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Metastatic rectal neuroendocrine tumor presenting as an inguinal mass: A case report and review of literature

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ABSTRACT

INTRODUCTION: Neuroendocrine tumors (NET) are a heterogeneous group of rare carcinomas that most often manifest along the gastrointestinal tract. Some of these tumors have the ability to secrete vasoactive peptides and hormones.
PRESENTATION OF CASE: The present report describes the case of a previously healthy 52-year old man who presented with a painful right inguinal mass. Upon surgical exploration, a lymph node metastasis of a high-grade NET was found. Further investigations revealed a rectal NET with pulmonary, pelvic and penile metastases.

The patient was treated with 6 cycles of carboplatin and etoposide. Although initial follow-up imaging after 3 cycles of chemotherapy revealed stable disease, there was progression of the metastases after completion of systemic treatment. Second and third-line chemotherapy regimens were instituted along with pelvic and whole-brain radiation therapy extending the patient's survival to 18 months after the initial diagnosis.
DISCUSSION: This case highlights the aggressive nature high-grade NETs as described in the current literature. Treatment modalities of colorectal NETs include local excision for non-metastatic disease and systemic palliative chemotherapy for advanced disease. However, there are no controlled trials in favor of palliative chemotherapy.
CONCLUSION: Rectal NETs are rare tumors which often have an atypical presentation or present in advanced stages. Currently, surgical options exist for local disease while treatment modalities for more advanced disease is still under investigation.

1. Introduction

Neuroendocrine tumors (NETs) are carcinomas that can arise anywhere in the body with most reported cases occurring along the gastro-intestinal tract. NETs represent a heterogeneous group of malignancies that, in certain cases, exhibit secretory properties, producing a variety of vasoactive peptides and hormones, such as serotonin, histamine, kinins and prostaglandins. They are rare in comparison to most other neoplasms, representing only 0.9% of all tumors and 2% of gastro-intestinal malignancies [1]. Historically, these tumors were referred to as carcinoids. However, the literature has progressively distanced itself from this nomenclature as only a minority of NETs displays the classic presentation of carcinoid syndrome (flushing, diarrhea and heart failure) [1,2]. This article reviews the case of a patient with a metastatic rectal NET that initially presented as a painful inguinal mass.

2. Presentation of case

A 52 year-old male patient presented to the emergency department with right groin pain for 1 week that began after strenuous activity. On physical exam, there was a firm non-reducible right inguinal mass. The patient had no symptoms of bowel obstruction and abdominal examination was unremarkable. No other complaints were formulated by the patient at that time. Complete blood count and serum creatinine and electrolytes were all within normal values. The differential diagnosis included an incarcerated right inguinal or femoral hernia or a right inguinal lymphadenopathy. As an uncomplicated non-reducible inguinal hernia was the primary diagnosis at the time, an open right groin exploration was performed 2 days later without preoperative imaging.

On surgical exploration, no inguinal or femoral hernia was detected. However, a mobile, indurated 2.5 cm right inguinal mass was found and an excisional biopsy of the entire mass was per-

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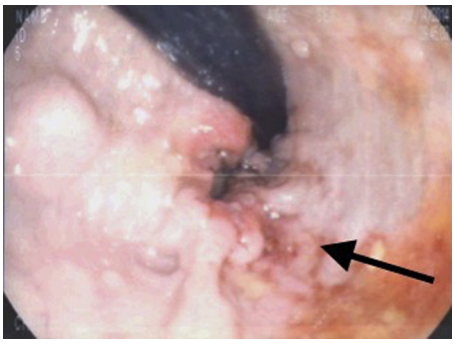

Fig. 1. Ulcerated lesion of the rectum found at endoscopy (black arrow).

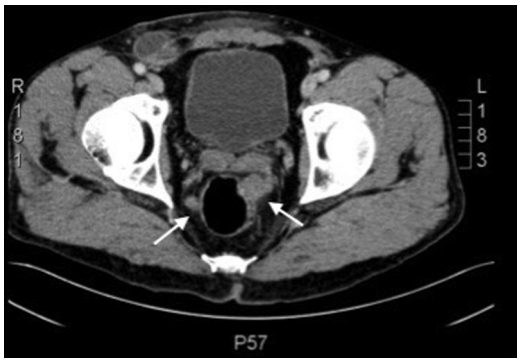

Fig. 3. CT of the pelvis showing multiple peri-rectal nodules (white arrows).

