CASE REPORT

Oesophageal presentation of Crohn's disease

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SUMMARY

Crohn's disease (CD) is characterised by a transmural inflammatory process, which can affect any part of the digestive tract; however, CD with oesophageal presentation is rare. We report a case of a previously healthy young woman with symptoms of dysphagia, odynophagia, chest pain and weight loss, who presented oesophageal ulcers at upper endoscopy and whose histology revealed granulomatous oesophagitis. After complementary study, a mild ileocaecal involvement of CD was demonstrated. The patient became asymptomatic with proton pump inhibitor and a course of prednisolone. Mucosal healing was obtained after maintenance therapy with azathioprine. In the absence of extraoesophageal symptoms, oesophageal CD may be overlooked. CD must always be considered as differential diagnosis in the presence of oesophageal ulcers.

BACKGROUND

Crohn's disease (CD) is a chronic granulomatous inflammatory disease that may involve any area of gastrointestinal tract; however, oesophagus involvement is uncommon, with a prevalence of ~1.8% in adults.[1] Most of diagnosis of oesophageal involvement is made in patients with known CD having symptoms referred to the oesophagus.[2] Rarely is it the presenting feature of the CD.

CASE PRESENTATION

A 23-year-old white woman was referred to our outpatient unit after 12 consecutive days of odynophagia, dysphagia and chest pain. The patient weighed 60 kg and she had already lost 5 kg since her symptoms began.

She denied other gastrointestinal symptoms. There was no history of oral ulcers or fever.

Her medical history and family history were not contributing and she denied taking any medication.

Physical examination was unremarkable.

INVESTIGATIONS

Laboratory test results were significant only for mild C reactive protein of 13.1 mg/L (normal value: <3.0 mg/L).

Upper endoscopy revealed multiple ulcers with punched out appearance in the medium and lower oesophagus with normal surrounding mucosa, as seen in figure 1. The gastro-oesophageal junction, stomach and duodenum were normal.

Histological examination demonstrated oesophageal mucosa with areas of erosion and presence of epithelioid granuloma without central necrosis in lamina propria, as seen in figure 2.

Ziehl-Neelsen stain, immunohistochemical staining for cytomegalovirus (CMV), herpes simplex virus (HSV) and PCR for *Mycobacterium tuberculosis* DNA were negative in biopsy specimens. HIV serology also came up negative.

Chest X-ray was normal and Mantoux test was negative.

DIFFERENTIAL DIAGNOSIS

The differential diagnoses that should be considered include gastro-oesophageal reflux disease, oesophageal carcinoma, viral infections (HSV or CMV), CD, sarcoidosis, tuberculosis, disseminated fungal disease, Behcet's syndrome and chronic granulomatous disease.[2–4]

OUTCOME AND FOLLOW-UP

She was followed up under close observation as outpatient and started pantoprazole 40 mg once daily with improvement of symptoms after 15 days of treatment.

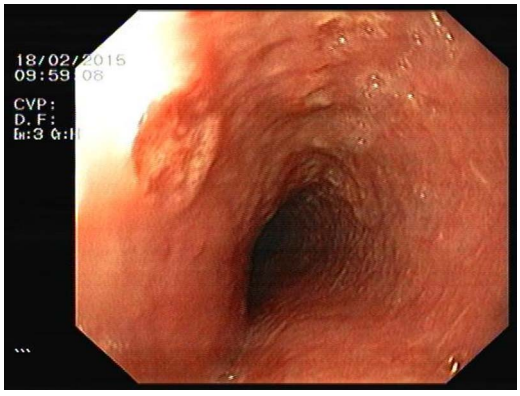

Figure 1 Oesophageal ulcers.

