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Case Report

Unique presentation of a plasmablastic lymphoma superficially involving the entire large bowel

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ABSTRACT

Plasmablastic lymphoma (PBL) is an uncommon, aggressive B-cell lymphoma mostly occurring in the oral cavity of human immunodeficiency virus (HIV) positive patients, but also described in extraoral sites and in HIV negative patients. One of the relatively common extraoral sites of PBL is the gastrointestinal (GI) tract. Few cases of PBL have been reported in association with inflammatory bowel disease (IBD). Here, we describe the unique presentation of a PBL involving the large bowel superficially along its entire length and without forming a tumor mass in an HIV negative patient with a recent diagnosis of ulcerative colitis.

1. Introduction

PBL is a rare B-cell lymphoma initially described in the oral cavity of HIV positive individuals [1], but occurring also in other sites [2] both extranodal and nodal and in HIV negative patients [3]. It is considered a specific and separate entity in the World Health Organization (WHO) Classification of Tumors of Hematopoietic and Lymphoid Tissue [4]. Rare cases of PBL have been described in long-standing IBD patients mostly following treatment with thiopurine and infliximab [5–11].

Here we report a case of PBL occurring in an HIV negative 72 year-old male superficially involving the entire large bowel without any identifiable tumor mass. The patient had a recent diagnosis of ulcerative colitis (UC) treated only for a very short time with immunosuppressive drugs.

2. Case description

In August 2013 a 72 year-old man was referred to the Gastroenterology Department of Arcispedale S. Maria Nuova, Reggio Emilia (Italy) because of severe diarrhea, malaise and rectal bleeding. The patient was diagnosed with ulcerative colitis (UC) three months earlier when he started having intestinal symptoms with bloody diarrhea and was treated with topical and oral steroids with temporary improvement of the symptoms. His past medical history was unremarkable. In August a repeated colonoscopy (Fig. 1) revealed an intense pancolitis characterized by a diffusely hemorrhagic and granular mucosa with multiple deep ulcers surrounding pseudopolyps. Due to a stricture of the lumen, the endoscopic procedure could not go beyond the transverse colon. Multiple mucosal biopsies showed marked glandular distortion with intense chronic lymphocytic and plasmacellular infiltrate together with cryptic abscesses. These histological features were consistent with an active UC. A magnetic resonance enterography (MRE) confirmed a diffuse large bowel wall thickening extending from the rectum to the descending colon, with no evidence of a clear-cut stenosis. Viral serology (EBV, HIV, CMV) and stool culture were negative. The peripheral blood exams were normal. Owing to the poor conditions, the patient required hospitalization and was initially treated with intravenous corticosteroids with

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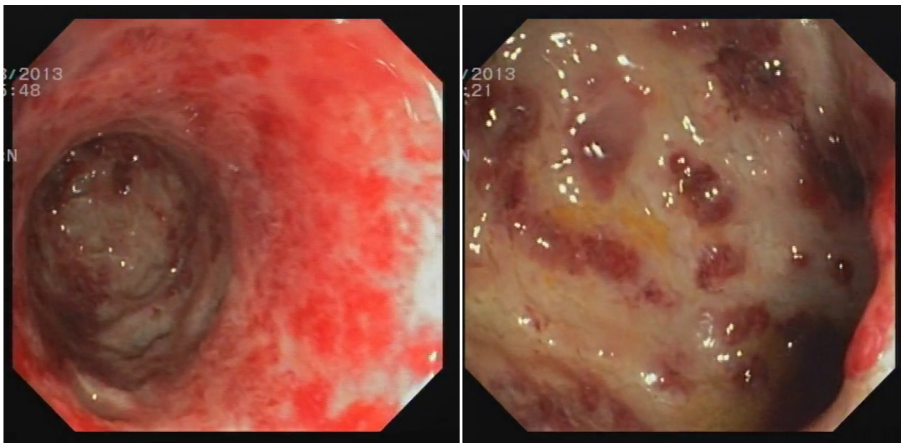

Fig. 1. Endoscopic view of rectosigmoid junction: the mucosa shows hemorrhagic and granular appearance and multiple deep ulcers surrounding pseudopolyps.

