Kaposi sarcoma is an unusual tumor associated to a human herpes virus-8 infection involving the skin or internal organs. Iatrogenic Kaposi’s sarcoma often occurs in patients receiving immunosuppressive therapy. So far, a few Kaposi’s sarcoma cases have been reported in the literature associated with inflammatory bowel diseases. We report a 53-year-old male diagnosed with a severe refractory ulcerative colitis who was treated with corticosteroids and azathioprine. The patient underwent a colectomy after the failure of medical treatment. Histological examination of the colon showed findings suggestive of Kaposi’s sarcoma. Immunohistochemistry for human herpes virus-8 was positive in the colonic lesions.

Introduction

Kaposi’s sarcoma (KS), first described by Moritz Kaposi in 1872, is commonly known as an unusual vascular tumor principally involving the skin. However, in some cases, it can also affect any organ system. It is strongly associated to human herpes virus-8 (HHV-8) infection. Iatrogenic form of Kaposi’s sarcoma often occurs in patients receiving immunosuppressive therapy. Although the association between Kaposi’s sarcoma and renal transplant has been well documented, there are less Kaposi’s sarcoma cases in the literature associated with ulcerative colitis (UC) or other inflammatory bowel diseases (IBD). We report a case of a human immunodeficiency virus (HIV) negative man, with refractory ulcerative colitis who developed Kaposi’s sarcoma, associated with HHV-8, following treatment with azathioprine and additional corticosteroids. This patient underwent a colectomy.

With the present case, we wish to draw the interaction of immunosuppressive therapy used in ulcerative colitis patients with the development of colonic Kaposi’s sarcoma.

Case report

A 53-year-old heterosexual man, without personal or familial medical history, was diagnosed with ulcerative colitis for three months ago revealed by chronic bloody diarrhea (6-8 stools daily) with abdominal pain, rectal syndrome and weight loss of 2 kg. He had no smoking or alcohol drinking history. Initially, before admission in our center, oral steroid and local mesalamine was prescribed without a complete relief of rectal bleeding. Upon physical exam, blood pressure was 130/80 mmHg and his body mass index was 18.7 kg/m². Abdominal exam proved to be normal. Mucus and blood soiled finger at DRE. Besides, there was no skin lesion or lymph node swelling. Laboratory investigations showed iron deficiency anemia (10.3 g/dL) and signs of inflammation: white blood cell count of 9800/mm³, erythrocyte sedimentation rate (ESR) of 60 mm and C-reactive protein (CRP) of 84 mg/L were noted. Albumin level was 28 g/L. Copro-parasitological examinations were negative. Ileocolonoscopy showed pancolitis with mucosal fragility, large superficial ulcerations and pseudo-polyps, without severe endoscopic signs and with normal ileum. Histology found clear signs of active ulcerative colitis with no malignancy signs.
He was initially treated with intravenous steroids (1 mg/kg/day of prednisone), local mesalamine and parenteral nutrition for a severely active disease with a partial relief of diarrhea relayed by oral corticosteroids. At week 4 of corticosteroid therapy decreasing, relapse occurred (6 stools daily, anemia 8.6 g/dL, ESR 40 mm). Dose escalation of steroid was prescribed in association with Azathioprine (2.5 mg/kg/day). After 4 weeks of free steroid treatment, and while patient with Azathioprine (at month 6) another severe relapse occurred (8 stools daily, anemia 6.5 g/dL, ESR 40 mm, CRP 89 mg/L). Copro-parasitological examinations were always negative. Cytomegalovirus and HIV testing was negative too. Detection of Clostridium difficile toxins was not conducted. We had considered that it was a refractory severe ulcerative colitis and we suggested a surgical treatment for the patient. A subtotal colectomy with double stoma of the ileum and of the sigmoid colon was performed. Colon macroscopic examination revealed multiple mucosal and submucosal hemorrhagic polypoid lesions that coalesce, associated with large ulcerations. Histologic examination of polypoid lesions (Figs. 1-2) showed sheets of spindle cells interspersed by clusters of extravasated erythrocytes. The spindle cells often run parallel to the mucosae. Many spindle cells show mitoses. Endothelial cells lining the spaces are flattened or more oval, with little atypia, deposits of hemosiderin surrounded the vascular structures. Slit-like spaces, lymphocyte and plasma cell infiltration and extravasated erythrocytes are also observed. There was a partial infiltration of the appendix. No lymph node metastasis was demonstrated. Equally important, histology also found clear signs of active ulcerative colitis. On immunohistochemistry, the spindle cells were positive for vascular markers (CD31, CD34) and HHV-8 (Fig. 3) and were negative for factor VIII, actin, desmin and c-kit. These results were consistent with the diagnosis of Kaposi’s sarcoma, associated with typical features of ulcerative colitis. Once again, the patient underwent a total proctocolectomy and ileoanal anastomosis. The patient tolerated the surgery therapy well and recovered after operation.

