Oesophageal involvement in mantle cell lymphoma

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ABSTRACT

The stomach and small intestine are common sites for gut lymphomas, but oesophageal lymphomas are very rare. In mantle cell lymphoma (MCL), although multifocal gut involvement is seen, oesophageal involvement is uncommon. Gut involvement may be primary or secondary to systemic involvement. Multiple lymphomatous polyposis (MLP) is the intestinal form of MCL. Most cases of MLP occur in the elderly, usually over 50 years of age, and the presenting symptoms are abdominal pain, melaena, haematochezia and fatigue. In MCL, tumour cells typically express CD5 and cyclin D1 markers. Our patient presented with generalised lymphadenopathy, dysphagia and rapid weight loss. Upper gastrointestinal endoscopy revealed submucosal polypoid lesions in the oesophagus, stomach and duodenum. Histopathology and immunophenotyping confirmed MCL. Although MLP presenting as a primary MCL of the intestine has been described in the literature, our patient also had multiple intestinal polyposis (including the oesophagus) due to secondary involvement from systemic MCL.

Keywords: CD5, cyclin D1 markers, mantle cell lymphoma, multiple lymphomatous polyposis, oesophagus

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INTRODUCTION

The gut mucosa contains more lymphocytes than any other organs in the immune system. However, lymphomas involving the gastrointestinal (GI) tract are relatively uncommon. GI lymphomas can either be primary or secondary to systemic involvement, and usually present with a solitary lesion, although they occasionally have multifocal involvement.[1] While the stomach and small intestine are common sites for GI lymphoma, oesophageal and colorectal lymphomas are rare.[2] Mantle cell lymphoma (MCL) comprises 2.5%–7% of all non-Hodgkin's lymphomas (NHL), and GI tract involvement is seen in about one-fifth of the cases.[3] Multiple lymphomatous polyposis (MLP) is seen in the intestinal form of MCL.[2] Oesophageal involvement in MCL has seldom been described in the literature. We report the clinicopathologic features of a case of MCL.

Fig. 1 Photograph of the patient shows submandibular cervical lymphadenopathy (biopsy was taken from the right submandibular lymph node).

CASE REPORT

A 40-year-old woman presented to our hospital with painless generalised lymphadenopathy since 2006 (Fig. 1). She had dysphagia to solid food and significant weight loss for two years, and tinnitus for one year. The patient had no history of subacute intestinal obstruction, melaena, haematochezia, fever or night sweat. She had recently been transfused with two units of whole blood. The general examination revealed moderate pallor, cervical and bilateral axillary, and left inguinal lymphadenopathy. The Waldayer's ring was enlarged, and the systemic examination was noncontributory. The liver and spleen were not palpable.

Laboratory investigations revealed a normal liver function test, blood sugar, urea, creatinine, serum Ca^{2+}, Na^{+}, K^{+} and uric acid levels. Serum lactic acid dehydrogenase was elevated (1552 U/L). Hepatitis B surface antigen, antibodies to hepatitis C, and

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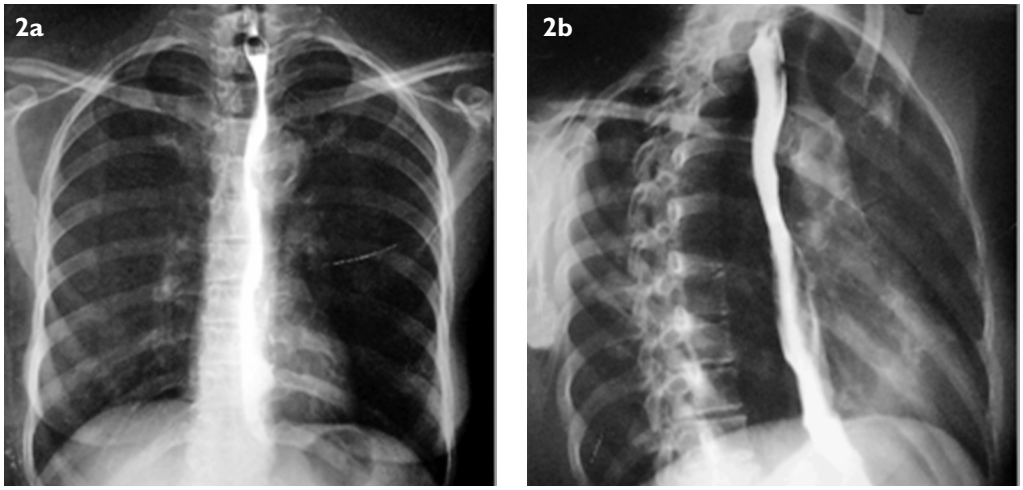

Fig. 2 (a) Anterioposterior view and (b) lateral view of barium swallow radiographs show a filling defect distal to the mid-esophagus.

enzyme-linked immunosorbent assay for human immunodeficiency (HIV) virus I and II were negative. The blood picture revealed haemoglobin 10.9 gm% and total leucocyte count 14,600/mm^3 (including neutrophil 83%, lymphocyte 10%, eosinophil 5% and monocyte 2%). Upper GI endoscopy showed exophytic polypoid submucosal lesions of the oesophagus involving approximately all quadrants of a 30–35 cm segment from the incisor teeth. The lumen was compromised and not well distended with air, and the stomach showed exophytic submucosal polypoid lesions.

