CASE REPORT

MULTIDISCIPLINARY MANAGEMENT OF METASTATIC NEUROENDOCRINE TUMOURS

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Abstract

A 65-year-old man presented to his GP with right upper quadrant abdominal pain and weight loss. Abdominal ultrasound showed multiple gallstones and some ill-defined liver lesions. Computer tomography scan diagnosed a terminal ileal lesion causing cicatrisation of the terminal small bowel but does liver abnormality. The patient was worked up with serum gut hormone profile and magnetic resonance imaging of the liver which demonstrated multiple liver lesions and biochemical suspicion of neuroendocrine tumour (NET). The patient underwent a right hemicolectomy and excision/ablation of 44 liver metastases. He made a good post-operative recovery and remains disease free after 18 months. We also present a brief literature review regarding advances in the management of metastatic NET.

Key words: Neuroendocrine tumours, Hepatic metastases, Radiofrequency ablation, Computer tomography, Magnetic resonance imaging

Introduction

Neuroendocrine tumours (NETs) represent a diverse group of neoplasms containing membrane-bound neurosecretory granules.[1] Clinical presentations depend on the staging of this disease and its functionality i.e., autonomous hormone secretion, which may lead to carcinoid syndrome characterised by nausea, vomiting, diarrhoea and abdominal cramps.[2] There has been a recent increase in the incidence of all gastrointestinal NETs, especially small bowel NETs (SB-NETs)[3] which may be due to an increased awareness and advances in diagnoses rather than a true rise in disease incidence. Modlin *et al*. reported SB-NET to be the most common SB neoplasm with a three-fold increase in incidence over the past three decades.[4]

The Surveillance, Epidemiology and End Results Programme showed that carcinoid syndrome typically present in sixth–seventh decades of life,[5] with an estimated prevalence of about 35/100,000 population.[2] The most common primary tumour sites are the SB and pancreas,[6] while the most common site of metastasis is the liver.[7]

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We report the case of a patient diagnosed with primary SB-NET and liver metastases who then underwent surgery with curative intent. This case adds to the literature on the management of functioning primary SB-NET with distant metastases, in particular to the choice of imaging modalities and pushing the boundaries for surgical resection when feasible.

Case Report

A 65-year-old man was referred to hospital by his GP with a 4-day history of right upper-quadrant colicky abdominal pain, episodes of diarrhoea and unexplained 3 kg weight loss over the past few months. His medical history consisted of hypertension, hypercholesterolaemia, bilateral inguinal hernia repair, sciatica, multiple basal cell carcinoma excision and diverticular disease.

Initial investigations showed abnormal liver function tests with mildly elevated alkaline phosphatase and alanine aminotransferase (142 U/L and 346 U/L, respectively). Abdominal ultrasound scan showed gallstones and a fatty liver with several solid and cystic lesions in both the lobes. To investigate this further, a computed tomography (CT) scan was organised which showed partially calcified lymphadenopathy in the mid-SB mesentery measuring 1.8 cm with spiculations and a similarly calcified poorly

visualised mass in the adjacent SB measuring 1.8 cm which was consistent with mid-gut NET. CT scan did not identify any metastatic liver [Figure 1], lung or bony lesions. However, magnetic resonance imaging (MRI) of the liver [Figure 2] demonstrated >25 T2 hyperintense lesions in both the lobes of the liver. On dynamic contrast-enhanced sequences, these lesions showed intense enhancement on arterial phase, complete rim enhancement on portal venous phase and complete washout on delayed phase, features consistent with hypervascular liver metastases. The patient also had radionuclide octreotide single-photon emission CT scan which showed a primary lesion in the SB, mesenteric nodal deposits and multiple liver metastases showing abnormal uptake. There was no evidence of overexpression of somatostatin receptors elsewhere. His chromogranins A and B were raised at 214 pmol/L (<61) and 164 pmol/L (<151), respectively. Rest of the gut hormone profile was normal.

The patient was seen by a NET specialist and was started on somatostatin analogues. His case was also discussed at the combined hepatobiliary and NET multidisciplinary meetings, and it was decided to offer him surgery to remove the primary tumour and debulk the liver disease as much as possible.

An upper midline laparotomy with extension to the right subcostal region was performed. On the pre-operative ultrasound, it was felt that even MRI had underestimated the size and number of liver lesions. The patient underwent right hemicolectomy and regional lymphadenectomy, cholecystectomy and excision of 34 liver lesions from both the lobes of the liver. Further, five superficial lesions were diathermy ablated and five deep seated lesions were radiofrequency ablated. A total of 44 liver lesions were treated and no disease was left at the post-operative ultrasound scan.

The patient made a remarkable recovery and was able to return home 5 days after the surgery with long-term octreotide treatment. Follow-up scans were scheduled biannually in the first 24 months post-operation and every 9–12 months thereafter. The histopathology showed a well-differentiated grade 1 (Ki-67 immunostaining showed >1% staining) NET of the terminal ileum with multiple mesenteric and liver metastases (T3N1M1).

