Gastrointestinal stromal tumor in a HIV positive patient in Kenya

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Abstract

The Human Immunoodeficiency Virus (HIV) epidemic has brought with it additional challenges of resurgence of previously rare medical entities. Gastrointestinal Stromal Tumour (GIST) is the most common mesenchymal or nonepithelial tumour in the gastro intestinal tract, and more so now with the advent of HIV co-morbidity. We present a case of a 62 year old lady with a long standing history of gastrointestinal (GI) symptoms who ended up being diagnosed with GIST and HIV co-morbidity. Surgical resection of the tumour and retroviral suppressive therapy was initiated with a good outcome. A discussion of GIST in a HIV positive individual is presented herein to increase awareness among clinicians, to heighten their index of suspicion when presented with a similar case. It is also important to thoroughly investigate patients with similiar presentation as Kaposi’s Sarcoma in the gastrointestinal tract can also mimic GIST. To our knowledge this is the first reported case of GIST comorbidity with HIV in the Eastern Africa region. Similar other cases of GIST have been documented such as that of a male HIV positive patient who presented with malignant GIST of the esophagus in Texas, USA.

INTRODUCTION

Human Immunodeficiency Virus (HIV) infection is epidemic in sub-Saharan Africa. At the end of 2010, globally there were about 34 million people living with HIV (WHO report, 2012). Of these, there were an estimated 23.5 million cases living in Sub-Sahara Africa. In the same year, low and middle income countries had about 6.65 million HIV infected persons on antiretroviral medicines (ARVs) and of these, 5.06 million (76%) are based in sub-Sahara Africa (WHO, 2012). In Kenya, December 2010 found 1.6 million persons living with virus with about 432,621 on ARVs (NASCOP, 2012). The low coverage of ARVs to those eligible, mean we often see Late Presenters in Africa; thereby our patients come to us with unusual medical conditions at their first presentation. There are a myriad of these HIV related immunosuppression associated diseases that went heretofore unrecognized.

Gastro-Intestinal-Stromal Tumours (GISTs) account for 1-3% of gastrointestinal tumours (Behazin, N. S and Katz J) and are the most commonly known mesenchymal tumours of the GI tract. GISTs are usually found in the stomach or small intestine but can occur anywhere along the GI tract and rarely have extra-GI involvement (Zhao X and Yue, C). In USA, there are an estimated 5,000-10,000 new cases (Univ Chicago) are reported each year. Data from the East African region is scarce.

This case study documents the presentation and management of a 62 year old, HIV immunocompromised woman with GIST.

Patient and Method

A 62 year old female patient presented with acute-on-chronic upper abdominal pain over a period of 6 months and diarrhea on and off for 1 year. Over the previous 3 months, she had experienced bloody loose motions intermittently, despite use of various treatments given at a rural clinic. In addition, she had also lost a total 15 Kilograms progressively over a period of 3 months and was treated severally for peptic ulcer disease with variable improvement. By the time she sought medical
advice from us, her symptoms had progressed considerably. She was experiencing intermittent abdominal pain and vomiting for about one month. Symptoms would subside on an empty stomach.

On physical examination, she was dehydrated, markedly pale. We also elicited vague supra-umbilical tenderness without guarding. Her stomach was dilated and palpable; however no distinct masses were palpated. Bowels sounds were normal. Examination of other systems was unremarkable.

Investigations done were as follows: Hemoglobin-6gms/dl (with an iron deficiency peripheral blood film picture; white blood cell count- 5.2 x10^9/l (lymphocytes 47.4%, neutrophils 29.2%); Urine analysis – ketonuria 1+ (due to dehydration); Stool – positive for Occult blood, No ova/cysts, Helicobacter Pylori Antigen- negative; abdominal ultrasound showed a vague mass arising from the stomach with non-specific gastric fullness. Computerized Tomography (CT) of the abdomen was advised. This was done and it showed a 7 by 7 cm pedunculated exophytic mass arising from the greater curvature of stomach and highly suggestive of GIST (Figure 1); Tumor Markers- CEA, CA-19, CA 125 all within normal limits; Chest X-ray – Normal findings; In the light of the iron deficiency in an adult with a gastric mass coming from an area with high HIV sero prevalence, an HIV test was indicated. Thus a rapid ELISA HIV test was done and it was found to be Positive. This led to called for further delineation of HIV stage of illness. CD4 lymphocyte count was found to be a markedly low 14 cells/mm³; the viral load being 2.3 million copies per cu mm³. Liver Function Tests were Normal; Renal Function Tests: Urea and Electrolyte, Creatinine were all Normal; Upper GI Endoscopy showed gastritis and a sub mucosal mass with inconclusive biopsy on histopathological evaluation (HPE).

