Oesophageal cancer: diagnosis and management

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Oesophageal cancer is the ninth most common cancer in the UK. With 8500 cases diagnosed annually, the UK has the highest rates of oesophageal cancer in Western Europe. Adenocarcinoma now accounts for 60–75% of all oesophageal cancers in the UK and is three to four times more common in men. Despite advances in diagnosis and treatment, five-year survival rates for all patients diagnosed with oesophageal cancer ranges from 15–20%. In this article the authors discuss current diagnosis and management.

There are two predominant types of oesophageal cancer: squamous cell carcinoma (SCC) usually affects the upper two thirds of the oesophagus and adenocarcinoma is more common in the lower third (Figure 1). Common aetiological factors are tobacco and alcohol for SCC and gastro-oesophageal reflux disease (GORD) for adenocarcinoma. There is a marked geographical variation in the incidence of oesophageal cancer. SCC is endemic in the Asian ‘cancer belt’, which extends through northern China, southern Russia, north-eastern Iran, northern Afghanistan and eastern Turkey; while in Western countries, adenocarcinoma of the oesophagus is more common and on the rise, along with the incidence of GORD and obesity.

SIGNS AND SYMPTOMS
Oesophageal malignancies present with disease-specific and constitutional symptoms (Box 1). For established oesophageal cancers, local symptomology manifests as progressive dysphagia, initially from solids and progressing to liquids, with a sensation of ‘sticking’ at different levels of the oesophagus when swallowing. Patients may also regurgitate and vomit back solids, as

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well as complaining of pain due to the mechanical stretch of the oesophagus. Dysmotility of the oesophagus may result in hiccoughs as the gullet attempts to propel the tumour down into the stomach. Chest infections may occur secondary to regurgitation and may be confounded by other lifestyle habits, such as smoking, potentially making this symptom easy to overlook. Reflux disease is a precursor to this and could result in Barrett’s oesophagus. Acid reflux resistant to proton-pump inhibitors (PPIs) should ring alarm bells for an upper gastro-esophageal pouches or reflux.

**BARRETT’S OESOPHAGUS AND CANCER**

Barrett’s oesophagus is a condition in which metaplastic columnar epithelium replaces the normal stratified squamous epithelium lining the distal oesophagus (Figure 2). Risk factors for cancer in Barrett’s oesophagus include chronic GORD, hiatus hernia, advanced age, cigarette smoking and obesity with intrathoracic body fat distribution, with Caucasian males being the most at-risk group. The annual risk of oesophageal cancer is approximately 0.25% for patients without dysplasia and 6% for patients with high-grade dysplasia. Endoscopic eradication therapy with radiofrequency ablation significantly reduces the frequency of progression to cancer for patients with high-grade dysplasia.

**THE ROLE OF SCREENING**

Screening for oesophageal cancer is not routinely undertaken in the UK as there is a lack of evidence that screening affects mortality.

Endoscopy is the gold standard for diagnosing oesophageal cancer and precancerous lesions. In the current endoscopic technique, four quadrant biopsies are taken every 2cm in the columnar-lined oesophagus. The tissue is stained with Lugol’s solution. Normal squamous epithelium has abundant glycogen which is stained brown by iodine; abnormal mucosa is not stained due to the low glycogen content.

Studies have shown that there is a benefit from implementing endoscopic screening in populations at high risk for oesophageal cancer. In Japan, a study stratified Japanese men into high-risk and low-risk groups based on diet, drinking and smoking. Chromo-endoscopy resulted in diagnosis of oesophageal cancer in 0.86% of the subjects. The detection rate was 4.27% in the high-risk group, as opposed to 0.67% in the lower risk group. A Chinese study detected precancerous lesions in 46.6% of subjects through chromo-endoscopy, 2.42% of which were cancerous.

