Herpes simplex oesophagitis

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ABSTRACT

Herpes simplex oesophagitis (HSO) is uncommon and commonly occur in immunocompromised patients. Presentations can be nonspecific and endoscopic findings range from diffuse ulceration to localised oesophagitis commonly affecting the distal oesophagus. We report four cases of histologically proven HSO that we have encountered over the years in practice where the Human Immune-deficiency virus (HIV) infection is still uncommon. As the diagnosis requires histological confirmation, and given that the manifestations are variable from oesophagitis to ulcerations, the actual incidence may be underestimated as some cases are not biopsied.

Keywords: Oesophagitis, odynophagia, dysphagia, *Herpes Simplex Virus*

INTRODUCTION

Oesophagitis is most commonly due to gastro-oesophageal reflux disease (GORD). Infection is a rare cause and usually occurs in immune compromised individuals. Infectious causes include to *Herpes Simplex virus* (HSV), *Cytomegalovirus* (CMV) and Candida infections. [1, 2] Patients typically present with acute onset dysphagia and odynophagia, with or without oral and skin lesions. Systemic manifestations such as nausea, vomiting, fever and chills may present. We report four cases of Herpes Simplex oesophagitis (HSO).

CASE REPORT

CASE 1: A 68-year-old Malay lady was admitted with a-two-day history of dizziness and vomiting, a month history of loss of appetite, with consequent weight loss and myalgia. She has a background history of spastic paraplegia for more than 10 years, osteoporosis, hypertension, and recent cataract surgery on the left eye. She gave no history of fever, cough, shortness of breath, diarrhoea, constipation and other urinary symptoms. Due to her paraplegia and resultant lower limbs deformities, her movement were limited. She was only able to mobilise using her hands power in a sitting position. She was still to carry out most of her daily chores such as cooking and washing.

On examination, she was alert and afebrile with a blood pressure of 86/48 mmHg, regular pulse rate 100 per min, respiratory rate of 20 per min and SpO_2 100% on room air. There was pallor in the conjuctiva, oral mucosa looked dehydrated but no

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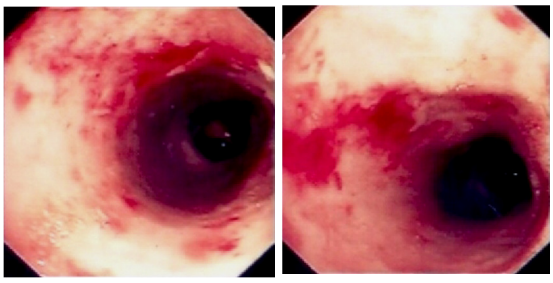
oral lesions were noted. Abdomen examination revealed mild epigastric tenderness without any rebound, guarding, masses and organomegaly. Musculoskeletal examination revealed bilateral lower limbs flexion contractures. She had a large infected sacral sore (Grade IV). The rest of the examination was unremarkable.

Laboratory investigations showed leukocytosis (25.4 x 10^9, with 93.9% neutrophils), anaemia (7.9 gm/dL), mild coagulopathy (prothrombin time [PT] 14.2 seconds, activated partial thrombin Time [APTT] 25.5 seconds and INR 1.25) and elevated C-reactive protein (7.87 mg/L). Liver profiles were normal except for severe hypoalbuminemia of 14 gm/L and hypoproteinemia of 46 gm/L. Electrolytes: Urea 11.9 mmol/L, Na 129 mmol/L, K+ 4.3 mmol/L, CL 97 mmol/L, Creatinine 62 umol/L; Iron studies: Iron <1.0 umol/L, transferrin 0.94 G/L; random glucose: 5.2 mmol/L; HbA_{1c} 5.4%. Pus culture was taken from the sacral sores.

