Palliative management strategies for oesophageal cancer in the presence of co-morbidities

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Abstract

This case was submitted as a 2018 trainee intern general medicine case history. It documents the presentation of a new diagnosis of oesophageal cancer, alongside the diagnoses of atrial fibrillation with congestive heart failure, in an 87-year-old NZ European man with known metastatic prostate cancer. The case is followed by a discussion on the definition, epidemiology, risk factors, clinical presentation and differential diagnosis for oesophageal cancer, with a focus on comparing the alternative palliative management options when faced with challenging co-morbidities.

Background

1. Metastatic prostate cancer diagnose in November 2017 with cervical, thoracic and lumbar metastases at time of diagnosis. On hormone therapy. Secondary L1 compression fracture
2. Ischaemic heart disease with stable angina (transthoracic echocardiogram Sept 2014, ejection fraction 45%, severe aortic stenosis). Two previous myocardial infarctions (1992 and 2012)
3. Asbestos exposure with extensive plaque disease
4. Hypertension
5. Bilateral total hip and total knee joint replacements
6. Gastro-oesophageal reflux disease
7. Hiatus hernia

Medication List on Admission

Regular

Bicalutamide 50mg PO BD
Goserelin 10.8 mg inj Q3Month
Aspirin 75mg PO OD
Metoprolol Succinate 47.5mg PO OD
Quinapril 20mg PO BD
Atorvastatin 40mg 2 tab PO nocte
Ezetimibe 10mg PO OD
Prednisone 5mg PO mane
Frusemide 40mg PO mane
Omeprazole 20mg PO BD
Docusate Sodium 50mg + Sennoside B 8mg PO BD
Zoledronic acid 4 mg/5 mL inj Q1Year

PRN

Paracetamol 500mg 2 tab PO QID
Oxycodone Hydrochloride 5mg PO TDS
Glyceryl Trinitrate 400mcg/actuation oral spray 1dose SL

Allergies/ADRs

None known.

Presenting Complaints

1. Dysphagia
2. Chest pain with increased shortness of breath on exertion (SOBOE)

History

Mr W is an 87-year-old NZ European man who presented to North Shore Hospital, Auckland, with multiple complaints on the above background. He had three weeks of progressive dysphagia to solids and liquids, with regurgitation of food and episodes of vomiting after eating meals. He had also noticed a new sense of early satiety. No haematemesis was described. He had two episodes of melaena prior to 4/7 constipation but reported no abdominal pain or urinary symptoms. He had 20kg of weight loss prior to his recent prostate cancer diagnosis in November 2017, which was 4 months prior to this admission, but his weight has been stable since.

His second presenting complaint was 3/7 of intermittent, dull, central chest pain associated with increased SOBOE. Orthopnoea and paroxysmal nocturnal dyspnoea (PND) were present. On admission he was only tolerating walking a distance of 5m due to breathlessness, with a baseline of 30m. Cough, sputum production, palpitations, haemoptysis, fever and recent illness were all denied on specific questioning.

Social History

Mr W is a retired builder living in his own home with his wife. He is independent for activities of daily living (ADLs) and receives 1 hour/week home help for meals. He mobilises with a walking stick around the house. He is an ex-smoker with a 30-pack-year past history and does not drink alcohol. His family history was unremarkable.

On Examination

He appeared comfortable at rest with a heart rate of 120 bpm that was irregularly irregular. Otherwise his observations were normal range and he was afebrile. Relevant findings included dual heart sounds with an ejection systolic murmur loudest at the aortic area, radiating to the carotids. JVP was +4cm. Bibasal crackles were heard on auscultation of the posterior chest. There was no pedal oedema present. He had a tender epigastrium without percussion tenderness, but otherwise normal abdominal examination. Per rectum and neurological exams were normal.