![Figure 1. CT scan abdomen showing GIST tumour (arrowed)](image)

![Figure 2. GIST tumour (Peri-operatively exposed)](image)

![Figure 3. Peri-operative excision of tumour cut surface](image)

![Figure 4. Partial gastrectomy with excised tumour in kidney dish](image)
Results

A diagnosis of GIST in a HIV positive, immunocompromised woman was made and treatment commenced with combination antiretroviral medicines (ARVs); Tenofovir, Emicitabine and Efavirenz. She also received intravenous fluids, multiple blood transfusions to build her hemoglobin up to 13 g/dL. Other medicines that she received were Esomeprazole, Domperidone and Hyoscine-N-butyl bromide.

Once the patient was stable, a laparotomy was performed on 29th November 2009 that revealed a firm vascular pedunculated 7 by 7 cm tumor arising from the greater curvature of stomach. There was no obvious infiltration of the tumor into adjacent tissue. Also no lymphadenopathy, peritoneal or liver metastases were seen.

A partial gasterectomy was done (See Figures 2, 3, 4). Histopathological Cytology showed spindle cell tumour with nuclei showing mild pleomorphism and open chromatin pattern with blunt edges. Occasional mitotic figures seen, approximately 5/10 high power field were seen. Tumor cells were negative for glycogen on special stain (PAS+/D). Resection margins were 3 cm clear. Immunohistochemistry showed positive CD 117 and CD 34. Alpha smooth muscle actin and S-100 were negative. This confirmed GIST with clear resection margins.

Patient recovery was slow, but uneventful. She regained 10 kilograms over the next 4 months and feeding well with no adverse symptoms. Six weeks later, the viral load was undetectable (less than 20 copies/mm³) and CD4 count had risen to 459 cells/mm³. She was retained on ARVs after healing from the surgical wounds. Two years after surgery (Aug 2011), she was doing well and remains adequately viral suppressed and maintaining good immune reconstitution.

DISCUSSION

Gastrointestinal stromal tumors were initially thought to arise from smooth muscle cells and previously classified as Leiomyomas or leiomyoblastomas. Histologically, they appear to arise from the muscularis propria and most likely arise from the cells of Cajal which are autonomic nerve-regulated gastrointestinal pacemaker cells that regulate intestinal motility (Fletcher et al, Kindblom et al and Sircar et al) and express the Kit (CD 117) protein (Townsend). The Kit protein is detected using immunohistochemistry and can reliably distinguish GISTs from true smooth muscle neoplasms. These receptors are positive in 95% of cases. Most GISTs (70-80%) are also positive for CD34, a haematopoietic progenitor cell antigen.

The incidence of GIST is found most commonly in the stomach (40%) and small intestine (30%). Other GI sites include the duodenum (9%), omentum (7%), colon (4%), rectum (5%) and esophagus (2%). The male: female ratio of GIST is equal (1:1:1) with highest incidence in 5th-7th decades.

Most recorded instances of GIST have not described co morbidity with HIV infection (DeMatteo et al). However, like in our case, Padula et al described a rare case of malignant GIST in the esophagus of a HIV positive male patient that resulted in an extremely unusual metastatic site that has not been reported for GISTs. Castronovo G et al also reported young patients presenting with GIST and HIV co morbidity. Also Kubben FJ et al. reported the case of a young AIDS patient that presented with GIST in a rare site; the small intestine. In this case the patient had also previously suffered from GIST with Epstein - Barr virus (EBV) infection. The possible pathogenic role of EBV in GIST remains to be established (Castronovo et al).

With the advent of accelerated HIV sero prevalence in our region, the increasing occurrence of previously rare malignancies and/or rare disease manifestations should heighten clinician’s index of suspicion. That said, all suspected cases of GIST in HIV immunosuppression should be investigated for Kaposis’s sarcoma of the gastrointestinal tract as this, too, has been shown to mimic GIST (Zoufaly et al).

