

## Collision tumour of the oesophagus: a challenge for histological diagnosis

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### Abstract

**An unusual case of mantle cell lymphoma metastasising to squamous cell carcinoma of the oesophagus, in a 62 year old Chinese man, is reported. A histological diagnosis based on examination of a small endoscopic biopsy specimen, in the absence of detailed clinical information, may be difficult, as the lymphoma component can be mistaken for reactive lymphoid infiltrate which is sometimes present adjacent to squamous cell carcinoma. Correlation with the clinical history, careful assessment of the subtle histological changes, and use of ancillary methods such as immunohistochemistry are most helpful in making the correct diagnosis. This case also illustrates further the possible occurrence of lymphomatous infiltrates surrounding other lesions in patients with a previous or concurrent history of lymphoma.**

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Various collision tumours, which are defined as the concrescence of two neighbouring independent neoplasms, have been described in the gastrointestinal tract. Examples may include squamous cell carcinoma and leiomyoma of the oesophagus,<sup>1</sup> adenocarcinoma and lymphoma of the stomach,<sup>2-7</sup> adenocarcinoma and carcinoid tumour of the stomach,<sup>8,9</sup> adenocarcinoma and lymphoma of the small intestine,<sup>10</sup> and adenocarcinoma and lymphoma of the rectum.<sup>11</sup> Many of these tumours were diagnosed on examination of the excised surgical specimens, with the second tumour being discovered as an incidental finding. Here, we describe a rare case of oesophageal "collision" tumour composed of squamous cell carcinoma and mantle cell lymphoma. The two components, however, were not truly synchronous primary tumours as the mantle cell lymphoma metastasised to primary squamous cell carcinoma of the oesophagus. To the best of our knowledge, this case is the first report in the literature of squamous cell carcinoma coexisting with malignant lymphoma in the oesophagus. Moreover, our case was initially diagnosed on the basis of endoscopic biopsy. The histological diagnosis of this lesion based on examination of a small biopsy specimen, in the absence of detailed clinical information, may be difficult. The malignant lymphoid component may mimic the reactive lymphocytic infiltrate which is sometimes present in the stroma

of ordinary squamous cell carcinoma of the oesophagus.<sup>12</sup> This is especially true for low grade non-Hodgkin's lymphoma, in which the cytological atypia of malignant lymphoid cells are subtle and may easily be missed.

### Case report

The patient, a 62 year old Chinese man, first presented to Queen Mary Hospital in 1991 with conjunctival nodules, hard palate mass, and bilateral cervical lymphadenopathy. Biopsy at that time revealed non-Hodgkin's lymphoma. Chest x ray, barium studies of the gastrointestinal tract, and a computed tomography scan of the abdomen did not reveal other sites of lymphoma involvement. Bone marrow examination was unremarkable. The clinical staging at that time was IIB. The patient was treated with nine monthly courses of cyclophosphamide (400 mg/m<sup>2</sup> orally for five days), vincristine (1.4 mg/m<sup>2</sup> intravenously) and prednisolone (100 mg/m<sup>2</sup> orally for seven days), and achieved clinical remission.

In 1995 the patient presented again with dysphagia and regurgitation. Solid food could still be tolerated, and there was no significant loss of weight or appetite. Physical examination was unremarkable and no superficial lymphadenopathy or organomegaly was found. Barium swallow showed an oesophageal lesion at the level of the T6 and T7 vertebrae. Upper endoscopy revealed a right nasopharyngeal lesion and a tumour growth at middle third of the oesophagus. Biopsy specimens of the right nasopharyngeal lesion and the oesophageal tumour revealed mantle cell lymphoma and mixed squamous cell carcinoma/mantle cell lymphoma, respectively. The previous biopsy specimens of conjunctival nodules and cervical lymph nodes were reviewed and showed similar features of mantle cell lymphoma. The patient was then treated with four monthly courses of intravenous cyclophosphamide (750 mg/m<sup>2</sup>), epirubicin (50 mg/m<sup>2</sup>), vincristine (1.4 mg/m<sup>2</sup>), and oral prednisolone (100 mg/m<sup>2</sup> for five days). The oesophageal malignant lymphoma apparently regressed on follow up endoscopy, although the carcinoma component was still present. The patient then underwent three-phase oesophagectomy. Intraoperatively, the oesophageal tumour was seen infiltrating into the left main bronchus. The subcarinal lymph node was enlarged. Histological examination of the resected specimen confirmed the presence of squamous cell carcinoma and residual mantle cell lymphoma. The postoperative course was uneventful. Further chemotherapy was planned after full convalescence.