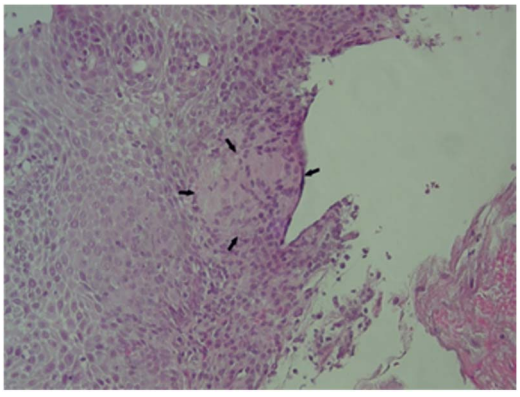

Figure 2 Microscopic examination of oesophageal mucosal specimens, arrows: granuloma.

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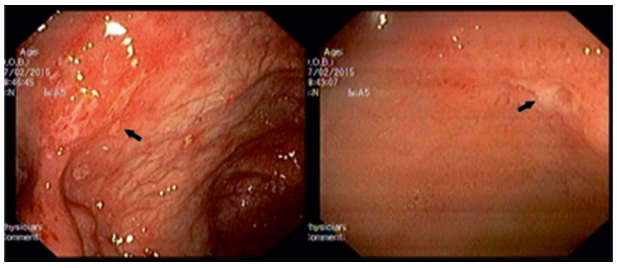

Figure 3 Erosions in caecum (left) and in the terminal ileum (right) at ileocolonoscopy.

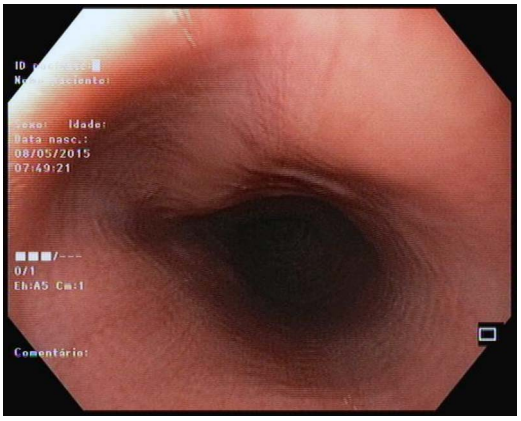

Figure 4 Oesophagus appearance at 12 weeks after treatment.

Following treatment, repeat upper endoscopy demonstrated the continuing presence of ulcers in the lower and middle oesophagus.

An ileocolonoscopy was performed which revealed superficial ulcers in the ascending colon, caecum and superficial erosions in terminal ileum, as seen in figure 3. Histological examination of terminal ileum biopsies revealed erosion, mild architectural distortion, mild decreased mucin secretory activity and marked expansion of the lamina propria by lymphocytic inflammatory infiltrate. The colon biopsies revealed mild decreased mucin secretory activity, focal Paneth cell metaplasia and intense lymphocytic inflammatory infiltrate. No granulomas were identified.

The patient underwent a complete investigation of the small bowel by MR enterography that revealed parietal thickening of the terminal ileum, with early hyperenhancement by the contrast product to an extent of ~10 cm. No complicated disease such as stenosis, fistula or intra-abdominal collections was observed.

In this context, the diagnosis of CD was considered and the patient was started on prednisolone 40 mg once daily tapering for 4 weeks and azathioprine 150 mg once daily with a full resolution of symptoms after a 1 week of treatment.

After 12 weeks of treatment, a repeated upper endoscopy revealed healing of the oesophageal mucosa, as seen in figure 4.

At present, she is asymptomatic, and under azathioprine 150 mg once daily.

DISCUSSION

The involvement of the oesophagus by CD is rare[2] and is even rarer to present as an initial manifestation of the disease,[3 5] because in the majority of cases the small bowel or colon involvement precedes oesophageal disease.[2] Few cases have been reported of isolated oesophageal CD;[2 6–9] however, there has been an increased number of reported cases since the widespread use of upper endoscopy.