Investigations:

1) Selected blood test results

Blood Test	Result	Reference Range
Sodium	140	135-145 mmol/L
Potassium	3.6	3.5-5.2 mmol/L
White Blood Cells	**15.8**	4-11.0 xE9/L
CRP	**27**	0-5.0 mg/L
Troponin I	**66** (first), **75** (second)	0-40 ng/L
Haemoglobin	143	130-175 g/L
NT-ProBNP	**235**	<35 pmol/L
T4 (free)	13.5	9-19 mol/L

2) ECG: Fast atrial fibrillation, rate 120, no ischaemic changes.

3) CXR: Extensive bilateral pleural calcifications, related to previous asbestos exposure. Stable cardiomegaly. No evidence of acute pulmonary changes.

4) Transthoracic echocardiogram: Heavily calcified aortic valve with severe aortic stenosis. Normal left ventricular size with an ejection fraction ~20%. Hypokinetic/akinetic globally with dilated atria. Mild mitral and tricuspid regurgitation.

5) Oesophagogastroduodenoscopy (OGD): Likely malignant oesophageal tumour found in the lower third of the oesophagus, in an area of Barrett's oesophagus, above a hiatus hernia. Biopsy showed HER2-negative, E-cadherin-positive adenocarcinoma.

Progress

Mr W was admitted under General Medicine. Furosemide 80mg BD IV was given to treat congestive heart failure and an IV amiodarone infusion given with telemetry to improve the rythm control of his atrial fibrillation. Mr W was already on metoprolol in the community. A decision was made to not anti-coagulate despite a CHA2DS2-VASc of 4, due to a HAS-BLED of 3.[1,2] Mr W was seen by General Surgery regarding his oesophageal adenocarcinoma. His case was discussed in their multidisciplinary meeting (MDM) regarding surgical options, with a conclusion deeming him not to be a surgical candidate due to his age, extensive co-morbidities and prior metastatic prostate cancer diagnosis.

Problem List

1. New fast atrial fibrillation; rhythm controlled on amiodarone
2. Congestive heart failure with severe aortic stenosis; left ventricular ejection fraction decreased from 45% to 20%
3. Dysphagia to solids and liquid and episodes of melaena; secondary to oesophageal adenocarcinoma
4. Metastatic prostate cancer with cervical, thoracic and lumbar metastases

Discussion

This discussion will focus on Mr W's diagnosis of oesophageal adenocarcinoma

Definition

Oesophageal cancers are mucosal lesions that begin in the epithelial cells lining the oesophagus. There are two main types; adenocarcinoma and squamous cell carcinoma (SCC). Oesophageal adenocarcinomas mostly occur in the distal oesophagus from a region of Barrett's metaplasia (but can occur without prior metaplasia), while oesophageal SCC is more evenly distributed throughout the length of the oesophagus.[3]

Figure 1 shows images from Mr W's OGD report. He had a classical location for his adenocarcinoma, in the lower third of the oesophagus at the gastro-oesophageal junction, within an area of Barrett's metaplasia. Barrett's metaplasia represents a change in the epithelial lining of the oesophagus from simple squamous, to columnar with addition of goblet cells.