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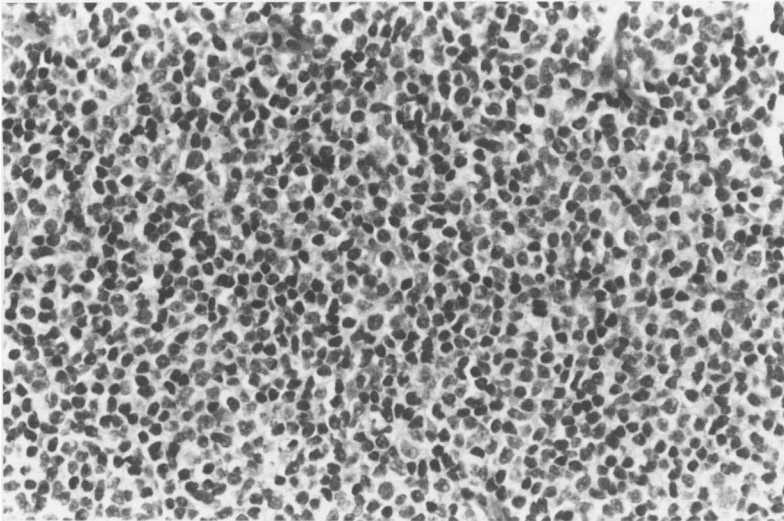


Figure 1 High power photomicrograph of the mantle cell lymphoma showing the subtle cytological changes. Note the irregular and occasionally cleaved nuclei containing fine chromatin. (Haematoxylin and eosin,  $\times 500$ .)

The initial, fresh oesophageal endoscopic biopsy specimen was submitted for examination. Half of the specimen was frozen for subsequent immunohistochemical studies and the other half was promptly fixed in 10% neutral formalin and embedded in paraffin wax. Sections, 3  $\mu\text{m}$  thick, were cut and stained with haematoxylin and eosin, Gordon and Sweets' silver, periodic acid Schiff, and methyl green pylonin stains. Immunohistochemistry was carried out on the frozen tissue using the Streptavidin-biotin complex technique for CD5 (Dako, Glostrup, Denmark), CD23 (Dako), immunoglobulins (IgD from Dako, IgG from Biotest Diagnostic, and IgM from Biotest Diagnostic),  $\kappa$  and  $\lambda$  light chains (Becton Dickinson), and a panel of B (CD19 from Becton Dickinson and CD22 from Dako) and T cell markers (CD3 from Becton Dickinson). The oesophagectomy specimen was also processed similarly after representative blocks were sampled from the fresh tissue. Macroscopically, the oesophageal tumour was an ulcerative growth, situated 6.5 cm proximal to the gastro-oesophageal junction, measuring 9 cm at its widest point.



Figure 2 Photomicrograph of the oesophagectomy specimen showing primary squamous cell carcinoma and residual mantle cell lymphoma. (Haematoxylin and eosin,  $\times 40$ .)

#### HISTOLOGY

Histological examination of the endoscopic biopsy revealed several tiny fragments of oesophageal mucosa with severe dysplasia of the surface squamous epithelium with focal suggestion of stromal invasion. In one of the tissue fragments, several clusters of lymphoid aggregates, composed mainly of a monotonous population of small lymphoid cells, were present. The cells had irregular nuclear membrane and scanty cytoplasm (fig 1). The cytological features were similar to those of the previous conjunctival and cervical lymph node biopsy specimens. Immunohistochemical studies showed that these lymphoid cells were positive for CD5, CD19 and CD22, but negative for CD3 and CD23. Surface IgD and IgM, as well as  $\kappa$  light chain restriction, were demonstrated. A diagnosis of squamous cell carcinoma of the oesophagus coexisting with mantle cell lymphoma was made.

