CASE REPORT

Malignancy-associated gastroparesis: an important and overlooked cause of chronic nausea and vomiting

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SUMMARY

A 69-year-old woman was referred to a gastroenterology clinic with a 1-year history of protracted nausea and postprandial vomiting. She had a background of gastro-oesophageal reflux disease, irritable bowel syndrome and chronic obstructive pulmonary disease with a significant smoking history. Her laboratory work-up including autoimmune screen, coeliac serology and synacthen test were unremarkable. Upper gastrointestinal endoscopy and CT imaging ruled out mucosal and obstructive causes. Gastric emptying studies demonstrated a delayed gastric emptying consistent with diagnosis of gastroparesis. Concurrently, she underwent a CT of the thorax for unresolved consolidation on her chest X-ray. This revealed a locally advanced primary lung carcinoma. In this context, with all other causes excluded, her gastroparesis was deemed to represent a paraneoplastic phenomenon. Gastroparesis is a frequent, under-recognised and important complication of cancer.

BACKGROUND

Chronic nausea and vomiting (lasting for more than 1 month) is a dilemma frequently encountered by physicians in multiple specialties. This case highlights how you would investigate someone in this predicament. It emphasises how motility disorders such as gastric dysrhythmias or gastroparesis are more common causes of chronic symptoms than obstructive/mechanical causes. We believe this is potentially the first case described of paraneoplastic gastroparesis associated with non-small cell lung carcinoma.

CASE PRESENTATION

A 69-year-old woman presented with a 1-year history of persistent vomiting which was always postprandial, occurring within 30–60 min after eating and also often at night time. She also reported general fatigue, anorexia and weight loss. This was on a background of more longstanding symptoms of colicky abdominal pain and altered bowel habit deemed secondary to irritable bowel syndrome. She also had a history of gastro-oesophageal reflux disease with hiatus hernia and had an episode of oesophageal candidiasis documented on endoscopy in 2008. Her psychiatric comorbidities include depression and anxiety. She remained an active smoker with a 120-pack-year smoking history despite significant and debilitating chronic obstructive pulmonary disease. She denied

any alcohol consumption or illicit substance misuse.

Her medications included ranitidine, lansoprazole, montelukast, theophylline, a seretide inhaler, tiopropium, pregabalin, quetiapine and alprazolam.

On examination, she was thin, afebrile and slightly tachycardic (96 bpm) with oxygen saturations of 93% on room air. Inspection of her hands was noteworthy for finger clubbing. There was reduced expansion of her chest and auscultation revealed expiratory wheeze with scattered crackles. She had some periumbilical tenderness on palpation of her abdomen. The remainder of her examination was unremarkable.

At this point, our differential diagnoses included gastrointestinal (GI), non-GI and psychiatric causes. From a GI perspective, we considered gastroparesis (and all its various causes/contributors), gastric outlet obstruction, malignancy, eosinophilic gastroenteritis and cyclical vomiting syndrome. We sought to exclude potential non-GI aetiology such as theophylline toxicity, adrenal insufficiency and thyroid dysfunction.

INVESTIGATIONS

The patient's haemoglobin was 12.9 g/dL. Her white cell count, differential, platelets and coagulation panel were normal. Her inflammatory markers were raised with a C reactive protein of 48.5 mg/L and erythrocyte sedimentation rate of 56 mm. Her electrolytes were remarkably normal despite her persistent vomiting—Na 140 mmol/L, K 4.5 mmol/L, Cl 102 mmol/L, urea 2.5 mmol/L and creatinine 52 mmol/L. She had only a mild contraction alkalosis with a serum bicarbonate of 27 mmol/L. Importantly, her serum calcium was normal at 2.31 mmol/L along with her serum amylase.

A further panel of screening tests both standard and recommended in the work-up of chronic nausea and vomiting was performed. This included an autoimmune screen, coeliac serology, thyroid function tests, haematinics and a short synacthen test—all of which were normal.

She then progressed to the next stage of imaging and endoscopy. She had a CT of her abdomen and pelvis demonstrating emphysema at lung bases along with residual food and fluid in her stomach despite fasting. Her barium swallow delineated a normal upper gut appearance confirmed by upper GI endoscopy (showing only mild gastritis).