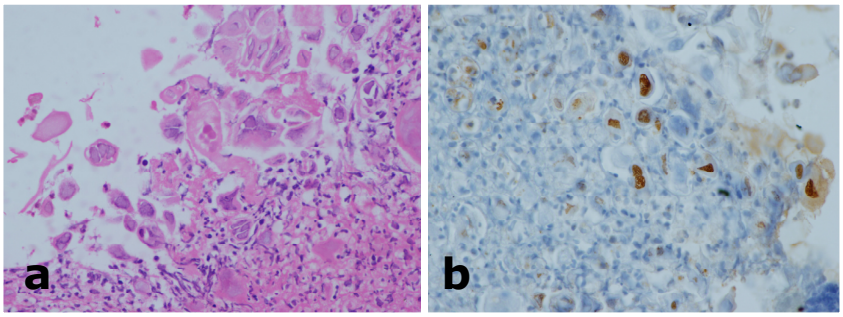
She was started on intravenous fluid and antibiotics (amoxicillin-clavulanic acid and metronidazole) to cover for sacral sore infection. The sacral sore was treated with dressing and intrasite gel. Sacral sore swabs isolated *Klebsiella pneumoniae*, *Proteus mirabilis* and *Bacteroides fragilis*, sensitive to the antibiotics prescribed. She was given blood transfusion and dietician input was obtained. Endoscopy to evaluate the anaemia showed severe oesophagitis with ulcerations in the proximal oesophagus, and erosive gastritis of (Figures 1). Oesophageal biopsies showed inflammatory changes and Cowdry inclusion bodies of HSO (Figures 2). On revisiting the history, the patient admitted that she also had some dysphagia. She was treated with intravenous acyclovir for a total of ten days after which she reported improvement with her appetite and dysphagia. Screening for HIV infection was negative.

CASE 2: A 65-year-old man presented with a three day history of epigastric pain and recurrent coffee ground vomiting. His past medical history included transitional cell carcinoma of the bladder diagnosed one month earlier, hypertension, benign prostate hypertrophy, cerebrovascular accident with left hemiparesis, subtotal thyroidectomy in 2008 and excision of verrucous carcinoma of the nasal bridge 2007. His current medication were enteric coated aspirin 100 mg daily, perindopril 6mg daily, thyroxine 125 mcg daily, ranitidine 150 mg twice daily, iron sulphate 200 mg three times daily, folic acid 5 mg daily, fluvoxamine 100 mg at night and lactulose 10 mg twice daily. He had not received any intervention with regards to his treatment for transitional cell carcinoma of bladder.

On examination, he was pale with a blood pressure was 155/100 mmHg, and a heart rate of 90 beats per minute. Examination of abdomen revealed mild tenderness in the epigastric region and per rectal examination revealed soft stool and irregular prostate.



Figs. 1: Endoscopy showing proximal oesophageal erosions and ulcerations.



Figs. 2: a) Histology slides showing inclusion (Cowdry) bodies of HSV (H&E stain magnification x60) and b) HSV stain (Magnification x60).

Blood investigations revealed HB of 10.6g/dl (normal range 12.5-16.3), WCC of 12.8 $x10^9$/L (normal range 3.6-10.2) and platelet of 252 $x10^9$/L (normal range 150-450). Her urea was elevated (22.4 mmol/L , normal range 3-9.2). Upper gastrointestinal endoscopy was performed the following day and it revealed severe erosive oesophagitis until proximal third of oesophagus. He was started on intravenous omeprazole 40mg twice daily. Biopsy of the oesophagus revealed an ulcerated squamous epithelium showing moderately dyskayocytics and nuclei showed multinucleation. Immunohistological stains showed positive reaction with HSV. However gastric biopsies are suggestive of intra-mucosal carcinoma. Test for HIV was negative. He was commenced on intravenous acyclovir 300 mg three times daily for five days. His vomiting persisted and he underwent laparotomy on day of his seventeen day of admission. Operative findings showed omental cake at antrum of stomach with tumour masses causing partially extrinsic compression at D3 duodenum. A gastrojejunosostomy was done to bypass the duodenal obstruction.

CASE 3: A 45-year-old lady presented two-day history of chest discomfort that was associated with odynophagia. She had been treated for chronic granulomatous mastitis treated with incision drainage. Before this, she had recurrent purulent discharge and was treated with a course of doxycycline. She was initially suspected to have doxycycline-induced oesophagitis. She also had cold sore ten days before presentation. Upper gastrointestinal endoscopy showed mid-oesophageal ulcerations circumferential scar. Biopsies taken from the ulcer edge revealed HSV inclusion bodies and also ischaemic changes. Testing for HIV was negative. Her symptoms improved with acid suppression therapy.

