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Ulcerative Colitis in Sub-Saharan Africa: Challenges of Management in a Low-Income Setting

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Inflammatory bowel disease (IBD) has traditionally been associated with high-income countries, and the highest prevalence is still found in countries such as the US and the UK.[1] Available evidence now points to a rising incidence in newly-industrialised countries in regions including east and south Asia, South America and Africa.[2] A growing IBD disease burden represents many challenges for healthcare systems in low-income countries, including the need to establish and maintain diagnostic facilities such as endoscopy units. Accessing treatment can be problematic for patients due to a lack of experience of IBD diagnosis and management amongst physicians and also to scarcity of specialist drugs. IBD patients often require treatment with immunosuppressive agents, and costly biological agents have now become a routine part of IBD care in high-income settings.

In low-income countries such as Zambia, the cost of biological agents including anti-TNF drugs is prohibitive for most patients and the majority are treated with sulfasalazine while a few patients have required

treatment with azathioprine and methotrexate. One of these patients, who developed severe complications while taking azathioprine and sulfasalazine treatment, is discussed in the case report below. There is a pressing need as case numbers rise to put systems in place to improve diagnosis and management of IBD in low-income settings.

Case Report

A middle-aged Zambian man presented to the gastrointestinal clinic at a tertiary hospital in Zambia with a 16-month history of chronic watery diarrhoea having previously visited two other hospitals. At one of these hospitals, he had undergone a colonoscopy which showed pancolitis and biopsies confirmed UC. He had no other major comorbidities and was HIV seronegative. The patient had no family history of bowel disease and had not travelled or lived abroad.His symptoms initially resolved with high dose prednisolone. At the time of first consultation he was taking 20mg prednisolone and was started on sulfasalazine 500mg BD. Serology was negative for HIV and hepatitis B surface antigen. He continued to experience increased stool frequency despite increasing the dose of sulfasalazine and ongoing treatment with oral steroids and underwent repeat colonoscopy which revealed pancolitis with a raised lesion in the descending colon suspicious for colorectal cancer. He was admitted to hospital and treated with high dose intravenous steroids (hydrocortisone 100mg QDS) for 1 week. Outpatient review by a surgeon was arranged with a view to possible colectomy.

Histology results from his repeat colonoscopy showed chronic changes associated with inflammatory bowel disease (basal plasmacytosis, marked crypt architectural distortion, crypt abscesses, and active colitis with neutrophils infiltrating the lamina propria). The biopsies taken from the lesion in the descending colon showed low-grade dysplasia. The patient was resistant to the idea of undergoing surgery, particularly when told this would involve having a stoma formed, and was reviewed by a surgeon who advised him to continue with conservative management. He continued to open his bowels 5-6x per day, and was started on azathioprine 2mg/kg and advised to come for weekly review following this with weekly full blood count and liver function tests. Thiopurine methyltransferase (TPMT) testing could not be carried out prior to starting azathioprine as this test is not available locally.Two weeks after starting azathioprine, the patient's full blood count results showed: Hb 11.0g/dL, White Cell Count 4.04 x109/L, Lymphocyte 1.22 x109/L. Liver function tests were as follows: ALT 20.1 IU/L, AST 15.9 IU/L, Albumin 23.3 g/L.Shortly after this, the outpatient clinic was closed due to the COVID-19 pandemic.

When the patient was next reviewed after three months had elapsed, during which time he had continued to take azathioprine,he had developed skin lesions consistent with Kaposi sarcoma (KS) (see **Figure 1**). Unfortunately no blood results were available at this time. The patient expressed the intention of going to his village for traditional medicine and was subsequently lost to follow-up.