**DIAGNOSIS AND STAGING**

When oesophageal cancer is diagnosed through endoscopy, the patient will need a thorough work-up to determine suitability for treatment. Accurate staging determines both treatment and prognosis. The T-stage looks at the depth of invasion of the tumour. This is best assessed by endoscopic ultrasound (EUS), which is often performed in specialist tertiary centres. CT imaging can also help by determining the involvement of structures adjacent to the tumour. The obliteration of fat planes between the oesophagus and adjacent structures is pathognomonic of a T4 tumour and can be detected by CT imaging. However, EUS is superior at differentiating between T1, T2 and T3 tumours. Nodal involvement (N stage) can be determined through fine needle aspiration. EUS can assess the response to chemotherapy, but is unreliable for staging oesophageal cancer after neoadjuvant chemoradiation. It is also limited when there is narrowing of the oesophageal lumen and the endoscope cannot be passed to visualise the tumour.

**MULTIDISCIPLINARY MANAGEMENT**

A confirmed diagnosis of oesophageal cancer is discussed in a multidisciplinary setting and the treatment modalities available depend on the stage of the cancer and health status of the patient (Table 1). T1 and T2 tumours are treated...
by surgery, with the surgical approach dependent on the size and location of the tumour. The most common approaches for surgery of the oesophagus are thoraco-abdominal, which opens the abdominal and thoracic cavities together, and the two-stage Ivor Lewis approach, in which the abdomen and thorax are opened separately (abdomen first). The McKeown operation is used in more proximal tumours, where a third incision is made in the neck for cervical anastomosis. The first minimally invasive oesophagectomy was performed in 1992. This surgery is performed in different ways using a combination of thoracoscopy, laparoscopy and hybrid procedures involving open surgery. A laparoscopic approach has been shown to reduce blood loss, respiratory complications, total morbidity rates and duration of stay in hospital. Advocates of open surgery do not believe as many lymph nodes can be retrieved with laparoscopy as during

**CASE HISTORY: A VIGILANT NURSE AND GP**

I was diagnosed with oesophageal cancer in November 2012. I was one of the ‘lucky’ 35%, as the cancer was discovered early enough to operate and get rid of it. For the other 65%, it is normally too late for this. A major reason for this is lack of knowledge about oesophageal cancer and what the symptoms are.

The discovery was a complete shock to both myself and my wife. We had never heard of such a cancer and I had never knowingly had anything that remotely resembled a symptom I needed to see a doctor about. I had been taking pills for high cholesterol and raised blood pressure for several years – my father and paternal grandfather both having suffered heart problems. I went for a routine six-monthly check-up at my surgery with one of the practice nurses. She said that everything was looking good (blood test result, urine, weight, blood pressure, etc), but asked if I would mind answering a few questions while I was there. ‘Not a problem,’ I replied confidently.

The first thing she asked was whether I had ever suffered indigestion. I would have answered no, because to my mind the odd bout of heartburn and indigestion was just a result of overeating and drinking. Taking Gaviscon, Rennies or other such antacids usually dealt with the problem and I would never have dreamt that it was something to be discussed with my GP. But because I was there and the nurse was asking the questions, I was keen for something – anything – to tell her to make it seem all worthwhile.

And so I told her that I had been away on holiday with my wife the previous week, and she had made a stew for our evening meal. One bit of meat had stuck in my throat, but was easily washed down with a sip of tea. It was the first time anything like this had happened. I had blamed it on the wife’s cooking and thought nothing more of it – until now.

She remarked that it was almost certainly nothing to worry about, but was worth mentioning to the GP. So, I went and saw him and recounted the story about the stew. He also said that it was almost certainly nothing to worry about, but it would be best to get it checked out. He sent me off for an endoscopy – and that’s how I found out about the cancer. If it hadn’t been for the diligence of both the nurse and my GP, I almost certainly wouldn’t be here today.

My chemotherapy started on 3 January 2013 and entailed a 10-day spell in hospital as I reacted badly. This was followed by an Ivor-Lewis procedure (it’s easier to say than ‘gastro-oesophagectomy’) in April. A small leak in the joint meant a slightly longer spell in hospital than would usually be expected. Six months later, in December 2013, I had my right kidney removed because of a non-related cancerous growth that had been discovered during all the tests I underwent for my oesophageal cancer.

