

CASE REPORT

A rare case of oesophageal neuroendocrine carcinoma: the value of somatostatin receptor scintigraphy

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Abstract

We present a case of metastatic neuro endocrine carcinoma of the lower end of the oesophagus, rare as for the primary tumour site. Somatostatin Receptor scintigraphy with ^{99m}Tc-EDDA/HYNIC-octreotate findings altered the patient's management from curative surgery to palliative chemotherapy. The patient presented with progressive dysphagia and was histopathologically diagnosed on biopsy of the mass at the lower end of the oesophagus as high-grade neuroendocrine carcinoma. Baseline investigations showed deranged liver function, but except for a thickened gastro-esophageal junction, there was no abnormality seen on the initial computerized tomography scan. Also, raiologically, there was no evidence of metastatic disease seen either in the liver or the bones. Prior to surgical intervention, which was decided in the institutional tumour board, the patient was referred to the department of nuclear medicine for somatostatin receptor scintigraphy with ^{99m}Tc-EDDA/HYNIC-octreotate. The images demonstrated widespread metastatic disease in the liver, bones and abdominal lymph nodes. The osseous lesions correlated well with abnormal tracer foci seen on subsequent bone scintigraphy. Moreover, scanning was completed within twenty-four hours with high-quality images produced owing to the ideal physical characteristics of technetium-99m. On the basis of the findings of the somatostatin receptor scintigraphy, the management changed from curative surgery to palliative chemotherapy. The patient however was unresponsive to combination chemotherapy and eventually expired five months after the initial diagnosis due to disease progression.

***Key words**: Neuroendocrine carcinoma, somatostatin receptor scintigraphy, ^{99m}Tc-EDDA/HYNIC-octreotate*

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Introduction

Neuroendocrine tumours (NET) are derived from enterochromaffin cells, traditionally described as originating from the foregut, midgut and hindgut. However, neuroendocrine tumour of the oesophagus is a rare entity in

 2221-0288(201201/02)1:1<69:RCONCS>2.0.TX;2-M

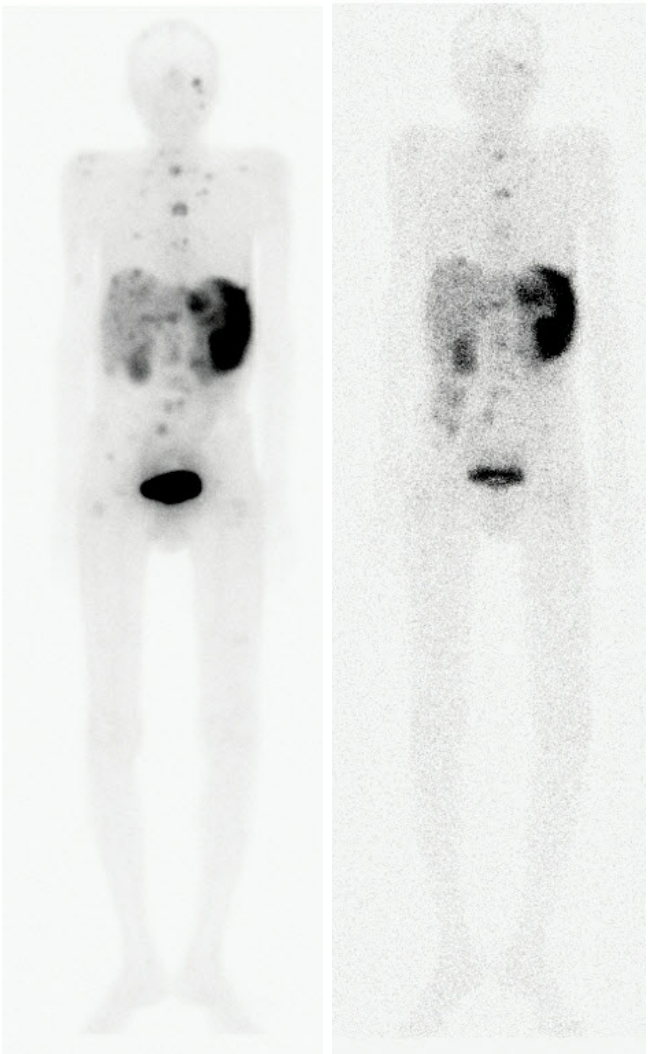

Figure 1 *Somatostatin receptor scinti graphy showing primary tumour at the lower end of oesophagus with multiple abnormal foci of the radiotracer throughout the liver, bones and abdominal nodes*

