ позитивних пацијената.

Приказ случаја: У раду је приказан пацјент мужког пола са ПБЛ танког црева као ретком узроком субоклузије, без ХИВ инфекције и са негативном серологијом за хепатитис Б, хепатитис Ц и инфекцију Епштајн Баровим вирусом. Пацјенту је урађена колоноскопија са терминалном илеоскопијом, при којој су узете биопсије слузнице терминалног илеума. Резултати патохистолошког и имунохистохемијског испитивања су потврдили дијагнозу ПБЛ. После хемио терапије, пацјенту је урађена ресекција илеума. Резултат постоперативне
INTRODUCTION

Small bowel obstruction is a major cause of morbidity in hospitals around the world. The etiology of small bowel obstruction includes adhesions (74%), Crohn's disease (7%), neoplasia (5%), hernia (2%), radiation (1%), and miscellaneous (11%) [1]. Plasmablastic lymphoma (PBL), a rare subtype of diffuse large B cell lymphoma, usually occurs in patients with HIV infection and is primarily found in the oral cavity [1-4]. There are also reported cases of PBL in immunocompetent individuals involving the cervical lymph nodes, stomach, lungs, cavity, small and large bowel, and liver [5-13, 14, 15]. This rare lymphoproliferative disorder is characterized by its plasmablastic morphology and immunohistochemical panel.

In this case report, we have a patient with symptoms of subocclusion and suspected Crohn's disease of the terminal ileum on endoscopy examination. Since the pathohistological findings of the terminal ileum biopsy did not confirm Crohn's disease, an immunohistochemical examination was required. Upon immunohistochemical analysis, PBL was diagnosed, isolated locally on the terminal ileum. Our patient had negative serology tests for HIV, Epstein-Barr virus, hepatitis B and hepatitis C and did not received immunosuppressive therapy or suffered from any chronic disease.

CASE REPORT

A 73-year-old male was admitted to our center with a one-year history of abdominal pain, weight loss, reported non-bloody diarrhea (six times a day), night sweating, and pruritus. His medical history revealed a laparoscopic cholecystectomy in 2012, sinus arrhythmia, hypertension, and benign prostatic hyperplasia. There was no family history of malignancies. The patient was an ex-smoker and had no recent consumption of beverages or drugs.
Six months prior to the admission to our center, patient had been examined in a regional hospital. However, the results of the previous examinations were unmarkable, except the finding on the radiographic examination of the small intestine which raised suspicion of Crohn's disease of the terminal ileum.

Upon the admission in our center, a general physical examination revealed an abdominal tenderness in the lower abdomen, with no palpable lymphadenopathy or hepatosplenomegaly. The patient had an arrhythmic heartbeat with a heart rate of 55 – 90 beats/min, sinus arrhythmia in electrocardiogram, an atrioventricular block type I and a suspected sick sinus syndrome.

The laboratory data included hemoglobin concentration (113 g/L), and normal values for the white blood cell and platelet counts, β2 microglobulin, lactate dehydrogenase, total proteins and albumins. The C-reactive protein values (28.2 mg/L) and the erythrocyte sedimentation rate (32 mm/h) were elevated. A serum protein electrophoresis did not show the presence of monoclonal protein. Both the serum carcinoembryonic antigen and CA 19-9 were within the normal range. The serological tests for HIV, hepatitis B, hepatitis C, and Epstein-Barr virus were negative. A purified protein derivative (PPD) skin test was also negative. Analyses of stool samples were negative for *Campylobacter jejuni, Yersinia enterocolitica, and Clostridium difficile*.

A conventional chest X-ray, abdominal ultrasonography and CT scan showed no abnormalities. Due to the clinical presentation and radiographic signs of subocclusion, the patient was examined by a surgeon who recommended further investigation and conservative treatment. An esophagogastroduodenoscopy revealed a small hiatal hernia and no macroscopic abnormalities of the esophagus, stomach, or duodenum. The colonoscopy examination and an accompanying biopsy revealed a normal colon. Endoscopy of terminal ileum showed diffuse erythema and vascular congestion of the mucosal architecture in the terminal ileum with ulcerations as a “skip lesions” between macroscopically normal presented areas of mucosa of terminal ileum.

Relative improvement of clinical symptoms including reduction of abdominal pain and decreasing number of liquid stools was achieved using mesalamine and methylprednisolone. The laboratory data, however, revealed an elevated erythrocyte sedimentation rate (66 mm/h) and fibrinogen values (7.5 g/L). Although the histopathology report did not confirm Crohn's disease, the findings of multiple endoscopic biopsies
revealed diffuse infiltration of lymphoid cells. Re-biopsies of terminal ileum and immunohistochemical (IHC) examination of the terminal ileum were therefore required. The endoscopic features of the terminal ileum during the repeated endoscopy revealed inflamed mucosa with an irregular nodular and polypoid pattern, spontaneous bleeding, and multiple large ulcers (Figure 1).

