CASE REPORT

A Rare Case of Hepatic Flexure Gastroenteropancreatic Neuroendocrine Carcinoma (GEP-NEC)

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ABSTRACT

A Colorectal neuroendocrine carcinoma (CRNEC) is a rare malignancy of the colon. It is a tumour with a heterogeneous presentation, further complicated by its disunified nomenclature, which imposed a challenge in detection and management. We present a rare case of hepatic flexure neuroendocrine carcinoma in a 47-year-old lady who complained of 5 months history of progressively worsening, intermittent colicky central abdominal pain, altered bowel habit, vomiting, and significant weight loss. She presented with lethargy, distended abdomen and fullness at its centre. The abdominal x-ray showed generalised bowel dilatation, with the subsequent CT scan abdomen showing obstructed hepatic flexure tumour. She underwent emergency exploratory laparotomy and right hemicolectomy with a double-barrel stoma. Intraoperatively, a hepatic flexure tumour, an engorged and nodular appendix with multiple mesenteric lymph nodes. Her recovery was unremarkable. Histopathology examination showed neuroendocrine tumour Grade 3 arising from hepatic flexure with no appendiceal involvement.

Keywords: Colon neuroendocrine tumour, Neuroendocrine carcinoma, Gastroenteropancreatic neuroendocrine tumour, Colon cancer

INTRODUCTION

Colorectal neuroendocrine (CRNET) tumours are a category of heterogeneous neoplasm previously referred to as carcinoid tumours that tend to transform into invasive carcinoma. It is a rare colon tumour, and its annual prevalence is approximately 0.86/100000 cases. Over the years, there has been an increasing incidence of colorectal neuroendocrine tumours. Nevertheless, they only accounted for about 20% of all neuroendocrine tumours. It affects the male gender predominantly. Attributable to its rarity, the colorectal neuroendocrine tumour remains enigmatic even more for neuroendocrine carcinoma. The lack of nomenclature and classification standardisation have hindered obtaining the best treatment and prognosticating this tumour group. We present a rare case of the colorectal neuroendocrine carcinoma of the hepatic flexure.

CASE REPORT

A 47-year-old lady with no previous comorbid, presented to us with five months history of intermittent colicky central abdominal pain, progressively worsening and associated with early satiety, vomiting, altered bowel habit and unintentional weight loss, 14 kilograms over four months period. Symptoms worsened four days before admission, predominantly more constant and higher intensity of colicky abdominal pain. She was lethargic, pink, warm peripheries, not cachexia on examination. Vitals sign was within normal parameter. On abdominal examination, there was abdominal distension with fullness at the centre abdomen, tender upon palpation. Otherwise, there was no hepatosplenomegaly or guarding. Per rectal examination showed collapse and empty rectum with no mass felt. An abdominal x-ray showed dilated large and small bowel with subsequent CT scan showed an obstructed hepatic flexure tumour with multiple mesenteric and paraaortic lymphadenopathy. Subsequently, the patient underwent emergency exploratory laparotomy with an extended right hemicolectomy (Figure 1). However, the nodes surrounding the root of the mesentery was unresectable. Intraoperatively noted long segment hepatic flexure tumour with dilated and oedematous proximal bowel. There were multiple rigid and fixed mesenteric nodes at the root of mesentery. The appendix was grossly enlarged with multiple irregular nodules (Figure 2). No mass felt distal to the tumour, and the rectum was collapsed. No peritoneal or liver surface deposit was seen (Figure 3). Double barrel stoma was
fashioned at the right abdomen because of oedematous and dilated bowel. Postoperatively, her recovery was unremarkable, and she was discharged on postoperative day 5. OGDS and colonoscopy were done and noted sub-centimetre pedunculated polyp at the rectum; no synchronous lesion was seen. Histopathology examination of the specimen was consistent with a poorly differentiated neuroendocrine carcinoma, grade 3, Ki67 77% and mitotic count of 20/10HF. There was evidence of lymphovascular and visceral peritoneum invasion, 24 out of 26 nodes positive. The disease was staged as pT4aN2b according to American Joint Committee on cancer (AJCC) 8th edition. The appendix was normal with no evidence of tumour infiltration. Polyp from the rectum turns out to be tubular adenoma with low-grade dysplasia. She was seen by the oncological team and adamantly refused subsequent chemotherapy. She succumbed to the disease within three months of her presentation to us.

DISCUSSION

A neuroendocrine tumour is a constellation of a less aggressive tumour than adenocarcinoma, arises from amine decarboxylation (APUD) cells, and unnecessarily secreting biologically active cytokines (1). The incidence of gastroenteropancreatic neuroendocrine tumour (GIP-NET) has increased over recent years,
owing to the standardisation of nomenclature of this disease, which was previously also known as carcinoid, and the improvement of detection modalities, namely endoscopic, computed tomography (CT), magnetic resonance imaging (MRI), scintigraphy and ultrasonography (1). Neuroendocrine carcinoma is the term given to carcinoid tumours with poorly differentiated, Ki67 index of >20% and >20 mitotic count/10HF. Improvement in worldwide conjoint effort and communication has proven to be prudent for the early detection strategy of this disease.