Scintigraphic gastric emptying studies were performed (figure 1). Anterior and posterior planar

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To cite: Kelly D, Moran C, Maher M, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-201815

Figure 1 Gastric emptying studies.

imaging was obtained at 1, 2, 3 and 4 h following the ingestion of standardised solid and liquid meals labelled with technetium-99 nanocolloid. The percentage of residual tracer within the stomach at 1 h was 89% (normal <90%), at 2 h was 79% (normal <60%), at 3 h was 56% (normal <30%) and at 4 h was 38% (normal <10%). These results are consistent with delayed gastric emptying, also called gastroparesis.

She was screened for potential underlying causes for her gastroparesis. Her fasting plasma glucose and glycated haemoglobin were normal at 5.7 mmol/L and 45 mmol/mol, respectively. Her total protein was 76 g/L and her serum electrophoresis did not reveal any paraprotein. Hypothyroidism and connective tissue disorders were ruled out. Her neurological examination was entirely normal. She had no history of recent viral illness or prior gastric surgery. None of her medications were particularly associated with a delay in gastric emptying.

In view of her background ongoing breathlessness and productive cough, she was simultaneously reviewed by our hospital respiratory team who recommended CT imaging to ensure resolution of the left mid-zone consolidation seen on a chest X-ray 1 month ago ([figure 2](#)).

A CT of the thorax showed a large left upper lobe lesion with hilar adenopathy consistent with a primary pulmonary neoplastic lesion ([figure 3](#)). There was distal airspace nodularity suggestive of lymphangitis. There was right hilar and precarinal lymphadenopathy. A bronchoscopy with biopsy was subsequently planned but in the interim her sputum cytology results returned positive for squamous cell carcinoma.

As part of her staging work up, a positron emission tomography-CT was performed confirming an FDG-avid perihilar mass in the left upper lobe consistent with primary lung carcinoma with probable nodal involvement. There was also a

solitary fluorodeoxyglucose (FDG)-avid stellate nodule in the right upper lobe concerning for a second malignancy. There was no evidence of FDG-avid metastatic disease outside of the thorax. A CT of the brain (precontrast and postcontrast) did not demonstrate any space-occupying lesions.

TREATMENT AND OUTCOME

We concluded that her diagnosis was probable paraneoplastic gastroparesis in the setting of locally advanced primary lung cancer.

Figure 2 Chest X-ray of the patient from 1 month prior to admission showing left mid-zone consolidation.

Figure 3 CT of the thorax demonstrating left perihilar mass.

We had tested autoantibodies associated with paraneoplastic GI dysmotility. She was anti-Hu and anti-Yo antibody-negative, but before she could be screened for a further panel of antibodies, she died in another hospital from an inter-current pneumonia.

Before her death, her management was discussed at our hospital's lung multidisciplinary meeting. It was felt that given her poor lung function status, she would not be a candidate for surgery or radiotherapy. Given her pre-existing considerable issues with nausea and vomiting, chemotherapy was also not advised.

She was treated symptomatically and reviewed by the palliative care team who added various prokinetic and antiemetic agents to her proton pump inhibitor/histamine receptor antagonist regime. Eventually, she settled with regular metoclopramide at a dose of 10 mg three times a day.

DISCUSSION

Gastroparesis is a disorder of the stomach caused by delayed gastric emptying in the absence of mechanical obstruction. The majority of cases are idiopathic (36%) followed by diabetic (29%) and postsurgical (13%).¹ Other associated conditions include parkinsonism, collagen vascular disorders and postviral syndromes. Many pharmacological agents can contribute including calcium channel blockers, opioid analgesics and tricyclic antidepressants.

As this patient was a middle-aged female smoker, she fitted the phenotype for 'idiopathic' gastroparesis and easily may have been misdiagnosed. Although necessary to rule out common causes first, this case highlights the importance of considering more rare associations.

Gastroparesis is, in fact, a common complication of cancer, often mislabelled as cancer cachexia or chemotherapy-induced nausea and vomiting. It is particularly prevalent in those with upper GI tumours, associated with 60% of those with advanced pancreatic cancer.²

It can have serious ramifications in this cohort who may well already have a poor nutritional status with anorexia and cachexia secondary to humoral effects of malignancy. Chemotherapy and radiotherapy can also be quite emetogenic. Gastroparesis

can contribute to electrolyte or acid-base disturbances, volume depletion and frequent hospitalisations that plague this group.