The histological diagnosis was subsequently confirmed by examination of the oesophagectomy specimen. The excised specimen showed a moderately differentiated squamous cell carcinoma of the oesophagus with transmural infiltration. Keratin pearl formation was frequently found. Vague nodules of small malignant lymphoid cells were also present in the submucosa, muscularis propria and adventitial soft tissue, representative of residual mantle cell lymphoma (fig 2).

#### Discussion

Histological diagnosis of squamous cell carcinoma and lymphoma of the oesophagus based on examination of a small endoscopic biopsy specimen may be difficult, especially if the lymphoma component is of low to intermediate grade and detailed clinical information is not available. Assessment of the lymphoid component based on cytological atypia alone is subjective and may not be conclusive. The use of immunohistochemistry and, most importantly, correlation with the clinical history is necessary if the correct histological diagnosis is to be made.

In general, B cell non-Hodgkin's lymphoma is characterised by a monotonous population of malignant lymphoid cells, in contrast to the polymorphous cell population seen in reactive lymphoid infiltrate. Germinal centres with well defined mantle zones are not seen. As for mantle cell lymphoma,<sup>13</sup> the tumour cells are small to medium in size and contain irregular and occasionally cleaved nuclei, fine chromatin, small nucleoli, and scanty cytoplasm. The nuclei are paler compared with those of small lymphocytic lymphoma.

The tumour may grow in diffuse and sometimes vaguely nodular patterns. Hyaline deposits may be seen around small capillaries. Thick reticulin fibres forming a coarse alveolar network surrounding large solid group of tumour cells may also be found. The monotonous cell population, absence of germinal centre, and the subtle cytological changes raise the possibility of a diagnosis of B cell non-Hodgkin's lymphoma; subsequent investiga-

tions including immunohistochemical analyses must be carried out before the final conclusion is drawn.

Immunohistochemically,<sup>14-17</sup> mantle cell lymphoma, which is probably derived from follicular mantle lymphocytes,<sup>18</sup> is characteristically CD5 positive and CD23 negative. Other B cell markers, such as CD19, CD20 and CD22, are also positive. The tumour cells may also express surface immunoglobulin, usually IgM and sometimes IgD. The monoclonality of the malignant B cells can be confirmed by demonstrating light chain restriction. Unfortunately, some of these antibodies—for example, CD5 and CD23, are more suitable for cryostat sections; and the demonstration of light chain restriction is often not satisfactory on paraffin wax sections. In controversial cases, demonstration of immunoglobulin gene rearrangement by molecular biological techniques may be needed as a last resort.

The coexistence of squamous cell carcinoma and mantle cell lymphoma in this case is most likely coincidental, with unrelated aetiologies. The squamous cell carcinoma component is the primary, while the lymphoma represents a metastatic lesion, probably originating from the cervical lymph node. This is, however, in contrast to the truly synchronous primary lymphoma and adenocarcinoma of stomach, in which *Helicobacter pylori* may be of some aetiological significance.<sup>19-23</sup>

In summary, our case represents an unusual example of lymphoma metastasising to squamous cell carcinoma of the oesophagus. This poses a diagnostic challenge to histopathologists and further illustrates the importance of a detailed clinical history. Clinical histopathologists must alert clinicians to the possible occurrence of lymphomatous infiltrates surrounding other primary lesions in patients with a previous or concurrent history of lymphoma. This is especially true for those patients with lymphoma presenting with a high clinical stage. Careful assessment of the subtle histological changes and the use of ancillary methods such as immunohistochemistry and molecular biology is essential before the final conclusion is drawn.

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