itself. Combining new diagnostic and treatment modalities in neuroendocrine tumours result in better quality of life and longer survival times. Moreover, the stage of the disease is of great importance for prognosis. Although the diagnosis is usually based on tissue examination or biopsy, the patient's symptoms combined with radiologic and scintigraphic findings are also very helpful. Somatostatin Receptor Scintigraphy (SRS) has gained popularity as an imaging method both for staging neuroendocrine tumours and determining the somatostatin type receptor (SSTR) status. The latter has therapeutic significance as well. ^{99m}Tc-Ethylene diaminediacetic acid/6-Hydrazinopyridine-3-carboxylic acid [HYNIC]-octreotate (^{99m}Tc-EDDA/HYNIC-octreotate) is a radiotracer with high affinity for SSTR 2. The physical bio distribution is similar to that of ^{111}Indium-Pentetreotide (^{111}In-Pentetreotide), which has been used for many years; however, its advantage is that it provides high-quality images with good target/background ratio and lesser time to scan patients owing to the favourable physical characteristics of technetium-99m for radionuclide imaging.

Case Report

A frail and rather emaciated looking 55-year-old man presented in the medical oncology outpatient clinic with a history of progressive dysphagia for the past one month. He had no family history of malignancy. The patient underwent baseline work up. The laboratory results showed deranged liver function but the computerized tomography (CT) scan of the chest and abdomen was unrevealing apart from thickening of the stomach wall, the gastro-oesophageal junction and the adjacent oesophagus.

The patient had oesophagogastroduodeno scopy (EGD), which demonstrated a nodular plaque-like tumour involving the lower end of the oesophagus, 34 cm from the incisors. The cardia was involved by a thick ulcerated tumour mass. The biopsy taken from the mass was histopathologically proven to be high-grade neuroendocrine carcinoma. A 15Fr percutaneous endoscopic gastrostomy (PEG) tube was placed for feeding purposes.

The patient was discussed in the institutional tumour board and as there was no evidence of metastatic disease radiologically, an initial decision for possible surgical intervention was considered. However, prior to implementing the plan, the patient was referred to the department of Nuclear Medicine for SRS for staging and determining the SSTR status.

The patient underwent SRS with 760 MBq of

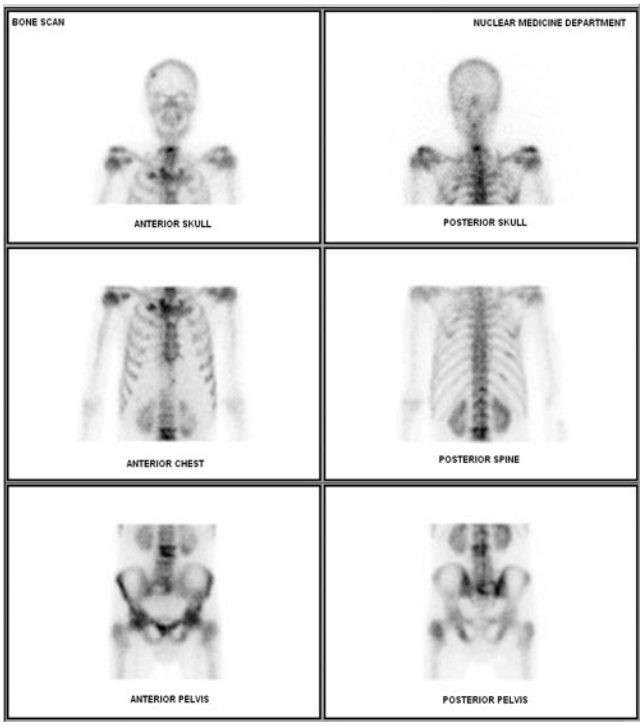

Figure 2 *Secondary skeletal involvement seen on bone scan in the skull, spine, multiple ribs, right sacroiliac joint and the left trochanteric region of the femur*

^{99m}Tc-EDDA/HYNIC-octreotate given by intravenous route. Static images of the whole body were acquired in both anterior and posterior projections (256 x 1024 matrix, six views with 300 seconds/view) at 10 minutes, four hours and 24 hours postinjection. Single photon emission computerized tomography (SPECT) images of the abdomen were also acquired using 3600 orbit (1800 for each head), step-and-shoot mode, 128 x 128 matrix, a total of 60 projections at 30-second/view; 4 hours after the injection. Scanning was performed using a dual-headed large field-of-view gamma camera equipped with a low-energy high-resolution collimator. Focal tracer accumulation was considered specific when visualized both on the 4- and the 24-hour images.

