TEACHING CASE

Classic Kaposi’s sarcoma presenting first with gastrointestinal tract involvement in a HIV-negative Inuit male – A case report and review of the literature

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Abstract

Kaposi’s sarcoma (KS) is a multicentric low-grade vascular malignancy. In North America, it is usually seen in AIDS and solid organ transplant populations. Classic KS is a subtype that traditionally occurs in elderly HIV-negative males of Mediterranean, Eastern European, and Jewish descent. Patients with classic KS characteristically present with skin lesions in the distal extremities. Involvement of the viscera is uncommon in classic KS, but may occur in the late stages of the disease. We report the first case of classic KS presenting in the gastrointestinal tract of an elderly HIV-negative Inuit male from Northern Quebec, Canada.

Keywords: Classic Kaposi’s sarcoma; Inuit

Introduction

In 1872, a Hungarian dermatologist, Moritz Kohn Kaposi, described an idiopathic pigmented sarcoma of the skin that now bears his name [6]. Although there is an on-going debate as to whether Kaposi’s sarcoma (KS) is a hyperplasia or a neoplasia, it is currently regarded as a low-grade vascular malignancy. KS is a multicentric and multisystem disease that involves the skin and, less commonly, visceral organs, such as the gastrointestinal tract, lung, and lymph nodes. There are four forms of Kaposi’s sarcoma: classic KS, endemic/African KS, AIDS-related KS, and transplant-related/immunosuppression-associated KS. All four forms of the neoplasm have recently been attributed to the human herpesvirus 8 (HHV 8), also known as Kaposi’s sarcoma-associated herpesvirus (KSHV) [2]. In North America, KS is usually seen in the AIDS and solid organ transplant populations. KS is an AIDS-defining malignancy and is particularly common in male homosexual AIDS patients. KS has been documented in heart, liver and lung transplant patients, but has the highest incidence in the renal transplant setting. It has also been documented in other iatrogenically immunosuppressed situations, such as in patients with long-standing steroid therapy for autoimmune conditions. Classic KS
is uncommon in North America, as it primarily affects elderly males of Mediterranean, Eastern European, or Ashkenazi Jewish descent. Classic KS is a slow-growing neoplasm that characteristically presents as bluish-red, well-demarcated, painless skin lesions on the distal extremities [5]. The lesions may progress from patches to plaques and ulcerated nodules. Visceral involvement occurs in approximately 10% of classic KS cases, usually in the late stages of the disease [5]. We report the first case of classic KS presenting in the gastrointestinal tract of a HIV-negative Inuit male from Northern Quebec, Canada.

Case report

A 61-year-old Inuit male from Povungnituk, a village in Northern Quebec, Canada, underwent endoscopy to investigate a gastrointestinal bleeding. His significant past medical history included long-term non-steroidal anti-inflammatory drug (NSAID) use for degenerative disc disease, gastroesophageal reflux disease, and a remote cerebrovascular accident. Laboratory investigations showed a normochromic normocytic anemia with a normal white cell count. At upper endoscopy, a hemorrhagic polyp in the distal antrum was identified, though not biopsied. Random biopsies of the background stomach showed Helicobacter-associated gastritis. Random biopsies of the duodenum showed no significant abnormality. Colonoscopy, performed at the same visit, showed a suspicious ulcerated lesion at the ileocecal valve, which was biopsied. On histology, fibrinopurulent exudate was present. In addition, a poorly defined collection of cytologically bland spindle cells was seen in the lamina propria and submucosa, associated with dilated capillaries. There were vague areas of interlacing fascicles, patchy infiltration by neutrophils, lymphocytes and plasma cells, as well as rare mitotic figures. A differential diagnosis was given: ulcer bed tissue with florid granulation tissue versus a spindle cell tumor. Although the former diagnosis was favored, further clinical and radiological work-up was recommended. Abdominal ultrasound subsequently revealed no diagnostic abnormality. Follow-up colonoscopy, performed 2 weeks after the initial endoscopy, showed partial resolution of the ulceration, and a less convincing macroscopic lesion. Rebiopsy, however, showed a more prominent spindle cell proliferation. Immunohistochemical work-up revealed the spindle cells to be positive for vimentin (DakoCytomation, Denmark) and CD-34 (DakoCytomation, Denmark), equivocal for CD117 (DakoCytomation, California, USA), and negative for muscle markers, S-100 (DakoCytomation, California, USA), and cytokeratin (ID Labs Inc., Ontario, Canada). The possibility of a gastrointestinal stromal tumor was raised. An abdominal CT scan showed mild non-diagnostic circumferential wall thickening of the cecal and ileocecal valve region, without a focal mass lesion. Specifically, a gastrointestinal stromal tumor was deemed unlikely by radiology. Given the partial endoscopic resolution of the lesion and the radiological evaluation, the patient was managed conservatively. A follow-up colonoscopy 5 months later revealed a near-normal ileocecal valve, and rebiopsy of the region was not performed.