**Discussion**

This paper report a case of iatrogenic colonic KS, associated to HHV-8, in an HIV-negative heterosexual man who had suffered ulcerative colitis. Kaposi’s sarcoma developed after starting steroid or immunosuppressive therapy, supporting the theory that colorectal Kaposi’s sarcoma associated with ulcerative colitis is iatrogenic. Table I summarizes the main data in literature of KS in association with IBD with or without HIV or HHV-8 infections. Kaposi sarcoma-associated herpes virus (KSHV) occurs in four distinct clinical forms: classic or sporadic KS, endemic KS, HIV-associated epidemic KS and iatrogenic KS associated with immunosuppressor therapy. Predominantly, Kaposi’s sarcoma is seen in the case of homosexual males suffering from AIDS.
The association of iatrogenic KS and immunosuppressive therapy in renal or liver transplant patients has been frequently reported. In much less cases in the literature, iatrogenic KS were associated with UC. Most of the cases we noticed refractory severe ulcerative rectocolitis on immunosuppressors or immunomodulator therapy. Our patient has received steroids and immunosuppressor therapy. The link between steroid-therapy and KS is well documented. However, there was no evident correlation between the development of KS and dose or duration of steroid therapy. Reduction or withdrawal of immunosuppressor therapy often leads to improvement in KS lesions. The diagnosis of colorectal KS may be difficult to establish in the absence of skin lesions, as in the case of our patient. At endoscopy, nodules on the bowel mucosa and polypoid lesions have been reported, as well as some cases of diffuse bowel involvement. In the case of intraluminal polypoids forms, polyps are red or blue, due to high vascular and conjunctive tissue proliferation. They can be confused with inflammatory pseudo-polyps associated with ulcerations. Biopsies may fail to sample diagnostic tissue before tumor infiltration of the mucosa. Large polypoid lesions may frequently undergo ulceration. Thus, superficial biopsies of such lesions may be diagnostically challenging to the histopathologist, and may, therefore, be misinterpreted as an inflammatory polyp. Upon histological exam, the tumor is made of cellular proliferation of neoplastic spindled cells arranged in fascicles. The tumor cells are relatively monomorphic with some mitoses. Erythrocytes are contained within slit-like channels between the individual spindled cells. Hyaline globules may be seen. The periphery of the tumor may show dilated vascular spaces. Kaposi’s sarcoma lesion may be mistaken for several other spindle cell mesenchymal neoplasms such as stromal tumor (GIST) or inflammatory fibroid polyp. The diagnosis is confirmed by positive immunohistochemical staining of the tumor cells for HHV-8. HHV-8 was positive in our current case. The HHV-8 is the major cause in the development of all epidemiologic variants of KS. Rezza et al. have reported a 30% risk of developing KS within 10 years in patients co infected with HHV-8 and HIV.

