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Case Report

Eosinophilic Oesophagitis: A False Negative Result on Biopsy

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Introduction

Eosinophilic oesophagitis (EoE) is a chronic, relapsing, inflammatory disease which causes oesophageal dysfunction as a result of oesophageal epithelial eosinophilic infiltration [1]. Normally, the oesophageal mucosa contains no eosinophils. In EoE, the accumulation of eosinophils occurs, due to several factors such as regurgitation, allergens, atopic conditions and other pathologies, and results in damage to the oesophageal tissue, with fibrosis and scarring [2]. Prolonged, uncontrolled inflammation can result in irreversible stricture formation which may cause severe functional disability [3]. EoE is usually diagnosed on the clinical features and histological findings.

Case Report

A 24-year-old male presented with gradually worsening, severe dyspeptic symptoms of 3 months duration. He had regurgitation, burning type chest pain, nausea and occasional dysphagia. Initially, the patient was treated by a general practitioner with proton pump inhibitors with a minimum response. There was no history of diarrhoea or abdominal pain. No history of itching, fever, loss of appetite or loss of weight. He denied cough or a history of bronchial asthma. He had no travel history outside Sri Lanka and had never consumed any raw meat. He was an electrician who never consumed alcohol or other substances. He had no contact with pets or other animals.

On examination, he was haemodynamically stable. There was no lymphadenopathy, pallor, jaundice, skin rash or evidence of cutaneous larva migrans. He did not have a hepatomegaly or a splenomegaly. No swollen joints were present. Cardiovascular system and respiratory system were normal.

Table 01: Patient's investigations

Investigation	On Admission	After 2 weeks of treatment	After 1 month
Haemoglobin (g/dL)	14		
Platelets (10^3/µL)	379		
WBC (10^3/µL)	56	36	10.4
Neutrophils %	15		
Lymphocytes %	10		
Eosinophils % Absolute count	71 40,000/µL	17%	2%
Serum Creatinine (µmol/L)	88		
AST (U/L)	23		
ALT (U/L)	25		
CRP (mg/L)	75		
ESR (mm/1st hour)	14		
LDH (U/L)	450		
Sodium (mmol/L)	137		
Potassium (mmol/L)	4		
T. Bilirubin (umol/L)	5.5		
ALP(U/L)	88		
GGT(U/L)	98		
Albumin (g/L)	35		
Globulin (g/L)	37		
Trop I	Negative		
INR	1.1		
Retroviral studies	Negative		
Toxoplasma antibodies	Negative		
Toxocara antibodies	Negative		
pANCA/cANCA	Negative		
ANA	Negative		
Filaria IgM/IgG	Negative		
Chest X-ray	Normal		
X-ray sinus view	Normal		

Blood picture showed a marked eosinophilia with some degranular forms. The 2D echocardiogram showed no evidence of cardiac damage with an ejection fraction of 60%. Contrast enhanced CT chest and abdomen showed no significant pathology.

The gastroscopy showed evidence of diffuse oesophagitis and pan-gastritis. Biopsy specimens were obtained from the oesophagus, gastric body and duodenum during the endoscopy. The histology of all six biopsy specimens showed no evidence of eosinophil infiltration. Subsequently the patient was referred to the haematology team and a bone marrow biopsy was performed. Bone marrow biopsy revealed a reactive marrow with eosinophilia. Reverse transcriptase-polymerase chain reaction for the *FIP1L1-PDGFRA* fusion gene was negative.

The patient was initially started on mebendazole and diethylcarbamazine, empirically. Since the absolute eosinophil count and white blood cell count (WBC) was increasing it was decided to commence oral steroids after the endoscopy and bone marrow biopsy. He was started on a 40mg dose of prednisolone. Following steroids, the patients' dyspeptic symptoms significantly improved and were completely resolved by two weeks. We followed up the patient monthly with a full blood count and tailed off steroids in 8 weeks. Once the patient was off steroids, he presented with severe dyspeptic symptoms and was found have eosinophilia of 57% in the peripheral blood. Steroids were recommenced and tailed off slowly over 6 months. At one year, the patient was free of symptoms and blood eosinophils were in the normal range.

Discussion

Eosinophilic œsophagitis (EoE) was initially described in 1978 but was not recognized as a distinct gastrointestinal clinico-pathological entity until 1993 [4]. A population-based, long-term study from 1989 to 2009 showed an average annual incidence of 2.45 per 100,000 participants [5]. EoE occurs in two peaks, first during childhood and subsequently between the third and fourth decade with a male predominance [6].

EoE is diagnosed by clinical features, endoscopic manifestations and histological findings. To diagnose EoE the clinician should have a high degree of suspicion, especially in patients with chronic oesophageal dysfunction who have a past history of atopic conditions, symptoms that do not respond to anti-reflux therapy, peripheral eosinophilia and a family history of EoE. The diagnostic criteria for EoE have gradually evolved. According to ~~the~~ recently proposed criteria, EoE is diagnosed in patients having symptoms of oesophageal dysfunction together with least 15 eosinophils per high power field (or 60 eosinophils per mm^2) in an oesophageal biopsy performed after exclusion of all other causes of similar symptoms and oesophageal eosinophilia [7]. The presence of persistent oesophageal eosinophilia despite the patient taking high dose proton pump inhibitors is no longer considered a criterion for EoE [8].

A broad spectrum of endoscopic features have been described in EoE . A majority of the patients have a macroscopically normal oesophageal mucosa. A grading scheme based on loss of vascular markings, whitish exudates, oesophageal rings, linear furrows and strictures has been developed and validated [9,10].

The correlation between the histological findings and the clinical manifestations is poorly understood. This has been studied on several occasions. In some studies, the degree of oeosinophilic infiltration correlated with the severity of symptoms [11,12]. A retrospective study of 112 patients using clinical records revealed a lack of association between the clinical symptoms and the histological manifestations [13]. Apart from an eosinophil count of >15 hpf, other histological manifestations such as lamina propria fibrosis, papillary lengthening and basal zone hyperplasia can occur.

Generally 2–4 biopsies are recommended, to be taken from both ends of the oesophagus. Some studies show that a sensitivity of more than 99% can be obtained if a higher number of biopsies, such as 5–6 biopsies, are taken [14]. In our patient, we obtained 4 samples from the distal and proximal oesophagus and one each from the stomach and duodenum. All six samples did not show evidence of eosinophil infiltration. But the fact that the patient had severe symptoms of oesophageal dysfunction with a very high eosinophil count and that the symptoms resolved completely with steroids suggested the possibility of EoE despite the negative biopsy result. The diagnosis is further supported by the relapse of symptoms and eosinophilia when the patient was taken off steroids in 8 weeks. Data on such cases are extremely limited, the only similar case report being of a 63-year-old immunocompromised patient who was managed as EoE with a false negative biopsy and highlights the possibility of a “burn out phenomenon” seen in the late stage of the disease [15].

Conclusion

In patients being investigated for EoE, a high number of biopsy samples is mandatory to diagnose the condition accurately. More reports and studies are needed to conclude that a false negative biopsy could occur in EoE, as in our patient in whom oesophageal dysfunction symptoms completely resolved with steroids. It is also important to exclude all other causes of eosinophilia in such circumstances.

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