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Primary HIV Infection as an Unusual Cause of Neutropenia in Crohn's Disease: A Case Report

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Authors' contributions

This work was carried out in collaboration between all authors. Author YAA developed the idea and wrote the manuscript, author GW developed the idea and wrote the manuscript, author SRT wrote and reviewed the manuscript, authors DL and SH reviewed the manuscript. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Although primary human immune deficiency virus (HIV) infection is a well described entity, it is frequently misdiagnosed or underdiagnosed. This has been attributed to the non-specific clinical features at presentation, inadequate history taking and a low index of suspicion by practicing clinicians. Haematological abnormalities are a recognised feature of HIV infection and may present in the form of pancytopenia or isolated cytopenias. One of the cardinal features of HIV seroconversion is leucopenia, however primary HIV infection as a cause of neutropenia and lymphopaenia in Crohn's disease, has to our knowledge, not been described in the medical literature. We present a case of profound neutropenia in Crohn's disease secondary to acute HIV sero-conversion illness.

Keywords: Crohn's disease; neutropenia; primary HIV infection; HIV sero-conversion; azathioprine.

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1. INTRODUCTION

Since its initial description in 1985 the diagnosis of primary human immune deficiency virus (HIV) infection remains a challenge in clinical practice [1]. Primary HIV infection, also known as HIV sero-conversion sickness or acute retroviral syndrome, encompasses all acute and recent HIV infections (within 6-12 months of exposure) [1]. This disease entity is often misdiagnosed or underdiagnosed, primarily due to the non-specific presenting features of the illness, inadequate history taking or a low index of suspicion by clinicians [2]. Haematological abnormalities are a recognised feature of primary HIV infection and typically present as either a pancytopenia or isolated cytopenias. The incidence of neutropenia varies from 5 to 10 percent in the early phase, to as high as 50 to 70 percent in the advanced stage of the infection [3]. HIV sero-conversion illness should thus be considered in the work up of any patient with unexplained neutropenia or lymphopaenia.

Crohn's disease (CD) is a form of inflammatory Bowel Disease (IBD) which may affect any part of the gastrointestinal tract in a discontinuous fashion from mouth to anus, most commonly the terminal ileum. CD is a life-long disorder which frequently follows a progressive and destructive course resulting in irreversible GIT damage. Over the past decade, there has been an evolution in treatment paradigms with conventional immunomodulators such as the thiopurines azathioprine and 6-mercaptopurine now being introduced far earlier in the disease course, in an attempt to change the natural history of CD. Unfortunately these drugs carry an appreciable risk of neutropaenia; especially in subjects with thiopurine methyl transferase (TPMT) mutations [4]. The use of thiopurines is the commonest cause of neutropenia in CD. However neutropenia secondary to HIV sero-conversion has not previously been described in CD. In this case report we describe a middle age male with longstanding CD whose work up for neutropenia demonstrated primary HIV infection as the aetiology.

2. CASE REPORT

The subject in question is a 53year old unemployed male, first diagnosed with ileocaecal and perianal CD in 1985. He is a long standing smoker. He also has a history of pulmonary tuberculosis treated in 1997 and chronic obstructive pulmonary disease. During the course of his illness he has undergone multiple surgical resections of his terminal ileum and caecum as a result of recurrent episodes of partial small bowel obstruction. As a consequence of severe, refractory perianal disease he underwent an abdominoperineal resection in 2004 and currently has a sigmoid end-colostomy. Although his compliance with medical therapy has been poor in the past he has been receiving azathioprine without side effects since January 2010. His TPMT genotype testing excluded common mutations. He has subsequently been in clinical remission.

He presented to our clinic in 2012 with a 5 day history of watery non-bloody diarrhoea. He denied having any concurrent abdominal cramps, fever, nausea, vomiting, or weight loss. He also described a week history of odynophagia and painful oral ulcers. There was no recent travel history of note. He did however admit having unprotected sexual intercourse three weeks before this presentation.

On examination he was afebrile with a temperature 36.5℃, he was not pale and there were no features of jaundice or pedal oedema. On further examination he had sunken eyes and reduced skin turgor in keeping with dehydration. He also had multiple painful oral aphthous ulcers. On examination of his abdomen mild generalised tenderness was noted and his stoma bag contained large volumes of greenish watery stool. Perianal examination revealed scarring as well as an active sinus with minimal drainage. There was no abscess present. Cardiovascular, respiratory, and neurological examinations were unremarkable.

Our initial concern was that he was having an acute flare of CD, however this was ruled out on radiological investigations, as well as a colonoscopy via the stoma which showed quiescent CD.No pathogens were identified on stool analysis. Blood cultures were negative and chest and abdominal x-rays were unremarkable. At this point we had a very low index of suspicion for primary HIV infection as the cause.

