HIV-Related and Epstein-Barr Virus-Associated Anal Burkitt’s Lymphoma: Report of a Case

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The incidences of anal carcinomas and malignant anal lymphomas are increasing as a result of the AIDS epidemic, but a case of HIV-related anal Burkitt’s lymphoma (BL) has not been reported in the literature so far. Apart from the typical facial BL manifestation, atypical locations have been described in the ovaries, bladder, stomach, gallbladder, pancreas, and upper colon (1-4). The highest incidence of BL is in childhood and adolescence, and the prognosis is rapidly fatal without adequate treatment. Few cases have been found in the rectum, none of which was associated with HIV or Epstein-Barr virus (EBV) (5-7).

Se describe y comenta un caso de linfoma primario de Burkitt localizado en la región anal, eventualidad como se sabe extremadamente rara, en un paciente de 38 años de edad portador de HIV, al demostrar la histopatología y la inmunohistología la presencia de un Epstein-Barr, virus asociado al linfoma de Burkitt.

Combinando la quimioterapia, la terapia virostática y el tratamiento quirúrgico, en tanto se le practicó al paciente una resección abdomino-perineal del recto, o lo que es lo mismo, una amputación recto- anal abdomino-perineal, se ha conseguido un resultado satisfactorio.

Report of a case

A 38-year-old African farmer from the southern part of Rwanda presented at the Surgical Department of the University Hospital of Butare with the symptoms of fecal incontinence, weight loss, and a rapidly growing anal tumor over six weeks. The clinical findings showed cachexia and an 8-cm x 13-cm anal tumor (Fig. 1). Because of fecal incontinence and necrotization of the tumor, the odor was unbearable.

Sphincter function was lost and rectoscopy showed infiltration of the whole anal canal. Although the linea dentata was not distinguishable, only the very lowest part of the rectum se-
Figure 1.—Thirty-eight-year-old African HIV+ patient with a fast-growing anal Burkitt’s lymphoma.

Emed to be infiltrated by the tumor. Normal rectal mucosa was seen 4 cm from the distal tumor edge. There was infiltration of the perianal epidermis. Adenopathy and other signs of metastasis were not evident. The patient was anemic with a hemoglobin of 9.2 mg/ml, which is not unusual for this region. Two HIV tests [HIV check, enzyme-linked immunosorbent assay (ELISA)] were both positive. Other signs of a manifest AIDS exacerbation were not observed. There was no available technology for a CD4 count or estimation of viral load. A biopsy of the tumor revealed a malignant lymphoma with a high percentage of mitosis. Adequate chemotherapy and antiretroviral drugs were not available and affordable in Butare for the patient at that moment. Under these circumstances and because of the patient’s suffering, a clinical decision to perform an abdominoperineal resection was made.

Surgery showed a normal abdominal cavity without lymphomas or liver metastasis. There was tumor infiltration in only the lowest part of the rectum and the lateral pelvic floor. Total mesorectal excision with descendosigmoidia was performed. The perineum had to be excised widely with parts of the levator muscles to resect the tumor in sano. Closure of the pelvic floor and suture of the perineum was possible without tension. The patient recovered quickly from the operation and the wounds healed without complications. The colostomy was dressed with a locally fabricated system consisting of glue and a simple plastic
bag. The patient was happy to be able to eat and digest again without bothering his family with the odor that had precluded normal social life.

The histologic finding from light microscopy performed by the Pathologic Institute of the University of Butare showed all the typical signs of Burkitt’s lymphoma. Resection lines were free of tumor. The sphincter muscle was completely destroyed and the lower rectum and the perineal skin were infiltrated. This diagnosis was verified by Butare’s academic partners at the University Hospital in Mannheim (Germany), which also performed immunohistologic staining. The hematoxylin and eosin staining showed the typical «starry-sky» pattern with sheets of monomorphic neoplastic lymphoid cells and interspersed with histiocytes. Giemsa staining revealed tumor cells with deep basophilic cytoplasm, round nuclei with prominent basophilic nucleoli, and numerous mitotic figures. Cellular apoptosis was frequent (Fig. 2). In situ hybridization for EBV early RNA (EBER) showed positive viral transcripts in the nucleus of tumor cells (Fig. 2, inset). At the interdisciplinary tumor board of Butare further che-