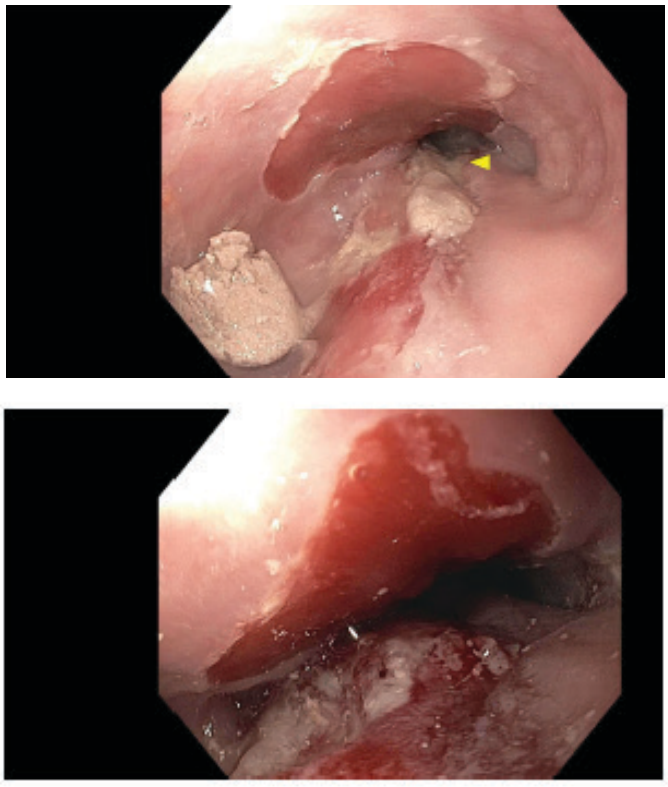

Figure 1 Lower third of the Oesophagus: Mass, Images from Mr W's OGD Report

Epidemiology and Risk Factors

The proportion of oesophageal cancers that are adenocarcinomas has risen from 10% of cases in 1960, to 80% of recent diagnoses. This change is thought to be due to the rising incidence of Barrett's metaplasia, particularly in Caucasian men.[4] Risk factors for adenocarcinoma include obesity (OR 2.34 for BMI≥30 kg/m2) and gastro-oesophageal reflux disease (GORD) (OR 5.0 for weekly symptoms). For SCC risk factors include smoking and alcohol consumption[4].

The risk factors specific to Mr W's development of oesophageal adenocarcinoma included his past history of GORD (a cause for Barrett's metaplasia) for 'over ten years', although he was compliant to his treatment (omeprazole 20mg BD). He had a hiatus hernia below the site, which is known to increase GORD symptoms. His additional risk factors included a 30-pack-year history of smoking, male sex, Caucasian ethnicity, and a diet low in fruit and vegetables. He had no family history of oesophageal cancer and was not on an oral bisphosphonate, which are further known risk factors.[3,4]

Clinical Presentation

Most patients with oesophageal cancers only start to report symptoms at an advanced stage. The classical presentation is progressive dysphagia to solids initially, then to liquids, with associated odynophagia and weight loss. Hoarseness of voice and cough can also occur and usually represents invasion of the recurrent laryngeal nerve.[5]

Mr W had a classical history with the addition of post-prandial food regurgitation and vomiting, which are symptoms of a severely obstructing cancer. He also described melaena which was likely the result of upper gastrointestinal bleeding from the adenocarcinoma, although he had only two episodes and was not anaemic on admission with a haemoglobin of 143 g/L. Mr W had significant weight loss of 20kg prior to his recent diagnosis of metastatic prostate cancer, but had a stable weight over the previous three weeks where he had progressive dysphagia. A possible explanation for his weight remaining stable, despite reduced oral intake, is weight gain due from his secondary diagnosis of CHF.

The oesophageal lesion likely represents a new primary cancer, as the oesophagus is not a common site for metastasis of prostate cancer.[5]

Differential Diagnoses

The differential diagnosis of dysphagia includes non-malignant strictures, achalasia, eosinophilic oesophagitis and oesophageal webs/rings.[5]

For Mr W's work-up, a stricture was possible with a history of GORD, but the dysphagia seen with this condition is often slower to progress and often occurs post-radiation therapy. Achalasia is often not associated with a history of GORD. Eosinophilic oesophagitis and oesophageal webs/rings tend to produce intermittent (rather than constant) dysphagia.[5]

Management Options

As oesophageal tumours are often diagnosed late, accurate staging is important for prognosis and treatment planning. The clinical stage groups for cases of oesophageal cancer, based on the TNM cancer staging system, is shown in Table 1. CT chest/abdomen is often used to stage disease. However, PET scanning is a recent alternative which has been shown to improve detection of nodal and distant metastases, and therefore identify possible surgical candidates.[5]