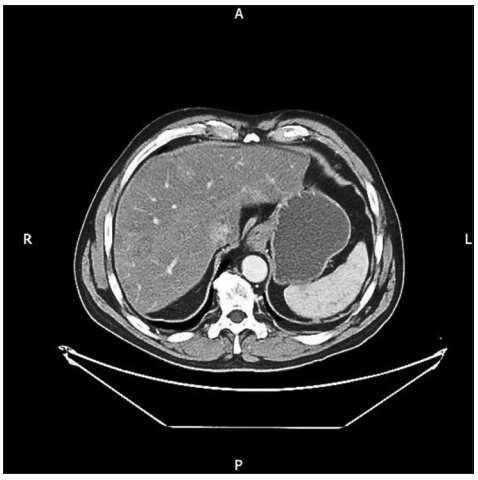

Figure 1: Pre-operative computer tomography scan (late arterial phase). No liver lesions seen

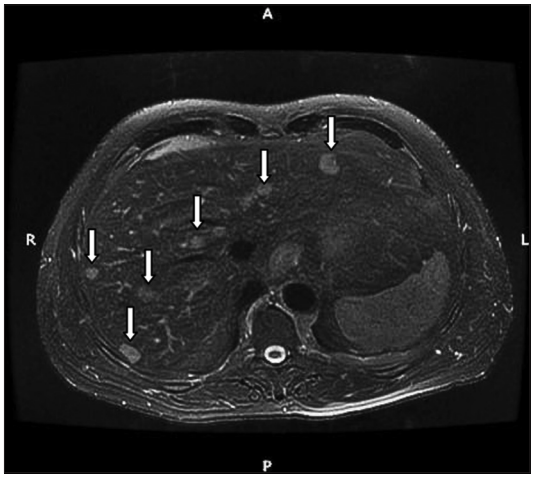

Figure 2: Pre-operative magnetic resonance imaging (short TI inversion recovery sequence): multiple hyperintense metastases in both the lobes of the liver

In the post-operative period, there was a significant reduction in the NET markers and improvement in the patient's symptoms. The patient reported the disappearance of episodic facial flushing but did complain of minor diarrhoea with fatty stools. Faecal elastase levels were found to be low (163 µg E1/g stool), indicating mild-to-moderate exocrine pancreatic insufficiency secondary to long-term octreotide use. This was addressed by an increase in the patient's pancreatin (Creon) dose.

The patient was advised to remain on long-term octreotide in case there were smaller undetected metastases that

could not be resected and to relieve any residual functional symptoms of carcinoid syndrome. At 6-, 12- and 18-month follow-up, the patient is asymptomatic. Chest, abdomen and pelvic scans remain negative for recurrence, and chromogranin A and B levels remain normal at 35 and 72 pmol/L, respectively.

Discussion

Surgical resection of SB-NET remains the treatment of choice when possible.[8] The survival rates improve further when the metastatic disease is also removed.[9] The treatment strategy has been outlined by the European NET Society and is recommended in patients with low morbidity and mortality, including the absence of extra-abdominal metastases, diffuse peritoneal carcinomatosis and right heart insufficiency.[10]

In this case, cytoreductive surgery (debulking) enabled resection of the primary tumour, liver metastases and lymph nodes. One study showed that aggressive intra-abdominal debulking of such tumours resulted in a median survival of 139 months, compared to 69 months for those who did not undergo debulking.[11] Of those with liver involvement, liver-directed intervention prolonged a survival by 216 months compared to 48 months.[11]

Cytoreductive surgery is not without its potential complications; these commonly include post-operative infections, abscess formation, bile leak and hepatic failure. Parenchymal-sparing techniques such as ablation, enucleation and wedge resections, however, offer greater safety and efficacy than other surgical techniques.[12,13]

It is interesting to see that multiple liver lesions were not seen at the CT scan, and even the MRI of the liver underestimated the bulk of liver disease. To our knowledge, there is no study directly comparing the utility of CT and MRI in localising primary NET lesions and distant metastases, but it is appreciated by experts that MRI of the liver gives better information than CT scan. Multiple studies have compared the usefulness of a variety of imaging modalities (CT, MRI, SRS and PET), all of which showed reasonable sensitivity and specificity in localising primary lesions and distant metastases.[14-20]

In summary, this case has demonstrated the superiority of MRI in detecting liver metastases with the benefit of zero radiation to the patient and, in our opinion, is the investigation of choice. It is also important to recognise that NETs are slow-growing tumours and do not behave like adenocarcinomas. It is, therefore, entirely reasonable to be aggressive in the surgical resection for these patients as cytoreductive therapy significantly improves their prognosis.

Learning points

- NETs are rare and may present with trivial symptoms.
- MRI is superior to CT imaging in detecting NET liver metastases.
- Cytoreductive surgery is effective in managing metastatic disease.

Conflict of Interest

The authors declare that they have no conflict of interest.

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