A histopathological examination revealed abundant atypical large lymphoid cells. IHC analyses of the biopsied tissue were positive for MUM1, CD38, and CD138, and negative for Pax5, CD20, CD3, bcl2, bcl6, CD56, and CD10; Ki67 was approximately 30% (Figure 2). The results based on the histopathological and IHC patterns confirmed a diagnosis of PBL. The patient was sent for further hematological investigation and treatment. After completing clinical staging procedures, the patient received cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) chemotherapy. Due to the persistence of abdominal pain, the patient was transferred to the surgery department, where an ileum resection (50 cm in length) was performed. The postoperative histopathology report confirmed PBL as the final diagnosis. After the postoperative recovery, the patient was receiving chemotherapy according to the CHOP protocol for the following 6 months, when the fatal outcome occurred, due to acute myocardial infarction and consequently cardiac insufficiency.

**DISCUSSION**

Our case report on localized PBL of the ileum presents a rare cause of subocclusive events. The patient was initially admitted to our hospital for further investigation to exclude previously suspected Crohn's disease. Due to the patient's persistent abdominal pain and radiographic signs of subocclusion, surgical treatment was discussed without previous ileocolonoscopy.

Crohn's disease is the second most common etiological factor of intestinal obstruction that can require surgical treatment [1]. According to the available literature, approximately 80% of patients with Crohn’s disease will undergo an operation during their lifetime [2]. For patients with Crohn's disease of the small intestine, intestinal obstruction is the primary surgical indication [3]. During an ileocolonoscopy, the endoscopic features of Crohn’s disease of the terminal ileum were described in our patient. The patient was therefore treated with mesalamine and corticosteroids. An explanation for the relative clinical improvement is that prednisolone is also included in the CHOP therapy. The final
PBL diagnosis was based on the histopathology and IHC analysis with additional confirmation by the postoperative findings. The case report of our patient once again proves the importance of pathohistology and immunohistochemistry in order to establish the final diagnosis.

Although PBL was initially described in patients with acquired immunodeficiency syndrome (AIDS) predominantly in the oral cavity, the clinical spectrum of this malignancy has since been expanded [4].

In the largest cohort study so far, conducted on 135 patients with PBL, the most of them were immunocompromised - either HIV-positive, transplanted or previously treated for systemic diseases and carcinoma [16].

However, there have been a number of patient series and reports including HIV-negative cases and extra-oral localizations. Over one-third of all PBL cases were first noted at extra-oral locations, predominantly within the gastrointestinal tract. According to the literature, HIV-negative patients can have PBL in the stomach, small bowel, and colon [6,9,10,13,14]. PBL of the small intestine is extremely rare. Korean authors have described PBL cases of the small intestine associated with other locations, such as the oral cavity, jejunum, and thorax [9]. According to a study conducted by Chinese authors, patients with localized PBL of the small intestine were immunocompromised from hepatitis B infections and had a recent radiotherapy for maxillary sinus cancer [11]. Our case report is specific because the illness, causing a small bowel obstruction, was localized to 50 cm of ileum in an immunocompetent patient with no previous medical history of radiotherapy or use of immunosuppressant drugs.

A group of Chinese authors analyzed 114 HIV negative patients with PBL from 52 published papers and concluded that PBL was localized in the gastrointestinal tract in only 15.79% of cases. [17].

In a study conducted by US authors, of 61 patients with PBL, the gastrointestinal tract was affected in 12 patients, of whom only 3 patients were immunocompetent [18].

Although the studies of other authors suggest a very low diagnostic yield terminal ileum intubation during colonoscopy, our case report points to the importance of insisting on the exploration of the small intestine in a patient with subocclusive symptoms in order to establish the final diagnosis. [19, 20]. Also, in our patient, the crucial importance for
further treatment was an accurate pathohistological verification of the detected changes in the ileum.

In conclusion, the differential diagnosis of subocclusive events can also include PBL of the small intestine, as a rare and unusual site of the disease, in HIV-negative patients without a previous medical history of immunosuppression.

Consent: Written informed consent was obtained from all patients for publication of these cases and any accompanying images.
The Ethics Committee approval was obtained by Ethics Committee of our center.

Conflicts of interest: The authors state that they have no Conflict of Interest (COI).

ACKNOWLEDGMENT: This work was supported by Ministry of Education, Science and Technological Development, Republic of Serbia (Grant No. III4100)

REFERENCES


Fig. 1. The endoscopic features of the terminal ileum during ileocolonoscopy. A: Ulcer; B: The polypoid altered mucosa and spontaneous bleeding C: The nodular altered mucosa
Fig. 2. Histopathological examination of the tumor tissue in the terminal ileum. A: Hematoxylin and eosin stain staining; diffuse neoplastic infiltration of ileum with atypical large lymphoid cells; B: Immunohistochemical (IHC) analysis of CD20; lymphoid tumor cells are negative, while normal B lymphocytes are positive for CD20 expression. C: IHC analysis for CD38; lymphoid tumor cells were positive for CD38 expression.