An initial complete blood count was unremarkable except for mild leucopenia with a white cell count (WBC) of 3.6×10^9/l (4.00-10.00). His baseline renal function tests were in keeping with dehydration and pre-renal failure; with a urea of 22.1 mmol/l (2.6-7.0) and a creatinine of 189 umol/l (64-104).His CRP was elevated 19.9 mg/l (0.0-5.0).He was initially managed with empiric antibiotics and intravenous rehydration.

On repeat blood investigations 3 days after admission his leucopenia was much worse with a reduction in all white cell lines. His total WBC was $1.9x10^9$/l (4.00-10.00), his neutrophil count was 1.29(2.00-7.50), monocytes count was 0.04 (0.18-0.8), and his lymphocyte count was 0.53 (1.00-4.00). His platelet count was normal. His electrolyte profile had normalised following rehydration.

The initial concern was that these abnormalities were secondary to the use of azathioprine and the drug was discontinued. However given that these findings were also suggestive of HIV sero-conversion, an HIV test was requested. The HIV Antigen/Antibody and ELISA were weakly positive; however the viral load was exceedingly high (552240 copies/ml) confirming acute sero-conversion. His CD4 count was 517 cells/ml. In consultation with our haematology unit, a bone marrow biopsy was deemed unnecessary, as the diagnosis of primary HIV infection was undisputed and the neutropenia would likely be transient. Anti-retroviral therapy (ARV) was not initiated. Over the following 10 days his haematological parameters rapidly improved and all white cell lines normalised. Table 1 shows serial monitoring of his WCC during admission. He was restarted on azathioprine successfully 3 months after seroconversion and his neutrophil count remains normal. He is currently attending both the IBD and HIV clinics on a regular basis and his CD remains in clinical and endoscopic remission.

3. DISCUSSION

Acute retroviral syndrome as a cause of neutropenia in CD has not previously been described .Here we report features of acute sero-conversion illness in a patient with long standing CD on azathioprine.

In primary HIV infection up to 40-90% of patients will develop acute retroviral syndrome which usually coincides with high levels of viremia and the host's initial immunological response [5]. Symptoms occur 2-6 weeks after exposure and usually last 4 days, but may persist for as long as 10 weeks. The formation of HIV-1 specific antibodies marks the completion of seroconversion, and these are generally detectable within 3-12 weeks [6,7]. The clinical features are non-specific and may mimic other clinical conditions. Multiple organs can be affected, resulting in a broad spectrum of symptoms and signs [8]. Constitutional symptoms of fever, malaise or fatigue are common. Patients may also suffer anorexia, weight loss or a maculopapular skin rash. As seen in our case, mucosal membrane ulcerations are common, as is diffuse lymphadenopathy. Gastrointestinal symptoms such as nausea, vomiting and diarrhoea are well described, while a productive cough is the main pulmonary manifestation. Neurological and psychiatric disorders such as meningitis or encephalitis are not uncommon. In addition liver involvement with raised transaminases have also been described. One of the commonest abnormalities seen in acute HIV infections are however haematological in nature, in particular leucopenia, neutropaenia, lymphopenia and thrombocytopenia. These are usually transient and tend to resolve rapidly [5,6].

Making the diagnosis of primary HIV infection is imperative as it represents a period of extremely high levels of viremia and genital shedding of the virus. Individual in this phase have a 10-fold increased risk of transmission, which will be reduced if a timely diagnosis is made [10,11]. However this remains a challenge in clinical practice. In one cohort of 46 patients with primary HIV infection, 85% sought medical attention but only 25% received the correct diagnosis. In another study, primary HIV infection was missed in 48% of patients at first presentation, suggesting a low index of suspicion [12,13,14]. How best to manage acute HIV infection remains unclear although some studies suggest benefit of early ARV treatment, others show no difference in outcomes [15]. This supports the decision to withhold therapy in this case at diagnosis.

Table 1. Total WBC and differential values on admission

Date	Total WBC	Neutrophils	Monocytes	Lymphocytes	Eosinophils
4/12/11	1.87	0.83	0.14	0.6	0.08
5/12/11	2.52	0.6	0.1	1.7	0.1
6/12/11	3.12	1.06	0.17	1.45	0.12
9/12/11	4.77	2.00	0.24	2.16	0.17

4. CONCLUSION

Primary HIV infection may be misdiagnosed,hence should be considered an important differential during work up for neutropenia in IBD.

CONSENT

Written informed consent was obtained from the patient for the publication of this case report.

ETHICAL APPROVAL

It is not applicable.

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We do acknowledge the contribution of the infectious disease unit in the management of this patient.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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