In addition, the first portion of the duodenum was studded with multiple small exophytic polypoid lesions, although the cavity and lumen were preserved. A barium swallow revealed space-occupying lesions distal to the mid-oesophagus (Fig. 2). The patient had no features of colonic involvement and refused colonoscopy. Computed tomography (CT) imaging of her chest did not show any mediastinal lymphadenopathy. Ultrasonography of the abdomen revealed periportal, para-aortic and mesenteric lymphadenopathy. A cervical lymph node biopsy was conducted, and histopathology and immunhistochemistry confirmed NHL of the mantle-cell type. Tumour cells expressed CD20, CD5 and cyclin D1, and were immunonegative for CD3, CD10 and CD23. Biopsies from the oesophagus, stomach and duodenum confirmed MCL involvement. A diagnosis of MLP of the GI tract due to systemic MCL was made.

DISCUSSION

GI lymphomas commonly involve, in decreasing frequency, the stomach, followed by the ileum, jejunum and duodenum. This pattern mirrors the relative amount of normal lymphoid cells in these anatomic areas. Oesophageal involvement by NHL is extremely rare.

GI lymphomas are commonly diffuse large B-cell lymphoma or mucosa-associated lymphoid tissue lymphomas, but rarely MCL. Histologically, MCL is usually characterised by the monotonous proliferation of small to medium-sized lymphocytes,[4] the co-expression of CD5 and CD20, and cyclin D1 in the malignant cells in immunohistochemistry. MLP is characterised by multiple polypoid lesions involving long segments of the GI tract.[5] In a series of 31 cases of MLP by Ruskone-Fourmestraux et al, the colon and rectum were the most commonly affected parts (in about 90% of cases), followed by the small bowel, stomach and duodenum in 69%, 57% and 52% of the cases, respectively.[6] Although oesophageal involvement in MLP is uncommon,[6,7] interestingly, our patient had oesophageal involvement in addition to the stomach and duodenum.

MLP cases usually occur in elderly patients over 50 years of age, with a slight male preponderance. Symptoms of MLP include abdominal pain, diarrhoea, melaena, haematochezia, fatigue, and a possible palpable abdominal mass. Oesophageal symptoms are uncommon because of the rarity of its involvement in MCL. Our patient presented with dysphagia to solid food, decreased food intake, weight loss and fatigue, with a background of generalised lymphadenopathy, suggesting the possibility of oesophageal involvement.

The differential diagnosis of oesophageal symptoms in patients with NHL generally includes fungal or viral infection, therapy-related mucositis and reflux esophagitis, but not lymphomatous involvement. The diagnosis of lymphomatous involvement of the oesophagus is often overlooked due to a low level of suspicion. In the age of HIV infection, oesophageal lymphoma has also become an important, although rare, part of the differential diagnosis of oesophageal

symptoms in immunocompromised patients. Lymph node biopsy and biopsy of the intestinal polyps with immunohistochemistry aid in the diagnosis of MCL. Full thickness surgical biopsies of the intestine may be required, as deeper lymphoid infiltrates may be missed in superficial biopsies. Cytologic brushing may occasionally help in the diagnosis.

The treatment of MCL is unsatisfactory. CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) with rituximab is quite effective, and response to chemotherapy is seen in up to half of the MCL patients.[8] Large tumours should be resected because chemotherapy may lead to gut perforation. As MCL commonly occurs in the elderly population, stem cell transplantation is not feasible.

Lymphomatous polyposis of the GI tract is uncommon, and oesophageal involvement is very rare. MLP is usually described in the literature as primary MCL of the intestine; our patient, however, had polyposis of the GI tract due to secondary involvement from systemic MCL. Late presentation of our patient had resulted in diffuse gastrointestinal involvement. The poor socioeconomic and educational status of our patient coupled with the delay in proper diagnosis, had led to the advancement of the disease. Patients with systemic lymphoma with oesophageal and gastrointestinal symptoms must be evaluated early and carefully so as to exclude secondary involvement of the oesophagus and other parts of the intestine.

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