The pathogenesis of this phenomenon, known broadly as 'malignant gastroparesis', is uncertain, but it may be due to either the cancer itself or a complication of its treatment. The aetiology is often multifactorial and can depend on the type of cancer. For example, pathogenesis in gastric cancer may include a mass effect from the tumour, infiltration into the myenteric plexus and vagotomy postgastric surgery.³ Important mechanisms overall include paraneoplastic phenomena, direct tumour infiltration of the coeliac plexus or vagus nerve, past GI surgery, viral infection and the toxic effects of chemotherapy and radiotherapy.⁴

Paraneoplastic GI dysmotility has been described in several cases of small cell lung cancer and less commonly with other tumours such as breast, ovarian and pancreatic cancer, carcinoid, Hodgkin lymphoma and cholangiocarcinoma.^{5–8} This group often have positive antineuronal antibodies, especially anti-Hu, anti-Yo and N-type voltage-gated calcium channel antibodies.⁹ Several mechanisms have been postulated including immune-mediated destruction of the interstitial cells of Cajal¹⁰ and antibodies directed against common epitopes of the enteric nervous system and the cancer.¹¹

In addition to nausea and vomiting, these patients can present with early satiety, postprandial bloating and fullness, abdominal pain and weight loss. On examination, there may be epigastric distension and tenderness. Occasionally, a succussion splash may be heard on auscultation.

Investigations should seek to exclude mechanical obstruction and rule out alternative causes of intractable nausea. The drug kardex should be scrutinised for potentially aggravating medications including narcotic analgesia. An upper GI endoscopy is helpful with visualisation of a dilated distended stomach with decreased peristalsis strongly suggestive of gastroparesis. The gold standard test for diagnosis is gastric scintigraphy following a standardised solid meal.

In terms of management, it is necessary to first assess for any nutritional or metabolic complications including electrolyte disturbances, vitamin deficiencies, volume depletion and weight loss. Treatment options may be guided by symptom severity for which there exists multiple scoring systems. One such system is the Gastroparesis Cardinal Symptom Index (GCSI) which is a sum of three subscale scores for the three main symptoms (early satiety, nausea/vomiting and bloating).¹²

Dietary and behavioural modifications are important including eating small, frequent, low-fat, low-residue meals and avoiding alcohol and smoking. Prokinetics and antiemetics form the mainstay of pharmacological therapy. One study concluded that erythromycin was the most potent agent for gastric emptying when compared with domperidone, metoclopramide or cisapride.¹³ Specific antitumour treatment may improve cases with paraneoplastic dysmotility.

In 2% of cases of severe gastroparesis, it is necessary to consider more invasive management strategies such as placement of a venting gastrostomy or jejunostomy tube, or referral to a specialist centre for gastric electrical stimulation. This is a pacemaker-like device that delivers high-frequency, low-amplitude stimulation via two electrodes implanted in the gastric muscle. The increased electrical stimulation leads to increased peristaltic pressure waves and gastric emptying. Those with diabetic gastroparesis and refractory symptoms have been shown to be the most responsive.¹⁴ There have been no prospective studies on its efficacy in malignant gastroparesis as yet.

Learning points

- ▶ Malignancy-associated gastroparesis is often an overlooked cause of persistent nausea and vomiting. It is frequently misdiagnosed as cancer cachexia or a side effect of chemotherapy.
- ▶ The aetiology is multifactorial and may include paraneoplastic dysmotility, postsurgical dysmotility and direct tumour infiltration of plexi, comorbidities, medications and viral infections.
- ▶ It is important to exclude mechanical bowel obstruction and emetogenic analgesia.
- ▶ Volume depletion, electrolyte disturbances and malnourishment should be screened for and corrected. Glycaemic control should be optimised in patients with diabetes.

Contributors All authors were involved in the diagnosis, management and care for the patient. DK wrote the paper. It was reviewed and revised by CM and SO'M. MM reviewed the radiology for the paper.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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