Rectal plasmablastic lymphoma in Ebstein Barr virus positive and human immunodeficiency virus negative subject after external radiation therapy for prostatic cancer

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Abstract

Plasmablastic lymphoma (PBL) represents a rare and aggressive subtype of diffuse large B cells lymphoma (DLBCL) most associated with the human immunodeficiency virus (HIV). Prognosis remains poor despite various treatment approaches. We describe an evolution at six months of HIV negative PBL and Ebstein Barr virus (EBV) positive PBL with chemotherapy. Role of radiotherapy is still unclear. (Acta gastroenterol. belg., **2021,** 84**, 663-665**).

Key words: Plasmablastic lymphoma, Ebstein Barr virus, rectal bleeding, external radiotherapy, chemotherapy.

Introduction

Primary gastrointestinal lymphoma accounts for 5% of all lymphomas and 10-15% of non-Hodgkin lymphomas. It must be differentiated from a generalized malignant process including the gastrointestinal tract because treatments and prognosis are different. Primary form occurs mainly in the stomach and small bowel. Rectal area is the least common localization (1,2).

Two histological subtypes are frequently encountered: mucosa-associated lymphoid tissue (MALT) and diffuse large B cell lymphomas (DLBCL) (1).

Plasmablastic lymphoma (PBL) represents a rare and aggressive subtype form of diffuse large B-cell lymphoma that was first described in the oral cavity. It is usually seen in association with human immunodeficiency virus (HIV) but other immunocompromised states such as the elderly or immunosuppressive medications are described.

Gastrointestinal tract is involved in approximately 14%. Rectal involvement has been noticed (3). Genetic profile remained unknown but chromosomic abnormalities have been recently identified. These mutations, including rearrangements on cMYC gene, are often linked with Ebstein-Barr Virus (EBV) (4).

Clinical features include weight loss, bleeding, abdominal pain, fever, malabsorption, anemia and obstruction. Diagnosis remains a challenge. PBL has features that overlap with other entities like myeloma or lymphomas with plasmablastic morphology (5). Therapeutic approaches are still subject of much debate and outcomes are poor despite standard therapy. Relapses are frequent and mortality is remarkably high (3).

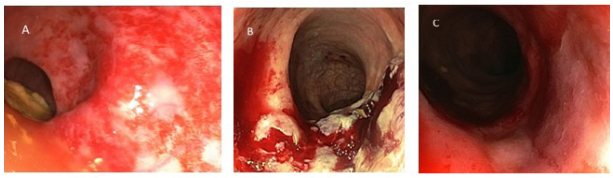

Figure 1. — A. Rectoscopy, angiodysplasias and radiation proctitis. B. Rectoscopy performed 3 months later, development of a large ulcer with buds and stigmata of bleeding near the anal canal. C. Rectoscopy after 3 cycles of chemotherapy.

Case presentation

A 84-year-old man was admitted in gastroenterology department after presenting rectal bleeding. He had no relevant medical history other than prostate cancer. He was treated three years before by external radiation therapy and hormonal treatment. He received 66 Gray (Gy) in the prostatic area (25 sessions of 2,64 Gy) and 50 Gy in the seminal vesicles and pelvic nodes (2 Gy). Hormonal therapy consisted of Bicalutamide 150 mg per day for 6 months. He had no fever, sweating, weight loss or abdominal pain. Defecation patterns were not affected. Physical and rectal examinations were normal. Laboratory tests revealed discrete normocytic anemia without inflammatory syndrome or elevation of lactate dehydrogenase.

The left colonoscopy found a radiation proctitis with diffuse bleeding and colonic angiodysplasia treated by Argon-plasma coagulation (Figure 1A).

The patient relapsed with recurrent bleeding three months later. A granular mass located on the anterior surface near the anal canal was found. Rectosigmoidoscopy demonstrated a large mucosal ulceration in the lower third of the rectum with stigmata of recent haemorrhage (Figure 1B). Biopsy revealed an excessively undifferentiated tumor process of cohesive cells with hyperchromatic nuclei.

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Immunohistochemical studies revealed the presence of CD10, CD138 (plasmatic cell membrane marker), MUM-1 (nuclei of tumor cells), CD79a (immature B-cell marker) and discrete CD20 with replication rate Ki-67 close to 100%.

The final diagnosis was an Ebstein Barr Virus (EBV) plasmablastic lymphoma.

Fluorescence in situ hybridization (FISH) revealed gene rearrangement on cMYC (translocation 8q24) found on 100% of the nuclei of tumor cells. Staging CT scan showed no pathological lymph nodes or other organic lesions. There was no infiltration of the fatty tissue and no local lymph nodes around the lesion on the echo endoscopy, pelvic magnetic resonance imaging (MRI) and positron emission tomography (PET-scan). EBV serology revealed a high IgG rate >750 U/ml (negative value: <20 U/mL) and negative IgM. HIV status, determined by enzyme-linked immunosorbent assay (ELISA), was negative. The patient was in stage IA according to the Ann Arbor staging system (extra nodal focal localization without B symptoms).