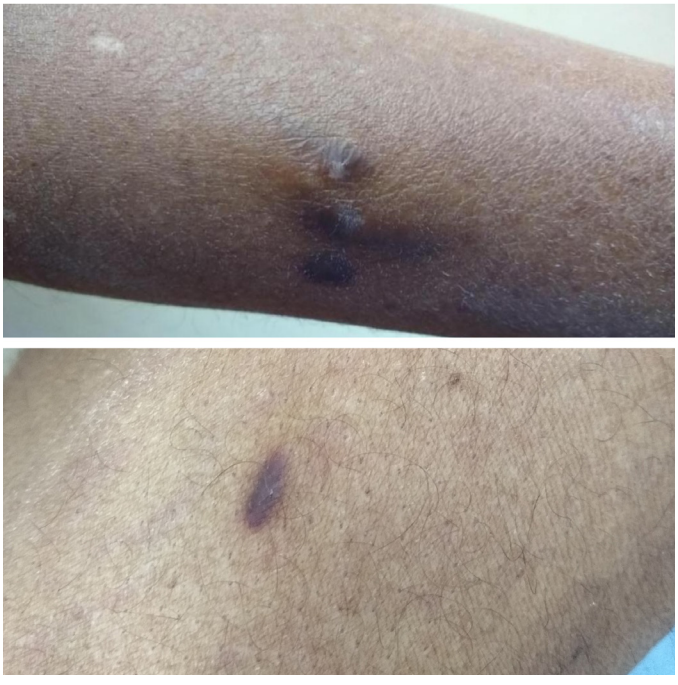

Figure 1: The patient had bluish-black nodular skin lesions (top image) and violaceous macular lesion, both in keeping with Kaposi sarcoma.

Discussion

Although there is no definite haematological evidence of immunosuppression in this case as full blood count results were not available at the time of the last consultation, it seems likely that this patient was immunosuppressed. Iatrogenic KS in patients with IBD treated with azathioprine as seen in this case appears to be a rare phenomenon, with the majority of cases reported being in male patients who were taking a combination of corticosteroids and azathioprine.[3,4] No previous case reports of KS secondary to azathioprine were identified from the African continent. Kaposi sarcoma is associated with human herpesvirus 8 (HHV8) and is the most common cancer seen in HIV seropositive individuals. In all patients with IBD where immunosuppressive drugs are indicated, screening for risk factors including HIV and viral hepatitis is vital. This is particularly true in sub-Saharan Africa given their endemicity in this region. Although the patient in this case report had been screened for HIV and hepatitis B at the time of diagnosis, ideally testing would have been repeated prior to starting azathioprine.

Low Grade Dysplasia

This finding in the setting of a patient with UC is a cause for concern and UK guidelines for management of dysplastic polyps in a patient with UC recommend either endoscopic resection of the polyp or surgical management.[5] In this case, the polyp looked suspicious for colorectal cancer although biopsies showed only LGD, and this was in the context of pancolitis, hence ideally the patient would have undergone colectomy. This was discussed with the patient who was reluctant to consider the idea of surgery, particularly with regards to stoma formation and affordability of ongoing stoma care. Outcomes from colorectal resection have been shown to be significantly worse in low-income countries. Although there is no published data pertaining to surgical outcomes specifically in patients with inflammatory bowel disease in Africa, one study of global variation in anastomosis and colostomy formation in patients undergoing left-sided colorectal resection found that 30-day postoperative mortality rates were 3 times higher in low-income countries (as defined by the United Nations Human Development Index).[6] Another study of complications of stomas in a tertiary hospital in Tanzania found a complication rate of 25.7% following colostomy formation, which is similar to rates found in studies from high-income countries, however post-stoma closure complication rates were high at 63.4%[7]. From a patient perspective, managing a stoma in a low-income country is challenging as they are likely to bear the financial burden of stoma care themselves, and this was a barrier cited by the patient in this case report when discussing surgery.

Impact of the COVID-19 pandemic

COVID-19 has had a significant impact on health systems globally and on management of chronic diseases, with healthcare providers attempting to reduce the volume of face-to-face interactions with patients through use of telemedicine and apps. For example, 13.2% of respondents in a recent survey of health care practitioners caring for IBD patients during the pandemic reported using apps to record patient-reported outcomes and communicate with patients.[8] For the case reported here, COVID-19 clearly impacted on patient care as follow-up and monitoring for complications of treatment had been disrupted. Mobile phone health approaches have been used previously to some effect in the management of chronic disease in low-income settings, for example, to improve concordance with antiretroviral medication for HIV in patients in Cameroon.[9] Mobile phone technology could be used for follow-up of patients with IBD on immunosuppression, with the patient relaying blood results to the supervising physician for review, and consultation could take place via voice or video call. This approach has begun to be utilised in our clinic following the case reported here.

Conclusion

Management of IBD, particularly of patients who are immunosuppressed, presents multiple challenges in a low-income setting like Zambia. Some of the challenges highlighted by this case include patient and physician barriers to surgery, and difficulty in monitoring due to

distance of the hospital from the patient's home and the current COVID-19 pandemic. As the incidence of IBD has been shown to rise in line with the demographic transition, it is vital that health care systems in low- and middle-income countries address these challenges in order to prepare for the inevitable increase in case numbers.

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