Often, patients with this disease will present at the later stage of the disease. Manifestation of this disease at an early stage is non-specific and has proven hard to detect. This is supported by the fact that less than 10% of the patient may present with classic carcinoid symptoms such as gastrointestinal hypermotility and cutaneous flushing due to the release of vasoactive cytokines. Most patients with gastrointestinal neuroendocrine tumours presented with mechanical obstruction symptoms such as constipation, pain and abdominal distension (1). Gastrointestinal neuroendocrine tumour can be classified relative to its embryological origin into foregut, midgut and hindgut. They elicit distinct clinical presentations, respectively. Commonly, midgut neuroendocrine tumour presents with spasmodic crampy abdominal pain owing to progressive mechanical obstruction from desmoplastic mesenteric lymph nodes reaction, which subsequently leads to tethering or kinking of the affected segment of bowel, eventually causing a complete obstruction (2). These symptoms are consistent with our patient presentation, where her episode was preceded by five months history of progressively worsening intermittent crampy abdominal pain associated with vomiting, early satiety and significant loss of weight. Unfortunately, no medical treatment was sought before her emergent presentation, where complete obstruction at the level of hepatic flexure has occurred. Nevertheless, symptoms such as diarrhoea, flushing, bronchospasm, and right-sided valvular heart disease should be actively sought to increase clinical suspicions of colorectal neuroendocrine tumours further.

Since the clinical presentations are non-specific, diagnosis of this condition relies on high accuracy investigations of biochemical markers, radiological and endoscopic assessment. A substance such as 5-hydroxy indole acetic acid (5-HIAA) is a product of serotonin metabolism and relies on the production of serotonin, which is produced by most neuroendocrine tumours. Twenty-four-hour urinary collection of 5-HIAA is the investigation of choice for a serotonin-avid neuroendocrine tumour, mostly midgut neuroendocrine tumour, with a staggering high sensitivity and specificity, 70% and 98%, respectively (3). Its reliability is contested by possible false-positive results from patients with malabsorption syndromes or those who consumed foods enriched with tryptophan (3). Hence, patients under investigation are advised to refrain from taking specific tryptophan-enrich food for a minimum of 5 days before ensuring the reliability of this test. Chromogranin A is another biomarker that can be used to diagnose neuroendocrine tumours. It is independent of serotonin production, which confers its higher sensitivity compared to 5-HIAA at the expense of lower specificity (3). Nevertheless, caution should be practised when interpreting its result in a patient with concurrent renal failure, hyperthyroidism, chronic liver disease, inflammatory bowel disease and for the patient on proton pump inhibitor as a result may falsely raise. Besides biomarker, radiological assessment of the targeted area of interest with triphasic computed tomography and magnetic resonance imaging has comparable sensitivity to detect either primary or metastatic lesion with 30%-70% and >90%, respectively (3). Molecular imaging has a vast option in their armamentarium, capitalising on the particular biological functionality of neuroendocrine tumours. The first choice would still be the Indium-111-diethylenetriamine Penta-acetic acid-octreotide (Octreoscan) which capitalised on the somatostatin receptor expressed up to 90% of GEP-NET (3). Besides, positron emission tomography imaging has gained popularity recently with the labelling of its isotopes (68Ga) to somatostatin analogues giving rise to 68Ga-DOTATOC and 68Ga-DOTATE PET scan. PET scan is superior to Octreoscan in terms of shorter duration for investigation, reduced radiation exposure, and better PET camera sensitivity and resolution. Lastly, endoscopy assessment of the gastrointestinal system is still considered an essential adjunct with the advantage of direct tissue visualisation, tissue biopsy and treatment (4). Curative treatment is possible for early-stage GEP-NET through endoscopic submucosal dissection.

Often, the patient presented at a later stage of the disease, which hampers curative treatment options. Treatment options mainly focus on local control and systemic therapies to alleviate symptoms associated with NET. Surgical oncological resections remain the primary treatment option in symptomatic resectable GEP-NET. Subsequent adjuvant treatment depends on the surgical clearance of the lesion and its ensuing lymphatic drainage, its proliferative markers such as Ki67 index and mitotic count and the presence of metastasis as summarised by figure 4 (5). Systemic therapies are achieved by administration of somatostatin analogues, peptide receptor radionuclide therapy, interferon-alpha and a molecularly targeted agent such as sunitinib (5). As for our patient, she underwent extended right hemicolecotomy with D2 lymphadenectomy; however, the final HPE is dismal. It was a high-grade neuroendocrine carcinoma, poorly differentiated with a Ki67 index of 77% and mitotic count of 20/10HF, 20 out of 24 lymph nodes affected with evidence of lymph vascular and visceral peritoneum invasion. She was planned for platinum-based chemotherapy; however, treatment was refused despite sufficient counselling and information.
Surveillance following treatment posed another challenge in managing patients with GEP-NET, even worst for GEP-NEC. Surveillance is aimed to monitor treatment response, recurrence and metastasis. The survival rate after successful surgical resection is 62.7% within five years (4). Surveillance strategy utilising respective biomarker, radiological imaging and PET scan at preset interval is essential. The North American Neuroendocrine Society (NANETS) consensus agrees to utilise PET scan at baseline then followed by multiphasic computed tomography (CT) or MRI 3 to 12 months after resection then 6 to 12 months for up to 10 years. (4) However, in the case of neuroendocrine carcinoma, Oberg K et al. has suggested a more vigorous regime by performing surveillance multiphasic CT scan or MRI every 2-3 months and somatostatin receptor imaging after 18-24 months (5). Biomarker assessment by chromogranin A is crucial to correlate with radiological findings. Our patient’s condition deteriorates two months postoperatively, complicated by unremitting abdominal pain, which affects her oral intake and nutritional status. Given the magnitude of her disease, without any systemic therapies, her prognosis is dismal. She succumbed to her disease approximately three months following the initial surgery.

CONCLUSION

Neuroendocrine tumour of hepatic flexure colon is a rare disease even rarer for neuroendocrine carcinoma with dreadful prognosis. A high index of suspicions is imminent to enable early detection of these tumours since mostly it presents at a later stage.

REFERENCES