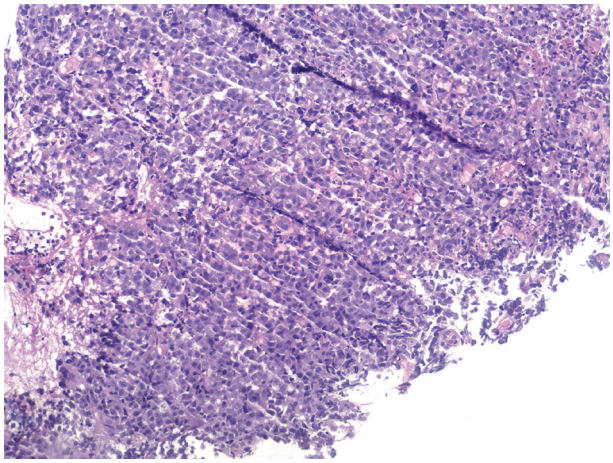

Figure 2. — Endoscopic biopsy. Plasmablastic lymphoma is a mature B-cells neoplasm. Tumor cells have large nuclei and abundant basophilic cytoplasm. Plasmablastic lymphoma have a specific immunophenotypical profile of plasmacytic markers (CD138+, MUM1 +, CD 79a+ and Ki67 close to 100%).

Discussion

Lymphomas of the gastrointestinal tract are predominantly non-Hodgkin's types and rarely primary, accounting for only 1 to 4 percent of malignancies. Plasmablastic entity is a rare variant of mature B-cells lymphoma with a predilection for mucosal sites including the digestive tract (extranodal localization) (1).

Manifestations of rectal lymphomas usually in-cludes alteration of bowel habits, pain, bleeding, hematochezia and general symptoms like fever, weight loss, nausea and vomiting (2,6).

Diagnosis is generally established with clinical examination, abdominal CT and endoscopic findings. The tumor has several macroscopic forms ranging from ulcerations to lymphomatous polyps or thickenings of some parts of the bowel wall (6,7).

The original cell comes from a B-immunoblast or a mature plasma cell. The replication rate is high. The immunophenotype is commonly negative for B-cell antigens and positive for markers such as CD138 and MUM-1 (5). B-cell marker CD20 is exceptionally positive (8).

PBL entity has a predilection for males and is most frequently associated with HIV positive individuals suffering from immunodeficiency syndrome. The disease can arise in other immunocompromised states such as the elderly (9).

Genetic modifications such as oncogene cMYC overexpression are often observed in EBV positive disease (4). EBV is associated with 50% of cases of HIV negative PBL (10).

In this case, the gender of the patient, advanced age and history of prostate cancer could be seen as risk factors.

Several studies concluded that prostate radiation therapy promotes the occurrence of secondary neoplasms including lymphomas. Some authors failed to demonstrate a statistical association probably because of a shorter follow up over time. The risk of secondary neoplasms increases with the age of the patient and the elapsed time after radiation. It is lower with brachytherapy than external radiation therapy (11).

The optimal treatment is still unknown and the prognosis is poor (8). Some studies suggest that HIV negative subjects with EBV infection have a better survival. It is the opposite with immunosuppression (10).

Some authors recommend CHOP chemotherapy (Cyclophosphamide - Hydroxyadriamycine - Oncovin - Prednisone) while others prefer more aggressive regimens including hyper-CVAD (Cyclophosmamide - Vincristine - Adriamycin - Dexamethasone) and DA-EPOCH (Rituximab - Etoposide - Prednisolone - Vincristine - Cyclophosphamide - Doxorubicin). Radiotherapy was tried in early stages but has not shown any efficacity. Bortezomib seems to be more efficient in HIV positive disease (9,12).

The patient was diagnosed at an early stage (IA classification) and received dose-adjusted CHOP chemotherapy.

Rituximab has been added to the protocol because of the expression of CD-20 marker. A favorable evolution was observed at 6 months (Figure 1C).

Conclusion

There appears to be a link between external radiation therapy and the occurrence of PBL. We recommend special attention to low digestive symptoms in the years following the treatment to diagnose possible secondary cancer at an early stage. Early discovery of PBL influences the prognosis (8).

Treatment remains a challenge with a global prognosis that is poor with current chemotherapy protocols. Novel therapies are urgently needed. Immunotherapy and stem cell transplant might be promising (12). The activity of Bortezomib should be more described in HIV negative PBL.

The patient's survival, in this case, is exceptional. We suggest that the early diagnostic and the expression of CD20 targeted by Rituximab are contributing to the good evolution.

Conflicts of interest

None.

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