Metastatic neuroendocrine tumor of soft tissue: a case report

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Neuroendocrine tumors (NETs) are relatively rare tumors arising from neural crest cells, mainly in the gastrointestinal tract and lung. Soft-tissue NETs have been occasionally reported in the literature. To our knowledge, we report the first case in the Middle East and the sixth case in the literature of a metastatic NET arising in the thigh. An Egyptian lady in the sixth decade of life came to our hospital with a NET in the thigh, metastatic in both the lung and the iliac region. Staged resection of the primary tumor followed by the nodal metastasis was done after a short period of neoadjuvant chemotherapy and Sandostatin. Diagnosis of these cases is difficult and no studies addressing their management are available. Our approach, pathological findings, and prognosis are discussed in comparison with previously registered cases worldwide. Surgical oncologists should bear in mind that NETs may occur in soft tissue and that surgical treatment is the only known effective treatment.

Keywords:
metastasis, neuroendocrine, soft tissue, somatostatin, thigh tumor

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Introduction

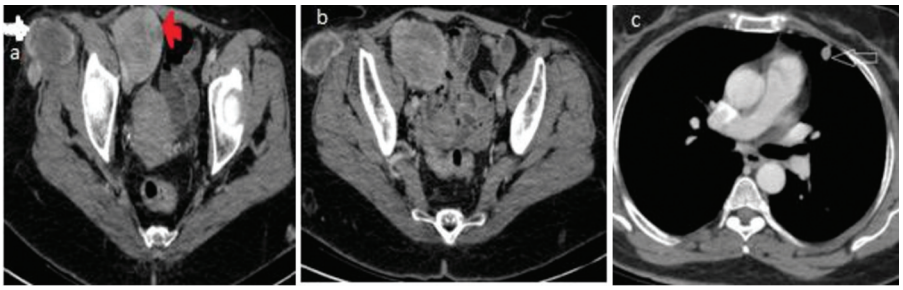
Neuroendocrine tumors (NETs) are thought to arise from cells of the diffuse endocrine system and are mostly of neural crest origin. They commonly arise in the gastrointestinal tract (GIT) (from Kulchitsky cells) and lung [1]. They are characterized by neurosecretory granules that stain positive on silver staining, chromogranin, and synaptophysin [2]. Occasionally, the tumor releases serotonin and other vasoactive substances in the systemic circulation, which may manifest as carcinoid syndrome.

This syndrome is often associated with bulky liver metastases or liver cell failure [3]. Skin metastases of NETs are occasionally documented at different primary sites, and more often coexist with other metastatic lesions [4,5]. Primary NETs arising in skin and soft tissue are even rarer. Our case is unique in presenting with lung and nodal metastasis, and our treatment is tailored in a multidisciplinary manner extrapolating experience from managing GIT NETs.

Case presentation

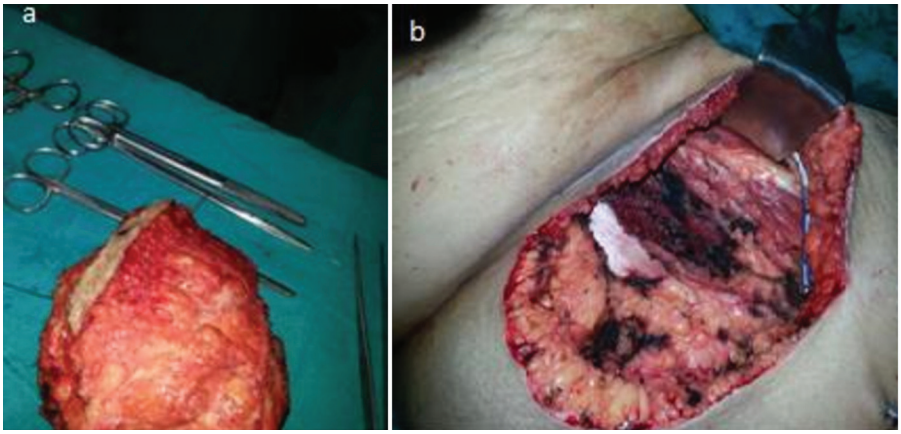
We present a case of an Egyptian woman aged 55 years with poorly controlled type I diabetes mellitus. The patient presented to her general practitioner in June 2014 with a right thigh mass encroaching on the inguinal region. MRI showed a right iliac fossa mass measuring 5×5×7 cm, with enlarged right inguinal lymph nodes with distorted shape measuring 3×4 cm. The patient was then referred to our center where computed tomography (CT) with oral and intravenous contrast on the chest, abdomen, and pelvis was performed. CT revealed a well-defined rounded soft-tissue mass in relation to the right external iliac vessels measuring 5×6×7 cm with an amalgamated right inguinal nodal mass measuring 4×6 cm, in addition to two pulmonary pleural-based nodules, the largest being 1.3 cm (Fig. 1). A core needle biopsy was taken from the inguinal mass, showing a NET with positive CD56, chromogranin, and BCL2, and negative CD34, TTF1, CK7, and CK20; Ki-67 index was 6%. Urinary 5-hydroxyindoleaceticacid was 9.6 (normal 6). The patient received three cycles of platinum-based chemotherapy plus Sandostatin, with no response. A multidisciplinary decision was taken to debulk the tumor, which was done as a staged procedure: first, excision of the soft-tissue mass in the thigh through a longitudinal incision (Fig. 2) revealing the NET with free safety margins (Fig. 3) and then excision of the right iliac fossa mass through a right paramedian incision with only a part of the capsule left on the right external iliac vessels (Fig. 4), which revealed the same pathology (Fig. 5). The patient suffered complications in the form of wound infection and gaping after the second operation, requiring several debridements, and was

