HIV associated malignancies presenting as acute pancreatitis: a case series

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Introduction

Pancreatic malignancies may present as acute pancreatitis (AP) in 2% of cases. The malignancies are diagnosed at initial presentation or over a varying period thereafter. Non-pancreatic malignancies may also be associated with hyperamylasaemia. In HIV-positive patients, there is an association with AIDS defining malignancies (Kaposi’s sarcoma, high grade B-cell non-Hodgkin’s lymphoma). The advent of highly active antiretroviral therapy (HAART) has seen a decline in the overall incidence of Kaposi’s sarcoma and non-Hodgkin’s lymphoma, and an increase in non-AIDS defining tumours. This case series aims to describe the pathological spectrum of tumours detected in combined prospective AP cohorts accrued over the last two decades from a high HIV-endemic region.

Methods

Two prospectively collected datasets (2001 to 2010 and 2013 to 2015), whose primary analysis was to study the outcomes of hyperlipidaemia in AP and the effect of HIV infection on the predictors of severity in AP, respectively, were used to identify those with pancreatic and extra pancreatic tumours. Demographic, clinical, investigative, and pathology details were collected and presented. The diagnosis of pancreatitis was by clinical criteria plus an amylase or lipase of ≥ 3 times the upper limit of normal, urine amylase > 1000 U/L, or evidence of AP on CT scan or at surgery. In the initial period, HIV infection and CD4 counts were documented or evidence of AP on CT scan or at surgery. In the initial period, HIV infection and CD4 counts were documented or evidence of AP on CT scan or at surgery. In the initial period, HIV infection and CD4 counts were documented or evidence of AP on CT scan or at surgery. In the initial period, HIV infection and CD4 counts were documented or evidence of AP on CT scan or at surgery. In the initial period, HIV infection and CD4 counts were documented or evidence of AP on CT scan or at surgery. In the initial period, HIV infection and CD4 counts were documented and presented.

Results

A total of 628 and 238 patients had AP in the first and second periods, respectively. Of these, 17% (106) and 38% (90) were HIV-positive, respectively. Tumours were detected in two patients from the first period and five patients from the second period. Table 1 describes the clinical presentation, diagnostic modalities used and pathology details of the malignancies from the two periods. In the first period 48% (51) of the HIV-positive patients had CD4 counts of...
Table I: The clinical presentation, diagnostic modalities used and pathology details of the malignancies from the two periods

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Symptomatic period (days)</th>
<th>Amylase level serum (urine) U/L</th>
<th>CD4</th>
<th>Cholestasis*</th>
<th>Presumed aetiology</th>
<th>Tumour diagnostic modality</th>
<th>Tumour type and site</th>
</tr>
</thead>
<tbody>
<tr>
<td>First cohort</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>m</td>
<td>7</td>
<td>396</td>
<td>13</td>
<td>no</td>
<td>Didanosine</td>
<td>Percutaneous biopsy</td>
<td>Renal cell/limb Kaposi</td>
</tr>
<tr>
<td>42</td>
<td>m</td>
<td>21</td>
<td>653</td>
<td>269</td>
<td>no</td>
<td>Tumour HOP</td>
<td>Percutaneous biopsy</td>
<td>Lymphoma</td>
</tr>
<tr>
<td>Second cohort</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>f</td>
<td>30</td>
<td>2265 (1374)</td>
<td>36</td>
<td>yes</td>
<td>Cotrimoxazole</td>
<td>EUS</td>
<td>Lymphoma</td>
</tr>
<tr>
<td>41</td>
<td>f</td>
<td>7</td>
<td>376</td>
<td>211</td>
<td>yes</td>
<td>Tumour HOP</td>
<td>EUS</td>
<td>Lymphoma</td>
</tr>
<tr>
<td>38</td>
<td>f</td>
<td>30</td>
<td>113 (3963)</td>
<td>170</td>
<td>yes</td>
<td>Tumour HOP on HAART</td>
<td>Percutaneous biopsy</td>
<td>Lymphoma</td>
</tr>
<tr>
<td>47</td>
<td>f</td>
<td>21</td>
<td>188**</td>
<td>119</td>
<td>no</td>
<td>Idiopathic</td>
<td>Endoscopic biopsy</td>
<td>Gastric Kaposi</td>
</tr>
<tr>
<td>34</td>
<td>m</td>
<td>Unknown</td>
<td>468 (5577)</td>
<td>3</td>
<td>yes</td>
<td>Tumour ampulla on ampullary biopsy</td>
<td>ERCP biopsy</td>
<td>Periampullary Kaposi</td>
</tr>
</tbody>
</table>

HOP – head of pancreas
*Cholestasis – 2 or more of the following criteria: bilirubin ≥ 21 mmol/l, γ Glutamyl transferase ≥ 78 U/l, alkaline phosphatase ≥ 121 U/l/HAART – highly active antiretroviral therapy
** Diagnosis of acute pancreatitis made on clinical and CT scan criteria

less than 200 cells/mm³ (mean 220 cells/mm³), and in the second period there were 30% (27) (mean 335 cells/mm³).