The scan findings were compatible with pathological focal increased uptake of the tracer at the lower end of the oesophagus with widespread osseous and liver metastases (Figure 1). Subsequent bone scan (with 740 MBq of ^{99m}Tc-Methylene Diphosphonate) confirmed the secondary skeletal involvement (Figure 2).

The patient was re-discussed in the tumour board and based upon the findings of the SRS, it was decided to treat the patient with palliative chemotherapy. The patient received five cycles of Cisplatin/Etoposide but with no any obvious clinical improvement. The follow-up CT scans and bone scintigraphs showed disease progression. The patient's performance status declined progressively, and he eventually expired five months after the initial diagnosis.

Discussion

The overall incidence of neuroendocrine tumours appears to have increased in the past decades [1] presumably due to changes in the detection rate. Under the age of fifty, the incidence is approximately twice as high in females as in males. At older ages, a male predominance is observed with a rate double that of women [2]. The sites most affected in neuroendocrine tumours are the gastrointestinal tract which accounts for about 65%, followed by bronchopulmonary tract, which accounts for about 25% of the cases [3]. However, oesophagus is a rare site for neuroendocrine tumours of the gastrointestinal tract with the neuroendocrine carcinoma of the oesophagus representing only 1-2.8% of oesophageal cancer cases [4, 5].

Presentation with metastases is found in 22% of the cases. The stage of the disease greatly influences the prognosis with best five-year survival rate of 93% in localized disease and a poor five-year survival rate of 20-30% in distant metastatic disease [3]. The incidence of skeletal metastases in neuroendocrine tumours has been reported to be approximately 10% [6]. Secondary skeletal involvement was evident in our case both on SRS as well as bone scintigraphy. Although, bone metastases most often arise from bronchial or hindgut primaries, recent data suggest no preferential primary site [7].

In most of the patients, as in this case, the diagnosis of neuroendocrine carcinoma is made on tissue examination [8]. However,

radiologic and scintigraphic findings help in staging and therefore subsequent management. Somatostatin receptors are located on the cell membranes of most of the neuroendocrine tumours. Imaging these helps not only to determine the stage of the disease but also has therapeutic implications. A positive SRS qualifies a patient for ^{90}Yttrium or ^{177}Lutetium based targeted therapy. Previously, ^{111}In-Pentetreotide and ^{131}Iodine-metaiodobenzylguanidine (^{131}I-MIBG) have been used to image neuroendocrine tumours with reported sensitivity of 80% and 70% respectively [9, 10]. The problems with ^{111}In-Pentetreotide and ^{131}I-MIBG are a high radiation burden, relatively poor-quality images and delayed scanning. It is due to these problems that ^{99m}Tc labelled somatostatin analogues with specific and high receptor affinity, high-quality images owing to the favourable imaging characteristics of ^{99m}Tc and early imaging have been in vogue from the past few years [11].

^{99m}Tc-EDDA/HYNIC-octreotate is a radiotracer with a high affinity for SSTR 2 [12]. The octreotate differs from octreotide by the more hydrophilic tyrosine in the third position and terminal threonine. The physiological biodistribution is similar to that of ^{111}In-Pentetreotide, but allows rapid imaging, detects more metastatic lesions with higher target/non-target ratios [13]. This was evident in our case where the scanning was completed within twenty-four hours and widespread metastatic disease was documented. Moreover, the involvement of the liver and bones was not seen on initial CT scan.

The use of chemotherapy in neuroendocrine tumours is limited and reserved only for either high-grade tumours or palliative setting. Single agent chemotherapy is not useful in the treatment of neuroendocrine tumours with very low response rates of about 5-10%. Although, combination chemotherapeutic agents could be used with slightly better response rates around 15-30%, the results are not encouraging [14] and same was observed in our patient who eventually expired due to unresponsive progressive disease.

In summary, SRS with ^{99m}Tc-EDDA/HYNIC-octreotate can be employed for staging neuroendocrine tumours. The findings of the somatostatin receptor scintigraphy have a significant impact in neuroendocrine tumours originating at rare sites such as the oesophagus, as these assisted in this patient's management, which led to an alteration in the treatment from curative surgery to palliative chemotherapy. Moreover, due to the ^{99m}Tc label, the images produced have a good target/background ratio with the ease of prompt scanning, which can be completed within twenty-four hours.

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