Figure 1



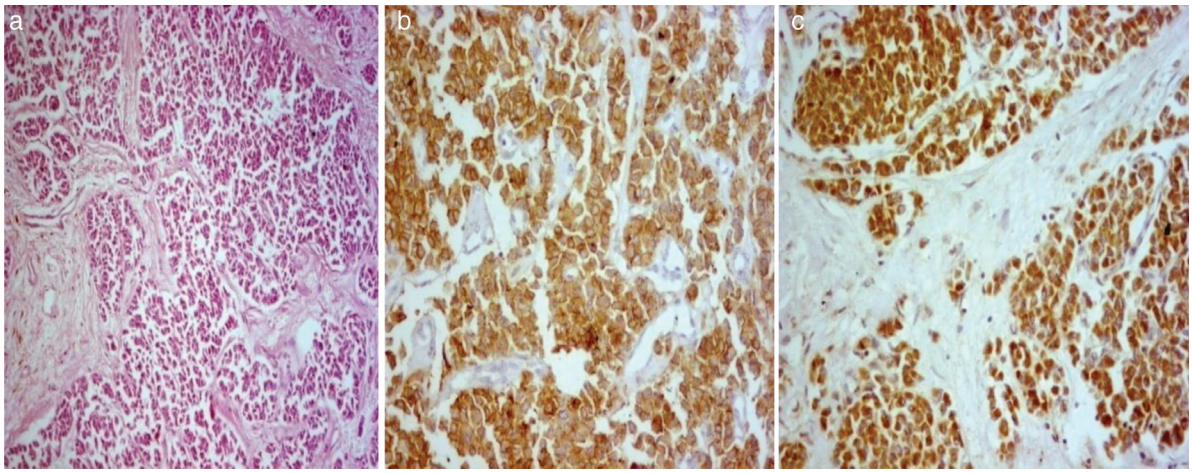
Computed tomography with intravenous contrast. (a) Right thigh mass (white arrow) and right iliac mass partially encasing iliac vessels (red arrow). (b) Section at higher level showing both masses. (c) Left pleural-based nodule (white arrow).

Figure 2



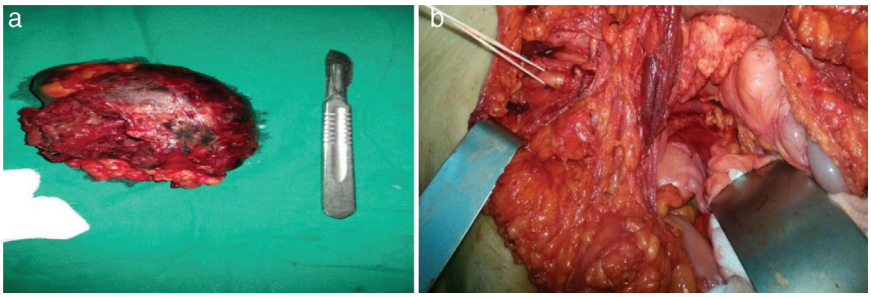
Gross appearance of thigh mass. (a) Excised thigh inguinal mass with overlying skin marked by threads. (b) Bed of the tumor in the right thigh after excision showing intact muscles.

