

An unusual metastasis in Oesophageal cancer

– case report and review of the literature

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Abstract:

Oesophageal adenocarcinoma most commonly metastasizes to the liver and lungs. Brain metastases - particularly cerebellar metastases - are very rare. We report the case of a patient presenting primarily with headache and neurological symptoms, who went on to be diagnosed with metastatic oesophageal adenocarcinoma. We also review the literature on this topic.

Case report:

A 44-year old male presented with a one-week history of constant occipital headache associated with blurred vision, unsteady gait, nausea and vomiting. There was no focal sensori-motor neuro-deficit and no speech disturbance. He denied any gastrointestinal symptoms and weight loss, but on direct questioning admitted to some heartburn and occasional dysphagia to solids. He was a non smoker and there was no history of alcohol excess.

Neurological examination revealed minimal dysidiadokinesia on the right, a broad-based gait and failure to walk heel-to-toe. Power, tone and reflexes were normal in both upper and lower limbs. Fundus examination revealed bilateral papilloedema.

Routine bloods were unremarkable with haemoglobin of 15.9 gm/dL, WCC $12.6 \times 10^9/L$, serum sodium of 143 mmol/l, serum potassium of 4.0 mmol/l, and normal liver function tests.

A CT scan of the brain with contrast showed both cerebral and cerebellar lesions measuring 6-35 mm in diameter, consistent with multiple metastases. There was surrounding oedema in the cerebellum associated with a mass effect and early obstructive hydrocephalus. (Figure 1)

In the absence of an obvious primary malignancy,

he went on to undergo a CT scan of the thorax, abdomen and pelvis. This showed thickening of the distal oesophagus above the gastro-oesophageal junction accompanied by a small cluster of enlarged left gastric nodes measuring up to 15 mm. There were also two lytic lesions in the 8th thoracic vertebra and the glenoid of the left scapula.

An upper GI endoscopy was carried out following the CT scan and this showed a circumferential oesophageal tumour extending from 4 cm above the squamocolumnar junction to the upper aspect of the stomach. Histology confirmed the diagnosis of moderately differentiated adenocarcinoma of the oesophagus.

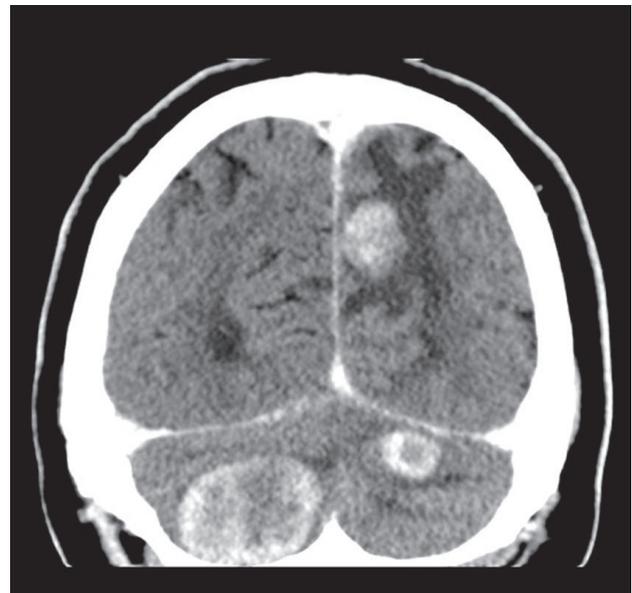


Figure 1

Coronal reformat of post contrast CT head showing enhancing masses in the cerebellum and left cerebral hemisphere with surrounding oedema.

Discussion:

Oesophageal cancer is the seventh leading cause of cancer death worldwide and in the UK. Squamous cell carcinoma used to be responsible for 95% of all oesophageal cancer but since the 1970s the incidence of squamous cell carcinoma has remained stable or decreased in most western countries while that of adenocarcinoma has increased, particularly in men¹. Over 7000 cases of oesophageal cancer are diagnosed in England each year. Oesophageal cancer is more common in men than in women and in the UK the male to female ratio is almost 2:1¹. The disease becomes more common with advancing age, with a peak incidence in the sixth and seventh decades of life.