One year later, the patient underwent upper endoscopy, and a 1.0 cm hemorrhagic sessile polyp was identified on the greater curvature of the body of the stomach. On histology, the gastric polyp was composed of a bland spindle cell proliferation, with slit-like spaces filled with red blood cells (Fig. 1A). There was associated hemorrhage and chronic inflammation. Diastase-resistant periodic acid-Schiff (PAS-D)-positive

![Fig. 1. A: Spindle cell proliferation with vascular slit formation and red blood cell extravasation. Hematoxylin and Eosin stain, 200 × original magnification. B: Immunohistochemistry stain for HHV 8 with positive nuclear staining.](image-url)
hyaline globules were noted within the spindle cells and also extracellularly. Immunohistochemistry showed positive staining with CD34 and HHV 8 (Fig. 1B) (Novocastra Laboratories Ltd., Newcastle upon Tyne, UK), confirming the diagnosis of Kaposi’s sarcoma. The previous ileocecal valve biopsies were re-evaluated and, in retrospect, a diagnosis of Kaposi’s sarcoma was made.

Further clinical work-up was immediately undertaken. HIV testing was negative, and a complete dermatologic exam was performed and showed no skin lesions at that time. Two months later, the patient developed groin lymphadenopathy, biopsy proven as Kaposi’s sarcoma. Characteristic KS skin lesions were noted on the left calf 20 months after the patient’s initial gastrointestinal presentation. The patient underwent an incomplete course of chemotherapy with doxorubicin, terminated due to worsening lung function by usual interstitial pneumonia. The patient is alive 2.5 years after initial presentation.

Discussion

Classic KS is an uncommon malignancy in North America, usually occurring in elderly males of Eastern European, Mediterranean, or Jewish descent. To the best of our knowledge, we report the first case of an immunocompetent, HIV-negative Inuit male with classic KS presenting with gastrointestinal tract involvement.

Only eight cases of KS have been reported in HIV-negative Inuit patients, and none of these had gastro-intestinal involvement. The first report of KS in the Inuit community was described by Masse et al. in 1974. A 46-year-old Inuit male presented with multiple skin nodules in the upper and lower limbs after treatment with cobalt radiation for squamous cell carcinoma of the larynx [9]. The history of malignancy and radiation treatment likely resulted in iatrogenic immunosuppression with subsequent development of KS, i.e., immunosuppression-associated KS subtype. KS was also reported in two healthy Inuit men from Arctic Greenland with long-standing histories of chronic lymphedema [10]. Both men presented with discolored lesions of the extremities and had no history of immunosuppression. Rosen et al. [12] recently described classic KS in five Inuit people from Northern Quebec. They described skin lesions in the extremities of three healthy males and two healthy females. Three of the five individuals were from Povungnituk, the same remote Northern Quebec community as in the present case. All five patients showed positive immunohistochemical staining for the HHV 8 in the tumor sections.

HHV 8 (also known as KS-associated herpesvirus) is a member of the gamma herpes virus family, and has been isolated in all four forms of KS [2,5]. The prevalence rate mirrors the rate of KS. However, the incidence and prevalence of HHV 8 infection in the Canadian population in general and the Aboriginal population in particular have not been documented. In a study of 150 renal transplant patients in Quebec, Canada, none of the patients were seropositive for HHV 8 [3]. None of the transplant patients were of Inuit origin (written communication, Deschenes, L. MD, August 23, 2005).

Gastrointestinal manifestations of classic KS occur in approximately 10% of cases, usually in the late stages of the disease [5]. Classic KS presenting in the gastrointestinal tract before skin involvement has rarely been reported [7,8,11]. Involvement of the stomach and small intestine is more common than involvement of the esophagus and colon. Presenting clinical features include anemia from chronic blood loss, bleeding, diarrhea, protein-losing enteropathy, perforation, and obstruction [4,7]. The endoscopic appearance of KS lesions can range from hemorrhagic patches to discrete papules, to volcano-like lesions with central umbilication, and to large exophytic lesions projecting into the lumen [1,7]. However, the majority of the lesions are submucosal and are difficult to appreciate on endoscopy and, therefore, biopsy.

On histology, KS is a bland spindle cell lesion. The spindle cells form vascular slits and are associated with red blood cell extravasation, hemosiderin-laden macrophages, and chronic inflammation. Intracellular or extracellular PAS-D-positive hyaline globules may be identified. The tumor cells are positive for CD31, CD34, and HHV 8 markers [12].

The main pathological entities in the differential diagnosis of KS involving the gastrointestinal tract include granulation tissue, angiosarcoma, and gastrointestinal stromal tumor (GIST). Granulation tissue is characterized by the presence of plump endothelial cells with an admixture of neutrophils, lymphocytes, plasma cells, and a proliferation of fibroblasts, without PAS-D globules. Granulation tissue may be difficult to distinguish from KS and may require clinical correlation. Angiosarcomas tend to form dissecting, anastomosing vascular channels often with marked pleomorphism and prominent mitotic activity, unlike KS [13]. GISTs are spindle cell neoplasms with CD34 positivity, but differ from KS in that they are characteristically c-kit (CD117)-positive. Also diagnostically useful, immunohistochemistry for HHV 8 is positive in KS, unlike the other entities in the differential diagnosis.

In conclusion, we describe a unique case of classic Kaposi’s sarcoma presenting in the gastrointestinal tract of an elderly HIV-negative Inuit man from Northern Quebec, Canada. KS must be considered in the differential diagnosis of spindle cell lesions of the gastrointestinal tract.
References


