CASE REPORT

Opsoclonus myoclonus syndrome due to squamous cell carcinoma of the oesophagus

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Accepted 6 February 2014

SUMMARY

We present the case of a 47-year-old woman with encephalopathy, ataxia and oscillopsia diagnosed with opsoclonus myoclonus syndrome (OMS). In adults, OMS in the context of encephalopathy is commonly paraneoplastic. A CT of the chest, abdomen and pelvis and a gastroscopy were performed and were normal. A fluorodeoxyglucose positron emission tomography CT scan demonstrated increased uptake in the mid-oesophagus and an endoscopic ultrasound examination demonstrated intramural thickening of 5 mm with no epithelial lesion. The patient was treated with three courses of intravenous immunoglobulin (Ivlg) with improvement in her symptoms. A year following the initial presentation a repeat endoscopic examination demonstrated an ulcerated oesophageal carcinoma with regional lymph node involvement. The patient was treated with neo adjuvant chemotherapy prior to oesophagectomy. The patient's symptoms resolved within 6 months of tumour resection without the need for further Ivlg. Unfortunately, after a further 6 months the patient developed liver metastases and died.

BACKGROUND

This case is important as it highlights the need for aggressive investigation and treatment of suspected malignancy in a paraneoplastic condition such as opsoclonus myoclonus syndrome (OMS). In this case an oesophageal malignancy was suspected early in the course of the disease when the 5 year survival following operative intervention would have been 87%. Unfortunately, due to the equivocal endoscopic appearances, surgical intervention was delayed until there was evidence of mucosal invasion, by which time the 5 year survival had dropped to 18%. Carcinoma of the oesophagus has never previously been reported in the context of OMS and this case suggests that the squamous cell carcinoma in our patient was causative.

CASE PRESENTATION

A 47-year-old woman presented with unsteadiness, vomiting, anorexia and what her husband described as 'dancing eyes'. On examination she was encephalopathic and had involuntary rapid erratic eye movements (opsoclonus), bilateral limb ataxia and startle myoclonus. A clinical diagnosis of OMS was made.

INVESTIGATIONS

Routine blood tests and MR brain imaging were normal. Cerebrospinal fluid examination was normal other than a monoclonal intrathecal IgG

band. A paraneoplastic antibody screen was negative (anti-GAD, anti-amphiphysin, anti-CRMP5, anti-Hu, Anti-Ta, Anti-Ri, anti-Yo, anti-voltage gated Ca and K channel antibodies). Further investigations included a CT scan of the chest, abdomen and pelvis that demonstrated a pulmonary embolism. A breast ultrasound and upper gastrointestinal endoscopy were normal. An FDG-PET CT scan of the whole body was initially reported as normal. An EEG demonstrated mild slowing of the background rhythm in the theta range. Nerve conduction and electromyography studies were normal.

DIFFERENTIAL DIAGNOSIS

On the basis of the clinical presentation a diagnosis of OMS was made. In children the aetiology is often paraneoplastic due to an underlying neuroblastoma. In both paediatric and adult cases, OMS can be seen following viral infection. The presence of OMS and encephalopathy in adults, however, is highly suggestive of a paraneoplastic aetiology.

TREATMENT

The patient was treated with clonazepam and a 3-day course of 1 g intravenous methylprednisolone with no improvement. After 14 days she proceeded to a 5-day course of plasma exchange. This was deemed to be unsuccessful after 11 days and she was treated with 2.0 g/kg Ivlg. This resulted in a sustained improvement over 3 months. After 3 months the patient developed worsening oscillopsia, startle myoclonus and visual hallucinations. She proceeded to a second course of Ivlg which resulted in the resolution of her symptoms. An FDG-PET CT scan was repeated and demonstrated increased uptake in the mid oesophagus that had been present on the initial examination when it was deemed to be physiological. An endoscopic examination was performed which revealed normal oesophageal mucosa. The patient then proceeded to an endoscopic ultrasound examination which demonstrated abnormal thickening of the oesophagus (at the submucosal level) that was not amenable to biopsy due to the high risk of oesophageal perforation (figure 1). A fine-needle aspiration was performed but was non-diagnostic. One option at this stage would have been to proceed to an oesophagectomy but this is a procedure associated with significant morbidity and mortality. Without evidence of progression of the lesion or any previous association of oesophageal cancer with OMS, a decision was made to monitor with 3-monthly endoscopic ultrasound examinations. Two further

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To cite: Rossor AM, Perry F, Botha A, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-202849

Figure 1 Radial endoscopic ultrasound image taken 7 months after the onset of symptoms and 5 months before the diagnosis of oesophageal cancer. An area of oesophageal thickening is seen at 11 o'clock directly beneath the epithelial layer. There was no macroscopic evidence of malignancy at the time of the endoscopy.

courses of IvIg were required at 3 monthly intervals due to the recurrence of symptoms.

A year following the initial presentation a repeat endoscopic examination and CT of the chest, abdomen and pelvis were performed which demonstrated an ulcerated oesophageal carcinoma (figure 2) with regional lymph node involvement. The patient was treated with neo adjuvant chemotherapy prior to oesophagectomy. Histology confirmed a squamous cell carcinoma of the oesophagus stage IIB (T2, N1).

OUTCOME AND FOLLOW-UP

The patient's symptoms resolved within 6 months of tumour resection without the need for further IvIg. Unfortunately, after a further 6 months the patient developed liver metastases and died shortly afterwards.

Figure 2 The endoscopic appearance of the oesophageal cancer immediately prior to surgery by which time there was mucosal invasion.

DISCUSSION

Oesophageal cancer is the 10th most common cancer in the UK with an annual incidence of 1 in 10 000.¹ The poor 5 year survival rate of 8% is thought to be due to delayed presentation.¹ The survival for early mucosal and submucosal cancer (T1N0) is 87%, whereas for lymph node positive cancer (TxN1) the survival is less than 18%. Oesophageal cancer has been described in several paraneoplastic conditions including cerebellar degeneration and necrotising myelopathy but not OMS.^{2 3} To the best of the author's knowledge, no paraneoplastic condition has been described in association with squamous cell cancer of the oesophagus.

The exact mechanism of opsoclonus is unknown but there is evidence that it arises from inhibition of the fastigial nucleus in the cerebellum. The fastigial nucleus forms part of the negative feedback loop which regulates saccadic burst neurons via GABAergic omnipause neurons.⁴

Oesophageal cancer was the likely cause of OMS in this case in view of the resolution of symptoms following resection of the tumour. No paraneoplastic antibody was identified which is in keeping with other case reports.⁴ Immunomodulation is reported to be only partially effective in paraneoplastic OMS in contrast to our patient who responded to IvIg but not steroids.⁵

Learning points

- ▶ Opsoclonus myoclonus syndrome was the first presentation of our patient's malignancy.
- ▶ Despite the positive fluorodeoxyglucose positron emission tomography(PET) scan, there was a delay in diagnosis and treatment due to the unusual endoscopic appearance (associated with a significant reduction in 5 year survival). This case highlights the difficulty of identifying a malignancy early in the course of paraneoplastic disease.
- ▶ Interval PET scanning in such cases is advised and early surgical resection or biopsy undertaken when there is persistent uptake with no other explanation.

Acknowledgements The authors would like to thank the patient and her husband for providing consent for publication of the case.

Contributors FN was the consultant neurologist with primary responsibility for the patient. AR wrote the first draft of the manuscript. FP, AB and FN revised the manuscript.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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