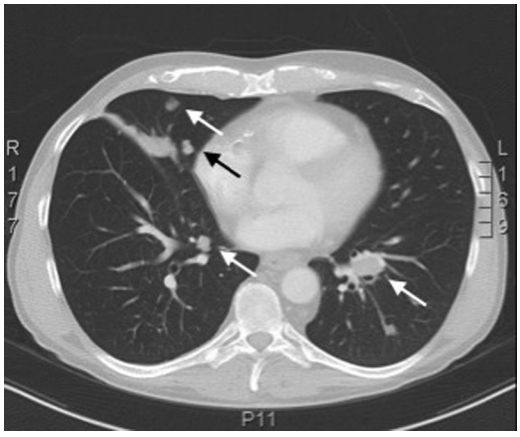

Fig. 2. CT of the chest showing multiple bilateral lung nodules (white and black arrows).

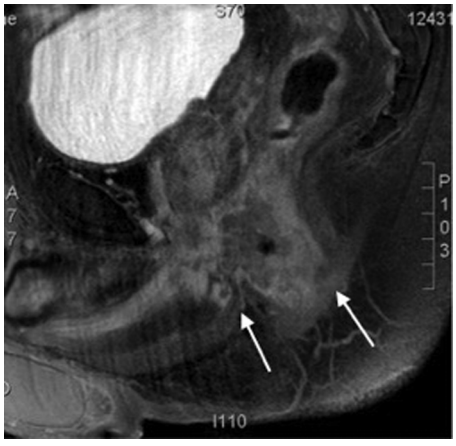

Fig. 4. Sagittal view of pelvic MRI showing rectal mass with invasion of levator ani muscle and satellite nodules of the peri-rectal fat and base of the penis (white arrows).

formed. Had preoperative ultrasound or computed tomography imaging been obtained, a percutaneous biopsy could have been carried out, albeit with the risk of insufficient tissue sampling. Preliminary microscopic evaluation determined the mass to be a lymph node metastasis with capsular invasion of an undifferentiated carcinoma of possible uro-genital origin. No lymphocytic proliferation was noted, excluding the possibility of lymphoma.

On further physical examination, the patient was noted to have three 0.5 cm subcutaneous nodules at the base of the penis and an indurated lesion extending 5 cm up from the anal verge on digital rectal exam. On colonoscopic investigation, an ulcerated lesion on the right rectal wall extending 4 cm up from the anal verge was found along with a submucosal nodule that was tentatively thought to be a lymph node (see Fig. 1). Endoscopic biopsies of the lesion were performed. Pathological diagnosis was that of a high-grade neuroendocrine carcinoma with keratin-7, chromogranin A and synaptophysin enhancement. Ki67 study showed a proliferation index of 80%.

Serum chromogranin A was elevated (114.0 ng/mL), as well as carcinoembryonic antigen (13.8 μg/L) and CA 19-9 (92 kU/L). Twenty-four hour urinary excretion of 5-HIAA was normal.

Computed tomography (CT) of the chest, abdomen and pelvis showed bilateral lung nodules measuring up to 1.4 cm and multiple peri-rectal nodules up to 2.3 cm in diameter (see Figs. 2 and 3). Magnetic resonance imaging (MRI) of the pelvis demonstrated an ano-rectal tumor extending 5.5 cm from the anus with invasion of the levator ani muscle and satellite nodules at the base of the penis and in the peri-rectal fat (see Fig. 4). Positron-emitting tomography confirmed the hypermetabolic and metastatic nature of all the aforementioned lesions.

The patient began complaining of ano-rectal pain as well as occasional blood per rectum. The patient agreed to palliative chemotherapy and a 6-cycle regimen of carboplatin and etoposide was started. The patient tolerated the treatment with the exception of transient afebrile neutropenia that delayed the final treatment by one week. The peri-rectal pain resolved completely with chemotherapy and CT of the chest, abdomen and pelvis after 3 cycles of chemotherapy showed stable disease. Follow-up CT after 6 cycles showed progression of the lung and peri-rectal metastases and a new large celiac trunk lymph node metastasis (3 cm).