The number of patients on HAART in each period was 60% and 59%, respectively. No tumours were diagnosed in the HIV-negative patients. The tumours were predominantly diagnosed by CT scan and EUS. In the first period, 179 CT scans were performed (60 HIV-positive and 119 HIV-negative), and in the second period, 33 CT scans were performed (16 HIV-positive and 17 HIV-negative). Most patients were younger than 40 years, and symptom duration ranged from 7 to 30 days. Five patients with malignancies had CD4 counts less than 200 cells/mm³. Three of the four patients with non-Hodgkin’s lymphoma (NHL) involving the head of the pancreas had associated cholestasis. One patient with Kaposi’s sarcoma (KS) and renal cell carcinoma died within 3 months of presentation. Two lymphoma patients died shortly after presentation, at 2 and 8 weeks, while the outcomes of the others who were referred for oncological therapy are unknown.

Discussion

This case series provides insight into the clinical presentation of HIV associated malignancies that will be encountered while managing patients with AP. In this dataset, cross sectional imaging was only performed in patients with diagnostic doubt or severe disease potentially resulting in an underestimate of the number of patients harboring tumours. In this sizeable, combined cohort there were no patients who had tumours of a pancreatic exocrine cell lineage. Previous studies have reported variable frequencies of pancreatic malignancies associated with AP. In a population-based study in the US, there is a reported association of AP with all-types pancreatic cancers of 0.15% in 945 253 patients in the period from 2002 to 2005, and 0.26% in 1070792 patients in the period from 2009 to 2012 (p = < 0.001) suggesting either an increase in incidence or better detection. In a series reporting on the corollary, 24 (13.8%) of 174 patients operated on for pancreatic cancer presented with AP. In the same study, hyperamylasaemia without clinical pancreatitis was observed in a further 17 patients (9.8%) with pancreatic cancers. This is in stark contrast to another case series of 302 patients with pancreatic cancers in which only 3% (10) had prior AP.

Primary pancreatic lymphoma (PPL) is rare, and the clinical and diagnostic criteria includes a predominant mass involvement of the pancreas with lymph node spread confined to the peripancreatic region. A systematic review of 107 eligible papers on PPL from 2001 to 2020 yielded 266 patients. Information on diagnostic procedures was available in 224. Sixty-eight (30.3%) were diagnosed on percutaneous biopsy, 39 (17.4%) with endoscopy, 33 (14.8%) with FNA, and 26 (11.6%) at surgery. Of the 218 patients with a complete dataset, 56 (26%) presented with AP. The predominant histological subtype was diffuse large B cell lymphoma (56%) in the age above 18 years, and Burkitt lymphoma (52.4%) in the age group below 18 years. Two of these patients were immunosuppressed following renal and pancreatic transplants. The HIV status of these 218 patients was not reported in the systematic review and the association with HIV infection is confined to case reports.

In our case series, all the cases were NHL in HIV-positive patients, although NHL has been reported as a cause of AP in HIV-negative individuals. The frequencies of non-exocrine pancreatic malignancies in our study was 0.5% in 866 in the overall cohort, and 2% in 196 of the HIV-positive cohort.

Several non-pancreatic cancers of the kidney, ovary, cervix, lung, adrenal phaeochromocytomas and multiple myeloma are known to secrete amylase. In the present series, one of the patients presented with stage four renal cell carcinoma in which was diagnosed by CT scan following symptoms of AP that persisted beyond one week. Kaposi’s sarcoma (KS), a malignancy of the vascular endothelium, is found in the skin and other organs. Human Herpes virus 8 is established as an important factor in the development of KS irrespective of HIV status. In a Tanzanian study of 248 patients with KS, 49% had AIDS; 12 (3.1%) involved the viscera (4 rectal, 6 intestinal and 2 gastric). In the present series, the KS lesion at the ampulla of Vater was thought to be the cause of the pancreatitis and the extra pancreatic lesions were thought to be incidental findings.
Three of the seven patients were on HAART and showed features of treatment failure with all having CD4 counts less than 200 (CD4 counts of 3, 13 and 170 respectively). The rest of the patients were below the threshold for HAART in 2014. This reveals that there are patients not on HAART despite advanced HIV infection. This low number of patients on HAART (less than two thirds), in combination with treatment failure, is likely to result in persistence of AIDS defining malignancies.

**Conclusion**

In these combined cohorts of patients with AP, it is notable that cancers of pancreatic exocrine cell lineage were not observed, regardless of HIV status. However, routine CT scan based on clinical grounds rather than routinely may have resulted in under detection. Despite this limitation, HIV-positive patients with a low CD4 count presenting with AP and cholestasis, are most likely to harbour a PPL. In this group of patients more liberal use of cross-sectional imaging and endoscopic ultrasound is indicated to evaluate for an AIDS defining malignancy as potential aetiology.

**Conflict of interest**

The authors declare no conflict of interest.

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**Ethics**

Ethical approval for the analysis was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, BE222/11.

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