The prognosis of oesophageal cancer is generally poor, with over 6000 deaths each year attributable to the disease, and with 50% of patients presenting with distal visceral metastases¹. One-year survival for oesophageal cancer is around 40% and five-year survival is around 12%. The most common sites of metastasis are the lungs, liver, kidneys, adrenal glands and bones. Brain metastases are reported less frequently, although case series have been published in the literature².

The overall prevalence of brain metastasis in oesophageal cancer has been estimated to be between 1 and 5%^{3,4,5,6}. Gabrielsen et al. reported brain metastases in 3.6% of patients with oesophageal cancer who underwent oesophagectomy with a trend towards a higher incidence in those with adenocarcinoma⁴. In other studies Weinberg et al. reported 27 cases (1.7%) with brain metastases in a group of 1588 patients with oesophageal cancer⁵ and Ogawa et al. reported 36 patients (1.4%) with brain metastases in a series of 2554 patients with oesophageal cancer³. While metastatic deposits to the brain are infrequent, metastatic disease to the cerebellum is even rarer.

A recent case series of 53 patients in the

United States revealed a higher incidence of brain metastasis than previously reported in patients with oesophageal cancer. Brain metastases were found exclusively in patients with adenocarcinoma. Although the association between histology and brain metastasis was not statistically significant due to the small sample size, this mirrors the pattern seen in patients with non-small cell lung carcinoma, where the incidence of brain metastasis is at least two-fold higher in those with adenocarcinoma versus squamous cell carcinoma. If the metastatic potential for CNS involvement is indeed higher in adenocarcinoma of the oesophagus, we may see an increasing trend in brain metastases as the incidence of this particular histology continues to rise.⁷

Other characteristics associated with brain metastasis are large primary tumors (greater than 8.2 - 8.5 cm), local invasion and lymph node involvement^{2,3,4}. Presenting symptoms include motor weakness 58%, headache 28%, seizures 22%, disorientation 17% and cerebellar dysfunction 16%^{2,3}.

CT and MRI remain the most useful tools for detecting brain metastases, but these should only be offered to patients with symptoms of neurological dysfunction. Routine preoperative CT brain in oesophageal cancer has not been found to be cost effective⁴.

Brain metastases in oesophageal cancer are associated with a particularly poor prognosis. Despite numerous studies designed to improve treatment outcome, the median survival of patients with oesophageal cancer with brain metastases is 3-6 months in published case series^{3,4,5}. Twelve and 24-month survival are reported as 13% and 3%, respectively. The best outcome is achieved in patients with single metastatic lesions who undergo surgical resection and adjuvant whole brain radiotherapy⁵.

The European Federation of Neurological Societies (EFNS) has established evidence-based

guidelines for treatment of brain metastases⁷. Dexamethasone is the corticosteroid of choice to control the cerebral oedema due to its minimal side effects and long half-life. An initial starting dose of 4-8mg per day, increasing to 16mg/day is recommended, followed by a reducing regime to the minimum dose required to control symptoms - often patients are weaned off completely. Up to 75% of patients with brain metastases show marked neurological improvement within 24-72 hrs of beginning corticosteroid therapy.

Surgical resection is indicated in patients with a single brain metastasis in an accessible location where systemic disease is absent or controlled and the patient's functional status is good. In patients with an inaccessible single brain lesion or more than three brain metastases, whole brain radiotherapy (WBRT) with a hypo-fractionated regime is the treatment of choice. Stereotactic radiosurgery (SRS) is an alternative treatment option to whole brain radiotherapy in patients with up to three brain metastases (again with controlled systemic disease and good functional status).

References:

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Stereotactic radiosurgery (SRS) permits the delivery of a single high dose of radiation to a target with a maximum diameter of 3-3.5 cm by using a gamma knife (multiple cobalt source) or linear accelerator (Linac) through a stereotactic device. It is performed at selected specialist centres only.

Conclusion

Brain metastasis in oesophageal cancer is rare and associated with very poor prognosis. It tends to occur in patients with large, locally invasive primary tumours. There is evidence to suggest that, as the incidence of adenocarcinoma of the oesophagus increases, so will the incidence of brain metastasis. As techniques to manage primary and metastatic oesophageal cancers advance and survival improves, recognizing and treating brain metastases becomes increasingly important. Surgical resection followed by whole brain radiotherapy has been associated with the longest median survival compared to surgery, WBRT or stereotactic radiosurgery SRS alone.