If fit for surgery, oesophagectomy is offered up to and including patients with stage III disease, with the addition of chemo and/or radiotherapy either prior to, or after resection. Chemoradiotherapy and oesophageal stenting are options available in not only stage IV patients, but also stage III patients who are non-surgical candidates due to existing co-morbidities.[5,6] Mr W's case was discussed at a General Surgical MDM for consideration of management options. A decision was made not to perform CT imaging, and to treat as per stage IV based on his extensive co-morbidities. He was deemed not to be a surgical candidate and with his significant heart disease and metastatic prostate cancer, he would also not tolerate chemoradiotherapy. However, symptomatic oesophageal stenting was recommended as a palliative option.

Squamous cell cStage group	cT	cN	cM
0	Tis	N0	M0
I	T1	N0-1	M0
II	T2	N0-1	M0
	T3	N0	M0
III	T3	N1	M0
	T1-3	N2	M0
IVA	T4	N0-2	M0
	T1-4	N3	M0
IVB	T1-4	N0-3	M1
Adenocarcinoma sStage group	cT	cN	cM
0	Tis	N0	M0
I	T1	N0	M0
IIA	T1	N1	M0
IIB	T2	N0	M0
III	T2	N1	M0
	T3-4a	N0-1	M0
IVA	T1-4a	N2	M0
	T4b	N0-2	M0
	T1-4	N3	M0
IVB	T1-4	N0-3	M1

Table 1 The clinical TNM staging system for cases of oesophageal cancer (taken from[4])

When talking with Mr W, he stressed how he wanted 'to live as long as possible, with as little symptoms as possible' post-diagnosis. This made me consider the evidence behind the current palliative management alternatives for oesophageal cancer.

Although not appropriate for Mr W, patients with localised oesophageal cancer can be given combination chemoradiotherapy. Patients treated with capecitabine combinations have been shown on meta-analysis to have superior survival times compared with 5-fluorouracil (5-FU) combinations.[7] Both of these regimens are potentially cardiotoxic so pre-existing heart disease, in particular congestive heart failure, is a relative contraindication. Trastuzumab can also be used in addition to standard chemotherapy. This drug is a monoclonal antibody which binds to the human epidermal growth factor receptor 2 (HER 2), which is present in 25% of oesophageal adenocarcinomas.[8] Increased survival time of two months has been shown in those assigned to trastuzumab plus chemotherapy, compared with chemotherapy alone, without additional toxicity or adversely affecting quality of life.[9] It is now standard practice to test for the presence of HER2 on biopsy samples taken from OGD,

and use trastuzumab first-line alongside traditional chemotherapy if results are HER2-positive. However, congestive heart failure is again a contraindication, and although testing for HER2 receptor presence is standard, the use of trastuzumab is not currently funded in New Zealand, so cost can be a barrier for some families.

Self-expanding metal stents (SEMS) can be inserted endoscopically to hold the oesophageal lumen open, and have been shown to provide higher symptomatic relief (based on patient dysphagia scores), with less requirement for re-intervention, compared with local dilatational management alone. Overall, oesophageal stenting provides symptom control quickly, but there are recognised disadvantages, such as the potential for acute haemorrhage during the procedure, perforation and stent migration into surrounding structures.[10] Stenting also damages the gastro-oesophageal junction, so can worsen underlying GORD and lead to aspiration.[10]

To conclude, oesophageal stenting +/- chemoradiotherapy are the main palliative management strategies for patients with oesophageal cancer in the presence of co-morbidities. Mr W's case was complex with several comorbidities limiting his individual management to solely oesophageal stenting. The use of the monoclonal antibody Trastuzumab can offer HER2-positive patients who can tolerate chemoradiotherapy approximately two-months of increased survival. This additional time might seem small, but to a dying patient, it can provide enormous opportunity.

Verbal and written consent was gained from the patient to write and publish this case report.

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