CASE 4: A 52-year-old man with diabetes mellitus and chronic hepatitis C presented with generalised weakness and passage of black stool in the previous few days. He was started on treatment for hepatitis C (Peg Intron 80 mcg weekly and ribavirin 1,000 mg daily) nine weeks previously, but had stopped two weeks before presentation. Monitoring of full blood count during treatment had shown mild drop of haemoglobin until before presentation when it showed haemoglobin 6.0 gm/dL with normal white cell and platelets count. Per rectal examination was normal and he was admitted for transfusions. An upper gastrointestinal endoscopy showed a small mid oesophageal ulcer on the left wall (Figure 3), grade B oesophagitis (Los Angeles classification) and a small heterotopic gastric mucosal

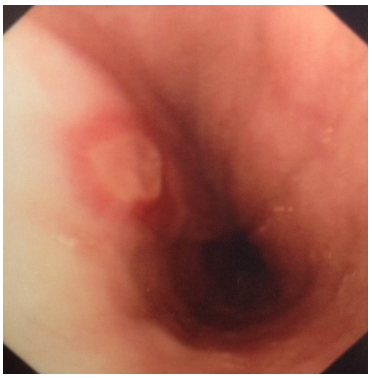


Fig. 3 : Endoscopy showing a small ulcer on the left lateral wall of the mid oesophagus.

patch of the proximal oesophagus. There was no ulcer seen in either the stomach or duodenum. Bleeding was presumed to be from the mid oesophageal ulcer but the treatment for chronic hepatitis C probably contributed to the anaemia. The patient was treated with acid suppression. Upon review two weeks later revealed that the biopsies taken from the ulcer base was positive for HSV inclusion bodies. Testing for HIV was negative. His symptoms settled on follow up.

DISCUSSION

Infectious oesophagitis is most commonly observed in immunocompromised and is extremely rare in immunocompetent hosts. [1-3] Abnormalities in host defense such as impaired T-cell lymphocyte function, impaired chemotaxis and phagocytosis, and neutropenia predispose an individual to opportunistic infections. [1-3] Altered immune function can be due to congenital or acquired immune deficiency (HIV and acquired immune deficiency syndrome [AIDS]), medications such as steroids or immunosuppressants post transplantations and cytotoxic agents used for treating cancers. [4] Poorly controlled diabetes mellitus and very old age can also predispose to these infections. [5]

HSV is well known to cause infectious oesophagitis in the immune-compromised patients, especially AIDS, solid organ and bone marrow transplants. HSO is generally considered rare in immunocompetent host. The infection may be primary disease or reactivation of a latent infection. HSO occurring immune-competent patients have been reported for both adults and children. [3, 6] Two of our patients were elderly with two others in the middle age groups. For the older patients, the risk factors were age, multiple comorbid conditions that included cancers, urinary system and an early gastric cancer (Case 2) and severe malnutrition (Case 1). Therefore, essentially both the older patients have factors predisposing an immune compromised state. For the other two younger patients, there were no definite risk factors apart for treatment for chronic hepatitis C (Case 4) resulting in anaemia with normal white cell counts. It is uncertain if the medications themselves had any contribution to the development of HSO. The other case (Case 3) did not have any risk factors. All our patients were negative for HIV.

HSO may manifests with dysphagia or odynophagia, heartburn and fever. [1-3] However, not all symptoms may be present or non specific. Other symptoms include myalgia and weight loss due to poor oral intake. Systemic manifestations such as nausea, vomiting, mild leucocytosis and herpetic vesicles on the nose and lips may be present. Bleeding and perforation may occur in severe cases but extremely rare. [7, 8]

The typical endoscopic appearance in

ulcers. Cobble-stoning can also be seen due to clustering of these lesions. However, HSO can also resemble oesophagitis of other causes such as GORD or medications related oesophagitis.

The diagnosis of HSO can be confirmed by histopathological studies or by viral culture of oesophageal biopsies from the ulcer edges. Biopsies from margin of ulcers will reveal ballooning degeneration, ground glass changes in the nuclei with eosinophilic intranuclear inclusions (Cowdry type A), and giant cell formation on routine stains. [10] Virus isolation by cell culture usually becomes positive within a few days and has been considered as the diagnostic 'gold standard'. However, PCR assays of HSV DNA in oesophageal tissue are more sensitive than viral cultures. [11]

HSO in immunocompetent individuals is usually a self-limiting disease, which resolves spontaneously within one to two weeks. [3] They may also settle without treatment. Treatment with acyclovir is well established in immunocompromised patient but not in immunocompetent host. [2, 3] Treatment may enhance healing and may prevent complications such as gastrointestinal bleeding and oesophageal perforation.

In conclusion, our four cases highlight the importance to consider HSO in patients presenting with oesophageal, with and without risk factors resulting in the immune system being compromised. Diagnosis typically require histology confirmation.

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