Clinical manifestations depend on location and size of tumor and are often non-specific. Common symptoms are those of dyspepsia causing indigestion, bloating, vague global abdominal pain, gastro intestinal bleeding and a palpable mass (rare). Metastasis occurs often to the liver, rarely lymph node and almost never to lungs. Often it is not detected until very late in the disease process. Unresponsive treatment for dyspepsia in a patient who is immunosuppressed, as in our case, ought to elicit a high index of suspicion and should lead to aggressive investigation to determine causality.

Investigations include Ultrasonography, CT scan with contrast, magnetic resonance imaging (MRI) and FDG-PET Scan (Fluorine 18 fluorodeoxyglucose). The latter is highly sensitive, but access is limited and unavailable in our resource constrained setting. Since the tumour grows intramurally, the true extent of the neoplasm is best assessed with contrast enhanced CT. Typical features reveal exophytic, large, hyper vascular masses that are often heterogeneous because of necrosis, hemorrhage or cystic degeneration. Often, tumour vessels can also be seen. Ulceration or fistulisation to GI lumen are common features. Up to 50% of patients present with metastasis mainly in liver and/or peritoneum.

Surgery is the principal mode of treatment that is curative for localized, resectable primary disease and with the goal of obtaining a margin-negative resection to include en-bloc resection of adjacent organs if involved by direct extension. Some patients present with locally advanced disease, or localized extensively spread disease that can only be resected by a functional
compromising surgery. Five year survival is 50-65% after complete surgical resection and less than 35% with incomplete resection or metastasis.

GIST is potentially malignant and is more aggressive with a tendency to metastasize in the presence of HIV co-morbidity. Benign gastric GISTs occur more frequently than malignant ones at a ratio of 3:5. Approximately 30% of GISTs are clinically malignant, and a substantial number of patients with apparent radical surgery will relapse with intra-abdominal spread presenting as multiple tumour nodules. Distant metastases most commonly spread to the liver followed by lung and bone in decreasing frequency (Kubben et al). Metastatic likelihood is given by size of tumour, visible mitotic activity, mixed cellularity and male sex (Townsend). According to WHO classification of tumors of 2000, our index case would be classified as having low-grade (Kubben et al) while the recently consensus approach of 2002 documented by Fletcher el al would classify her as having intermediate risk of malignancy (Fletcher et al).

Though our index patient has remained asymptomatic and recurrence free for the past two years, we still continue to carry out regular surveillance to look for possible recurrence. The co-morbid HIV disease makes it easier to follow her up as her HIV status requires 3-6 monthly check ups. Follow up imaging looks for increase in development of new lesions.

Most recurrences are within the first two years, presenting as local disease frequently associated with liver metastases. Other common patterns of failure include peritoneal recurrences. Salvage surgery to resect recurrent disease has not been demonstrated to improve survival after complete surgical resection ranging from 32% to 63%.

Until recently, there was no good adjuvant therapy for GISTs. Radiation therapy has not proven to be effective in their management, and only 5% of tumours respond to doxorubicin-based cytotoxic chemotherapy. The only efficacious agent is Imatinib mesylate which is approved for use in CD117-positive unresectable and/or metastatic GISTs. Its response rate ranges from 50-60%, with 54% of patients exhibiting partial response (Zoufaly et al). For responders, treatment with Imatinib results in dramatic tumour shrinkage and markedly improves long term survival of GIST patients. Response to Imatinib typically takes several months, but changes are visible within one month of commencing treatment.

In the light of HIV co-morbidity, if recurrence occurs in our patient we intend to commence patient on Imatinib therapy. Complete resection of the tumor with negative margins and no evidence of spread informed our decision to withhold Imatinib therapy in the meanwhile.

In conclusion this case was presented to heighten clinician’s index of suspicion for GIST in HIV epidemic settings when confronted by patients with diverse GI symptoms irrespective of age or gender. Thorough laboratory and radiologic investigation will also assist to rule out other possible diagnoses such as Kaposi’s sarcoma. Early diagnosis increases chances of good treatment outcomes.

References


19th Edition 2012
Accessed March 2012