Case Report

Clofazimine Induced Enteropathy – A Case Highlighting the Importance of Drug Induced Disease in Differential Diagnosis

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ABSTRACT

A patient on treatment for multibacillary leprosy for the past three years, presented with episodes of abdominal pain. Since the patient improved with conservative management, clofazimine induced enteropathy was considered as a remote possibility. A review of the mucosal biopsies showed macrophages with crystal-storing spaces consistent with clofazimine deposition in the duodenum. This case highlights the need to consider and investigate drug-induced disease as part of the differential diagnosis.

INTRODUCTION

Adverse reactions to drugs are responsible for a significant number of hospital admissions with reported rates ranging from 0.3% to as high as 11%.1 They often mimic other diseases and therefore go unrecognised. We would like to illustrate the importance of considering drug induced disease especially for drugs given long term such as clofazimine.

CASE REPORT

A 56 year old male patient diagnosed with lepromatous leprosy was started on multidrug regimen in January, 2002. He presented to the emergency department of a tertiary hospital in on April 2005, with symptoms of abdominal pain in the periumbilical and left hypochondrial regions, nausea, vomiting and anorexia. The pain had been present for the past two months and had increased in severity, two days prior to his presentation. He denied taking dapsone and had voluntarily discontinued rifampicin since January, 2005.

A CT scan of the abdomen revealed mid jejunal wall thickening, extensive mesenteric abnormality involving root of the small bowel mesentery, jejunal mesentery inferior to the pancreas showing septal thickening and lymphadenitis (Fig1).

Fig 1: CT Scan of the abdomen showing thickening of the jejunal loop

Gastroduodenoscopy revealed oedematous mucosa with blackish discoloration and reduced peristalsis from D2 segment of the intestine. Biopsies were reported as chronic atrophic gastritis. The patient improved significantly with conservative management. Clofazimine induced enteropathy was considered as one of the possible differential diagnoses and the drug was discontinued.

In June, the patient presented again to the emergency room with a similar history of abdominal pain which was more severe in intensity than the first episode. Taking into consideration the clinical findings, radiology, endoscopy and biopsy findings, the differential diagnosis included ischaemic bowel disease, acute pancreatitis, vascularis, abdominal tuberculosis, lymphoma and clofazimine induced abdominal symptoms. The patient once again improved with conservative management without the need of any surgical intervention. This led us to pursue the possible diagnosis of clofazimine induced enteropathy.

The biopsy slides were reviewed at this point. The original duodenal biopsy showed clusters of macrophages in the deep

Fig 2: Duodenal biopsy with aggregates of vacuolated macrophages in the deep mucosa between crypt bases and the muscularis mucosa. H&E*400
mucosa with empty crystal-storing spaces in their cytoplasm (Fig 2). The gastric biopsy showed chronic gastritis but no evidence of these macrophages. Review of the second biopsy showed only occasional vacuolated macrophages in the duodenal mucosa. As clofazimine crystals are known to be dissolved in organic solvents and the vacuoles appeared empty, special stains were not done on the duodenal biopsy, but tissue from the first biopsy with numerous macrophages was processed for ultrastructural study. Ultra-thin sections stained with uranyl acetate and lead citrate were viewed under a Philips EM201C electron microscope. The cytoplasm of the macrophages was seen to have numerous oval to elongated crystal spaces, some with pointed ends (Fig 3) consistent with crystal storing histiocytosis induced by clofazimine.2

**DISCUSSION**

The patient was treated with clofazimine 50mg daily with an additional 300mg, once every month, for three years. From literature, there is evidence that symptoms can appear after the intake of clofazimine in total doses ranging from 600mg per week5 to 600mg per day.4 The time frame for developing gastrointestinal side effects has been reported from anywhere between one month5 to eight years after onset of therapy.3 Gastrointestinal side effects are even known to occur three months after stopping a 15 month course.2 In our patient it was more than three years after starting clofazimine that he first developed gastrointestinal symptoms which then recurred two months after stopping clofazimine. Clofazimine accumulates in the tissues and tends to cause symptoms for a prolonged period after its discontinuation.

From the 16 reports available worldwide of enteropathy caused by regular intake of clofazimine,4 the diagnosis depended on a strong suspicion from the clinician along with a conclusive report from the pathologist. The radiologic and endoscopy findings in our case led the clinician to suggest a primary diagnosis of mesenteric ischaemia with an impending gangrene. The next step to confirm the diagnosis if there was a worsening of the symptoms would have been an exploratory laparotomy. In this patient, the symptoms gradually improved on conservative management with no surgical intervention. Therefore the possibility of bowel ischaemia was ruled out. The rare diagnosis of clofazimine induced enteropathy which simulates an acute abdomen was then subsequently considered.2 At this point of time, biopsy was reviewed which confirmed the presence of crystal storing histiocytosis.

From this case report, we wish to highlight the fact that physicians prescribing clofazimine should be aware that clofazimine enteropathy may be easily mistaken for other common causes of an acute abdomen and should be thoroughly investigated for pigment deposition with associated enteropathy. Not considering and investigating this could lead to unnecessary surgical interventions, as in 11 out of 16 reported cases described in literature. To conclude, this case highlights the need to keep in mind drug induced disease in any differential diagnosis.

**REFERENCES**