Figure 2.—Characteristic starry-sky pattern with sheets of monomorphic neoplastic lymphoid cells and interspersed histiocytes (arrows) in anal Burkitt’s lymphoma. The tumor cells have round nuclei with dense chromatin and multiple small nucleoli. Note also apoptotic figures (arrowheads). Hematoxylin and eosin; x 200. Inset: Nuclear transcripts of Epstein–Barr virus early RNA in nuclei of tumor cells (black). In situ hybridization of fluorescein isothiocyanate conjugated RNA complementary to EBV early RNA. Magnification x 400.
motherapy was discussed, but because the patient could not afford further chemotherapy or antiviral therapy, he was discharged without supplemental treatment. Eight weeks after discharge the patient showed up with a generalized lymphadenopathy and progressing weakness. Within two days he fell into a coma and died.

Discussion

Burkitt’s lymphoma (BL) accounts for 1-2 percent of all cases of non-Hodgkin’s lymphomas (NHL) in the general population but for as many as 35 percent among HIV-infected populations. One percent of African HIV+ adults develop BL but most of the patients show cerebral or visceral BL (8-12). The classic facial BL is not an AIDS-associated tumor in Africa (13). Although EBV is often associated with malignant lymphomas in HIV+ patients, this association seems to be less frequent in HIV+ patients with BL (6, 14, 15). Nevertheless, in this case an association of EBV with the lymphoma was confirmed by in situ hybridization of EBV early RNA. The histologic and immunohistochemical results showed the characteristic signs of BL. Analysis of the typical translocations t(2;8) or t(8;22), however, was not possible under the circumstances in rural Rwanda.

An important differential diagnosis of BL includes a large-cell immunoblastic lymphoma. The tumor cells in this entity, however, are larger with more abundant and less basophilic cytoplasm. Nuclei have one prominent, centrally located nucleolus. Also, nuclear pleomorphism is seen and the starry-sky pattern is not apparent. Most of the visceral manifestations of BL are found in the stomach (2). A few cases of colonic BL are described, mostly in the upper colon and only in a single case in the rectum (1, 7). Primary anorectal lymphomas are rare and are usually found in immunocompromised patients (16, 17). Anal BL, as described here, is a rare event. In 12 major studies that included a total of 1043 cases of primary gastrointestinal lymphomas, there was no reference to anal BL (6). In our opinion the term «anal Burkitt’s lymphoma» is justified in this case by the fact that more than three-fourths of the tumor grew below the lower rectum and had infiltrated the whole anus.

Treatment of visceral BL is the same as for other locations. Standard treatment is chemotherapy, in which several combinations of drugs are considered effective. Cyclophosphamide, doxorubicin, vindesine, bleomycin, and prednisone (ACVBP) (18) or cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) (19, 20) are chemotherapeutic drug combinations with high response rates. Most patients with HIV-associated NHL benefit as well from low-dose as from standard or high-dose chemotherapy with less toxicity (11, 20). After a week of chemotherapy, tumor mass reduction of 75 percent can be expected (1). The response rate is lower in HIV+ patients compared with that in HIV- patients, with a median survival time for HIV+ patients of approximately seven months, and
with a long-term survival rate of only 15 percent (8, 10).
It is proven that antiretroviral therapy (ART) decreases the incidence of HIV-associated tumors, and ART is recommended in the treatment of manifest BL as well (20-23).
Surgery is inevitable in cases of BL complications or is used as palliative treatment when chemotherapy is not available. In our case, the anal sphincter was completely destroyed. In addition, surgical reduction of the mass of the large abdominal BL before chemotherapy seems to improve survival rate (24).
In Butare the cost of a major operation is approximately $40 U.S. The cost of chemotherapy in combination with the obligatory antiretroviral therapy is over $1,000 U.S. For our farmer, like for most citizens of Rwanda for whom the average daily income is less than $1 U.S., chemotherapy and ART were not only unavailable but were also unaffordable. In spite of the poor prognosis, surgery was the only plausible intervention.
With the persistence of the AIDS epidemic, an increased incidence of anal malignant tumors can be expected. Especially in Africa, anal BL may be a more common diagnosis in the future. Because of the high costs, adequate treatment will be reserved for only a small number of patients.

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