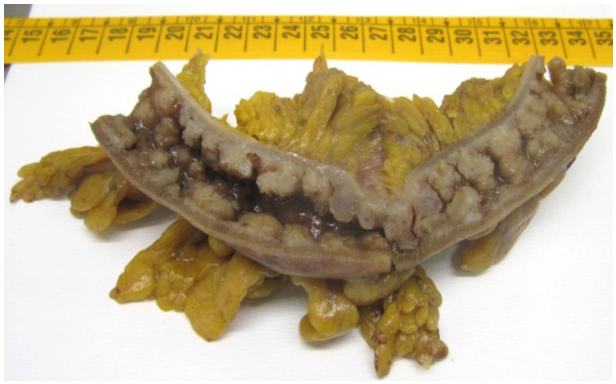

Fig. 2. Macroscopic examination: a diffuse thickening of the large bowel wall and multiple ulcers are visible.

no beneficial effect. Subsequently he received two infusions of infliximab and only a one-week course of azathioprine due to severe gastric azathioprine intolerance. Despite therapy, the clinical conditions progressively worsened with bloody diarrhea, fever and rapid weight loss. In November, a total proctocolectomy with ileostomy was performed. Macroscopically the surgical specimen (Fig. 2) revealed a diffusely granular mucosa with multiple linear ulcers and pseudopolyps associated with a variable, but diffuse thickening of the intestinal wall. There was no evidence of a definite tumor mass. Histological examination (Fig. 3) of the large bowel confirmed the UC mucosal alterations already identified in the previous biopsies. In addition, there were sheets of large cells with prominent nucleoli and an immunoblastic/plasmablastic morphology infiltrating in a band-like fashion mainly in the submucosa and only focally in the muscularis propria. Mucosal involvement by large, atypical cells was also focal and mainly confined to the ulcers. The neoplastic infiltrate involved the entire large bowel from cecum to rectum as demonstrated by extensive sampling. Immunohistochemically the atypical cells showed a plasma cell phenotype, positive for CD138 (clone [B-A38]/PD – Prediluted Ventana BenchMark) and IRF4/MUM1 ([MRQ-43]/PD), weakly positive for CD79alfa ([SP18]/PD) and negative for CD20 ([L26]/PD), PAX5 ([SP34]/PD), CD45 ([PD7/26/16 + 2B11]/PD), CD3 ([2GV6]/PD), CD2 ([LFA-2]/1:50, Novocastra), CD30 ([L26]/PD), ALK-1 ([ALK-01]/PD), CD56 ([123C3]/PD), EMA ([E29]/PD), CD34 ([QBend10]/PD), MPO ([Polyclonal rabbit]/1:4000, Dako), cytokeratin ([AE1/AE3/PCK26]/PD) and Human Herpes Virus 8 (HHV8) ([13B10]/PD). The proliferation index, assessed by ki67/MIB1 staining, was approximately 70%. In situ hybridization (ISH) for Epstein–Barr virus encoded RNA (EBER) was positive. A clonal IgH gene rearrangement was found. A diagnosis of PBL was finally made.

A staging bone marrow biopsy was negative for neoplasia and a total body computed tomography (CT) scan and positron emission tomography (PET) showed no other site of disease. According to the Ann Arbor staging system the patient had stage IVA lymphoma, with a low/intermediate age-adjusted International Prognostic Index (IPI), frail according to comprehensive geriatric assessment (CGA). He received two cycles of cyclophosphamide plus prednisone and six cycles of cyclophosphamide, bortezomib and prednisone. Local radiotherapy was performed. At 19 months from diagnosis, the patient is in complete remission and in good clinical conditions.

3. Discussion

PBL is a rare, highly aggressive lymphoma originally described by Delecluse et al. [1] as a specific clinicopathologic entity seen in the oral cavity of HIV positive patients. However over the years, several cases of PBL have been described in extraoral sites [2], both nodal and extranodal. The GI tract, in particular the rectum, is a relatively common extraoral site of PBL [12]. Although PBL has been commonly reported in the clinical setting of HIV infection [13], it can also occur in patients with other causes of immunosuppression or even in patients, mostly elderly, without any history of immunodeficiency [4].

The clinical course is generally very aggressive with most patients being at advanced stage at presentation and dying in the first year after diagnosis [4]. Differences exist between HIV positive and HIV negative patients in terms of response to therapy, as HIV positive patients have a better response to therapy and an overall survival of 14 months compared to 9 months of HIV negative patients [3,13,14]. Treatment of PBL is considered challenging given the poor outcome with traditional chemotherapy regimens. Recently the incorporation of Bortezomib into frontline therapy has proved to be beneficial in patients with PBL [15,16].

Histologically PBL consists of a diffuse proliferation of cells with an immunoblastic/plasmablastic morphology and high proliferative fraction. The consistent expression of plasma cell markers and frequent absence of B-cell markers are key pathological features of this entity together with EBV infection detected in a high percentage of cases [4]. EBV positivity varies according to HIV status [14], being detected by EBER ISH in 82% of HIV positive and in only 46% of HIV negative patients.