The patient was then switched to a 12-cycle regimen of FOLFIRI, of which he received only 11 cycles due to hepatic toxicity and 2 cycles of topotecan. However, follow-up imaging showed progression of the lung and intra-abdominal lymph node metastases and multiple new cerebral and hepatic lesions. The patient went on to receive intensity-modulated radiation therapy to the pelvis (for ano-rectal pain and disease progression) and whole-brain radiation therapy.

Disease progression and the patient's general deterioration led to a discontinuation of chemotherapy and institution of comfort measures. The patient died 18 months after the initial diagnosis.

3. Discussion

As previously mentioned, NETs are a rare entity representing less than 1% of all cancers, with a preponderance for the gastrointestinal system. Although they can present anywhere along the alimentary tract, rectal NETs are most common, representing 17.7% of all NETs according to one American survey [1,3]. The vast majority of rectal NETs are non-secreting and can be either low-grade,

indolent malignancies (often discovered on routine endoscopy studies) or high-grade tumors, which can be aggressive in nature with high metastatic potential [4]. Overall, colorectal NETs are often diagnosed at an advanced stage. One series reported 66% of newly discovered colorectal NETs were metastatic at the time of presentation [5]. This figure is relatively high because of right-sided colic NETs that are often clinically silent.

Low-grade rectal NETs are amenable to either endoscopic or surgical local excision and often do not respond to systemic chemotherapy. A variety of surgical procedures have been described for lesions too large to be removed endoscopically. These include a low anterior resection, abdomino-perineal resection or trans-anal endoscopic micro-surgery (TEMS). Recurrence after each of these surgical interventions is rare if negative margins are obtained [1,6].

Pathological diagnosis of NETs is important as treatment regimens differ greatly from the more common gastro-intestinal neoplasms. Ki67 staining assesses the proliferation rate of the neoplastic cells [7]. Higher-grade lesions, especially if metastatic in nature, will often respond, at least transiently, to a platinum-based chemotherapy regimen. Although no randomized controlled trials studied the effect chemotherapy on colorectal NETs, regimens combining carboplatin or cisplatin with etoposide are usually employed, based on their use in other advanced NETs or small-cell lung carcinoma, a pathologically similar entity [8,9]. There is currently no role for the surgical management of advanced metastatic colorectal NETs albeit for palliation in the case of bowel obstruction, pain or bleeding [9].

Targeted therapies for NETs are developing. Preliminary studies have shown that the use of tyrosine-kinase inhibitors such as sunitinib or mTOR inhibitors (everolimus) may confer a survival advantage in well-differentiated pancreatic NETs. No trials have yet studied their effect on colorectal NETs [10,11].

Gastro-intestinal NETs tend to metastasize in characteristic patterns following the lymphatic drainage of their anatomic location. Intestinal and colic NETs will metastasize to the mesenteric lymph nodes and to the liver. Furthermore, ano-rectal NETs can spread to pelvic and inguinal lymph nodes and tend to bypass the liver and present with metastatic disease to the lung, as observed in the present case [1,9].

In comparison to rectal adenocarcinoma, NETs generally have a poorer prognosis. However, even high-grade tumors remain relatively indolent, as metastatic colorectal NETs have a 2-year survival of 80% [12]. One study of 8 patients receiving cisplatin and etoposide for metastatic colorectal NETs demonstrated a median progression-free survival of only 4.5 months and a median overall survival of 9.5 months [8].

4. Conclusion

Rectal NETs are uncommon tumors with often atypical presentation or an incidental discovery at endoscopy. Most are diagnosed at an advanced stage with the tumor showing many high-grade features and already metastatic. Pathologic diagnosis is important as treatment is different from the much more common rectal adenocarcinoma. Although early stage tumors can be resected, treatment of more advanced disease is systemic palliative chemotherapy. No controlled studies have demonstrated survival advantage of chemotherapy although there is a trend in progression-free survival in certain series.

Conflicts of interest

None.

Funding

None.

Ethical approval

There was no ethics approval required for this case report.

Consent

Informed consent was obtained from the patient's next of kin for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

A. Di Palma: Reviewing patient data, writing the manuscript; H. Sebajang: Contributing author; F. Schwenter: Surgeon involved in patient's care, revising manuscript.

Guarantor

Frank Schwenter.

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