Patients with oesophageal CD have symptoms related to their oesophageal involvement.[10] Dysphagia and odynophagia are the most common symptoms.[2 6] Other symptoms include heartburn and chest pain.[2] Up to 30% of patients have oral aphthous ulcerations[2 10] at the time of oesophageal CD symptom onset. Weight loss associated with these symptoms can be found.[3 6 11] Extra intestinal manifestations of CD are often present, including arthritis, uveitis, and erythema nodosum.[12]

Endoscopic findings of CD oesophageal involvement include ulcers or erosions surrounded by normal-appearing mucosa, and cobblestoning of mucosa.[13] The most common sites of involvement are the middle or distal oesophagus.[2 10]

A small percentage of patients may complicate with fistulas to the stomach,[14] respiratory tract,[15–22] or have stricture formation.[6 9 23]

There are no pathognomonic histological features of oesophageal CD. The most common histological finding is a lymphocytic infiltrate in the lamina propria, though this is not specific.[2]

Non-caseating granulomas are seldom detected,[1] possibly owing to the patchy nature of disease or the superficial nature of biopsies. Thus their presence is not strictly necessary for the diagnosis.

The management of oesophageal CD is not established owing to a limited number of heterogeneous cases and lack of clinical trials reported in the literature.

Proton pump inhibitor therapy has been shown to relieve symptoms,[2 24] similar to this case. However, in this case there was no improvement in the endoscopic findings. Proton pump inhibitors efficacy in mucosal healing has not been proven,[25] and there is no recommendation for proton pump inhibitor monotherapy.[1 12 26]

Similarly, there is no recommendation for topical treatment of oesophageal CD involvement. However, Rholl *et al*[14] reported a case of oesophagogastric fistula successfully treated with a liquid form of mesalamine suspension dose of 4 g daily, prednisolone (30 mg prednisone daily), and ranitidine suspension. Zezos *et al*[11] also reported a case of mucosal healing of oesophagus treated with swallowed aerosolised budesonide.

Oral systemic steroids are frequently used for oesophageal CD with most patients improving rapidly,[2 27] as has occurred in this case.

There are also reported cases of efficacy of thiopurines on patients with oesophageal CD.[2]

Antitumour necrosis factor therapy has been shown to be effective in severe[16 17 28–30] and refractory[30] oesophageal CD. As oesophageal CD portends a poor prognosis, the threshold for initiating anti-tumour necrosis factor therapy should be low.[26]

Endoscopic dilation may be indicated in cases of symptomatic oesophageal strictures.[2] Surgical resection may be needed in fistulas, refractory strictures, and disease refractory to medical treatment.[2]

Temporary enteral nutrition through percutaneous gastrostomy proved to be useful to complement medical therapy in two cases of oesophageal CD.[31]

In our case, prednisolone induction and azathioprine maintenance enabled a clinical and endoscopic remission.

D'Haens *et al* reviewed clinical and endoscopic follow-up of 14 patients with CD of the oesophagus. According to these authors, there are three patterns of evolution of CD of the

oesophagus: resolution of symptoms and lesions with no relapse during follow-up in 57.1% of cases (complete healing), persistent lesions despite treatment in 21.4% (persistent lesions), reappearance of symptoms and oesophageal lesions after initial resolution in 21.4% of cases (relapse).[27]

In conclusion, CD should be considered in the differential diagnosis of oesophageal ulcers, even in the absence of known CD.

Upper endoscopy should be performed in all patients with CD with oesophageal symptoms. On the other hand, routine upper endoscopy can also be useful in diagnostic work-up of all patients with CD in order to evaluate the extent of disease.

After a confirmed diagnosis of CD based on clinical, endoscopic, imaging, and histological findings, treatment should be personalised, taking into account the patient's symptoms, disease activity, course of disease, phenotype and complications.

Learning points

- Oesophagitis as an initial manifestation of Crohn's disease is rare.
- Crohn's disease should be considered as differential diagnosis in presence of oesophageal ulcers, even in absence of known disease.
- Treatment of oesophageal Crohn's disease should be tailored to each patient, such as co-medication with proton pump inhibitors and immunomodulators as optional therapy in an appropriate clinical setting.

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Contributors SM performed literature search and drafted the manuscript. MJM, JMR and JC critically revised the manuscript and approved the final version to be submitted.

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Reminder of important clinical lesson