I have nothing but praise for everyone in the NHS who was involved in my testing and treatment – but in particular for the Upper GI team at the Queen Alexandra Hospital in Portsmouth. I have become a Trustee of the Oesophageal Patients Association (OPA) and am concentrating on raising awareness of oesophageal cancer and its symptoms. Before my diagnosis, I did not know such a cancer existed or that there were definite symptoms to watch out for – and my experience since has shown this to be a widespread problem. If, by creating greater awareness, just one person’s life is saved, then it will be worth it.

So far, I have raised over £2000 through a 25km sponsored walk in the Peaks, money that will be used towards the production of a leaflet/pamphlet by the OPA, designed to help raise awareness of oesophageal cancer and its symptoms. The intention is to distribute this widely, so that as many people as possible – including pharmacists and GPs, as well as the general public – are encouraged to investigate possible symptoms. Through this, the hope is that more people can be diagnosed at the earliest stage possible and treated accordingly.

**Philip Coverdale**

To make a donation to the Oesophageal Patients Association visit: https://mydonate.bt.com/charities/theoesophagealpatientsassociation
an open procedure, and regard previous chemoradiotherapy as a contraindication for minimally invasive oesophagectomy.

**FUTURE MANAGEMENT**

Advances in metabolomics have shown potential for using analysis of exhaled components of human breath in oesophageal cancer patients. This has identified four volatile agents (hexanoic acid, phenol, methylphenol and ethylphenol) that are significantly different in the exhaled breath of patients with oesophago-gastric cancers than control subjects. Although there is still much work to be done, these point-of-care tests will be cost-effective, prevent many unnecessary procedures and can be performed in primary care with ease.

Immunotherapy is an emerging field for the treatment of many solid tumours. The high somatic mutation rate in oesophageal cancer means that immunotherapy may better target malignant cells than conventional chemoradiotherapy, with less off-target side-effects. Antibody-based immunotherapy for growth factors, such as endoscopic submucosal dissection, are being considered for early cancers. For example, a stage T1b oesophageal cancer (ie the tumour has invaded the submucosa) would traditionally undergo radical surgery. However, with mucosal resection combined with chemoradiotherapy these tumours can be managed with endoscopy alone. Cancers that have spread beyond the muscularis mucosa have been treated successfully using this technique.

**CONCLUSION**

In conclusion, as a non-specialist, it is very difficult to detect upper gastrointestinal cancer at an early stage, as much of the symptomatology is identical to that of benign disease. With oesophageal cancer on the rise, principally due to lifestyle risk factors, vigilance is required. Referral to an upper gastrointestinal clinic on the urgent symptomatology is identical to that of benign disease. Immunotherapy may better target malignant cells than conventional chemoradiotherapy, with less off-target side-effects. Antibody-based immunotherapy for growth factors, such as endoscopic submucosal dissection, are being considered for early cancers. For example, a stage T1b oesophageal cancer (ie the tumour has invaded the submucosa) would traditionally undergo radical surgery. However, with mucosal resection combined with chemoradiotherapy these tumours can be managed with endoscopy alone. Cancers that have spread beyond the muscularis mucosa have been treated successfully using this technique.

**Declaration of interests:** none declared.

**REFERENCES**


### Table 1. Staging and management of oesophageal cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>Management</th>
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<tbody>
<tr>
<td>0 (Mucosal)</td>
<td>Endoscopic resection +/- radiofrequency ablation</td>
</tr>
<tr>
<td>I (Submucosal)</td>
<td>Radical oesophagectomy + lymphadenectomy</td>
</tr>
<tr>
<td>IIA (Locally advanced)</td>
<td>Neoadjuvant therapies + radical oesophagectomy</td>
</tr>
<tr>
<td>IIB (Locally advanced)</td>
<td>Neoadjuvant therapies + radical oesophagectomy</td>
</tr>
<tr>
<td>III (Advanced)</td>
<td>Oesophageal stents +/- brachytherapy</td>
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<tr>
<td>IV (Advanced/recurrant)</td>
<td>Chemo-/chemoradiotherapy</td>
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</tbody>
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