The therapeutic approach is challenging. Conservative therapy with immunosuppressive drugs withdrawal has been successfully described. Proctocolectomy associated to immunosuppressive drugs discontinuation is usually effective to treat both tumor and coli-

### Tab. I. Main data in the literature on iatrogenic Kaposi’s sarcoma and inflammatory bowel diseases (IBD).

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year of publication</th>
<th>IBD *</th>
<th>Skin lesions</th>
<th>Immunosoppression</th>
<th>Treatment</th>
<th>Improvement</th>
<th>HHV-8 †</th>
<th>HIV ‡</th>
</tr>
</thead>
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<tr>
<td>Gordon 14</td>
<td>1966</td>
<td>UC</td>
<td>No</td>
<td>Colectomy</td>
<td></td>
<td>NR **</td>
<td></td>
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<tr>
<td>Weber 15</td>
<td>1985</td>
<td>UC</td>
<td>Yes</td>
<td>Steroids enemas</td>
<td>Human alpha interferon + Radiotherapy +</td>
<td>initial response with relaps</td>
<td>NR ††</td>
<td>Positive</td>
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<td>Biggs 16</td>
<td>1987</td>
<td>UC</td>
<td>Yes</td>
<td>Steroids</td>
<td>Alpha interferon + Vinblastine + Proctocolectomy</td>
<td>Yes</td>
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<td>Meltzer 17</td>
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<td>Thompson 18</td>
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<td>Proctocolectomy</td>
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<td>Puy-Montbrun 19</td>
<td>1991</td>
<td>CD</td>
<td>Steroids AZA</td>
<td>Steroids and AZA withdrawal</td>
<td>Yes</td>
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<td>Tedesco 20</td>
<td>1999</td>
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<td>No</td>
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<td>Yes</td>
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<td>Cohen 21</td>
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<td>Proctocolectomy</td>
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<td>Pedulla 22</td>
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<td>No</td>
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<td>Bursics 5</td>
<td>2005</td>
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<td>Grelli 6</td>
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<td>No</td>
<td>Steroids Cyclosporin</td>
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<td>Svrek 5</td>
<td>2009</td>
<td>UC</td>
<td>No</td>
<td>Steroids AZA</td>
<td>Proctocolectomy</td>
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<tr>
<td>Rodriguez-Pelaez 6</td>
<td>2010</td>
<td>UC</td>
<td>Yes</td>
<td>Steroids Methotrexate</td>
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<td>Positive Negative</td>
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<tr>
<td>Cetin 7</td>
<td>2011</td>
<td>UC</td>
<td>Yes</td>
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<td>Radiotherapy of skin lesions and immunosuppressive drugs withdrawal</td>
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<td>Pioche 11</td>
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<td>No</td>
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<td>Herculano 12</td>
<td>2014</td>
<td>UC</td>
<td>No</td>
<td>Steroids</td>
<td>Immunosuppressive drugs withdrawal</td>
<td>Yes</td>
<td>Positive Negative</td>
<td></td>
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<tr>
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<td>-</td>
<td>UC</td>
<td>No</td>
<td>Steroids AZA</td>
<td>Proctocolectomy</td>
<td>Yes</td>
<td>Positive Negative</td>
<td></td>
</tr>
</tbody>
</table>

* Inflammatory bowel disease; † Human herpes virus-8; ‡ Human immunodeficiency virus; ¶ Ulcerative colitis; †† Crohn’s disease; †‡ Not reported; ‡‡ Aza-thioprine
tis 3-5 11 17 18 20 21. After initial subtotal colectomy, the patient would undergo proctectomy when Kaposi’s sarcoma associated to ulcerative colitis is confirmed.

Conclusion

This report has illustrated that it is important to consider a concomitant colorectal Kaposi’s sarcoma in patients with refractory ulcerative colitis receiving immunosuppressive drugs. This tumor may be related to immunosuppressor therapy and opportunistic infection with HHV-8, independently of HIV status. Subsequently, in our practice, immunosuppressor therapy should be carefully planned and HHV-8 should be recognized as a possible underlying opportunistic infection in immunocompromised patients with IBD. Surgery and immunosuppressive drugs discontinuation may be indicated to treat both Kaposi’s sarcoma and refractory colitis.

References