Figure 3



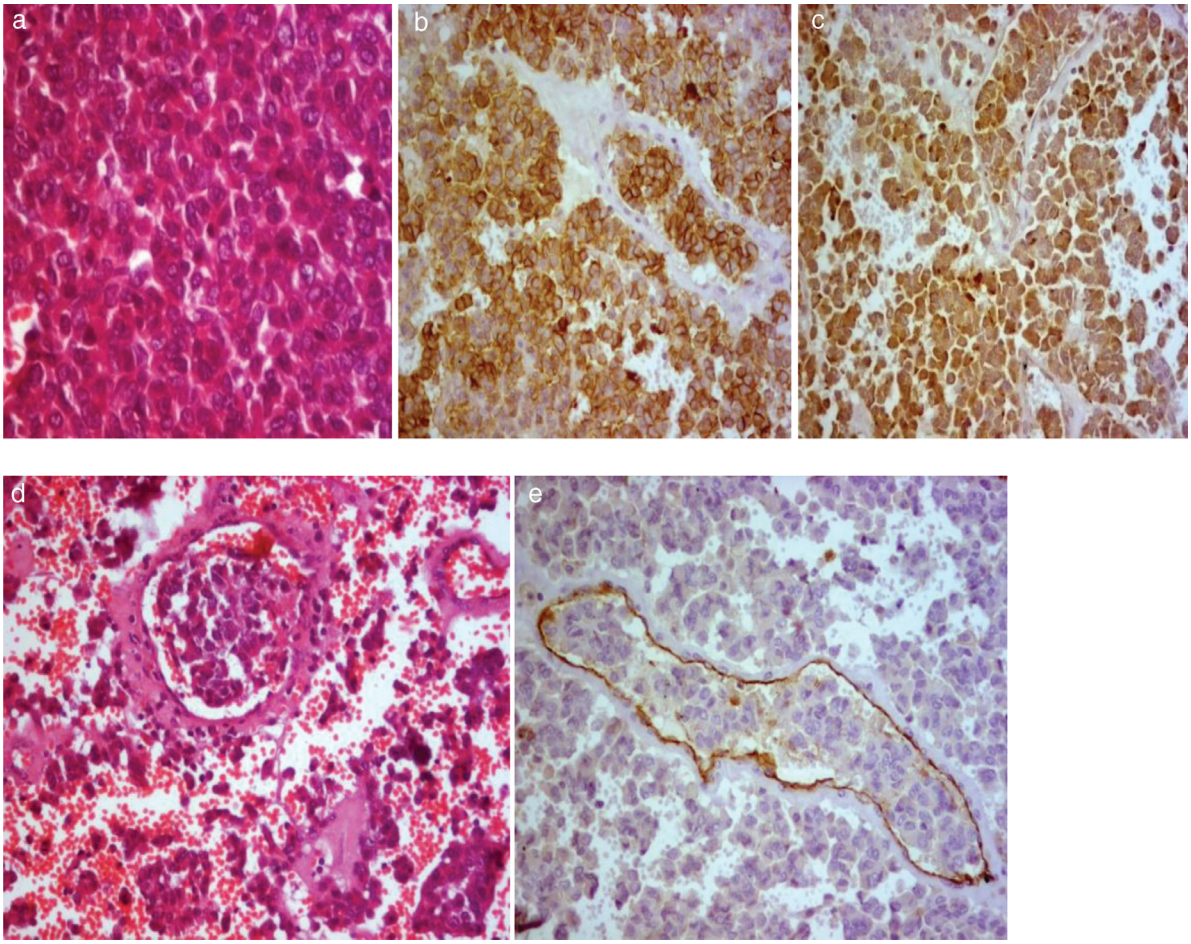
Microscopy of the thigh mass. (a) Insular pattern where nests of tumor cells are separated by fibrovascular stroma; focal rosetting is evident (H&E ×100). (b) Strong reaction for CD56 (×200). (c) Strong reaction for chromogranin (×200).

Figure 4



Gross appearance of the iliac mass. (a) Excised right iliac mass. (b) Bed of tumor showing preserved external iliac artery and exposed femoral artery exposed (hanged by white band).

Figure 5



Microscopy of iliac mass. (a) Higher magnification showing mitotic figures; however, mitoses were infrequent in the range of 3–20/10 HPF (H&E ×400). (b) Strong reaction for CD56 (×200). (c) Iliac mass positive for chromogranin (×200). (d) Vascular tumor emboli (H&E ×200). (e) Vascular tumor emboli highlighted by CD31 (×200).

discharged from the hospital 3 weeks later. Follow-up for 1.5 years with a CT scan every 6 months along with biochemical studies (chromogranin and 5-hydroxyindoleaceticacid) showed no locoregional recurrence and a stationary course of the pulmonary nodules.

Discussion

NETs, although uncommon, have been rising in incidence since 1975. The SEER database suggests that in the USA alone there are more than 100 000 cases of NETs [6]. With increasing number of NET

cases, abnormal sites have been detected, including skin and soft tissue. NETs of the soft tissue may be primary as our case or secondary (mostly from GIT primary). As NETs are slow-growing indolent tumors, metastasis is usually late and often with locally advanced disease. The primary tumor will usually have attained a diameter of at least 1 cm and not infrequently 2 cm, especially if arising in the appendix or rectum. Thus, the primary tumor is usually large enough for detection by radiology [7,8].

The presentation of NETs depends on the site of origin, release of 5-HT and other vasoactive substances into the systemic circulation, and metastasis [9]. In our case report the tumor was nonfunctioning, and nodal and lung metastasis were incidentally found during radiological workup.

The main differential diagnosis of these tumors is Merkel cell carcinoma, which in our case was excluded by: analyzing the skin overlying the thigh tumor which was not infiltrated, and by immunohistochemistry revealing negative CK7 and CK20 (Merkel cell carcinomas are usually CK20 positive and CK7 negative) [10].

After a thorough search of the literature only five cases with NET arising primarily in the soft tissue were found [2,3,11] in addition to our case. As for NETs of the GIT, surgery is the mainstay of treatment with radiotherapy spared for those with narrow margins or unresectable disease, with good results seen in the literature [12,13]. In our case, resection of the primary soft-tissue tumor was done, as well as resection of the pelvic nodal metastasis. The role of octreotide therapy in these tumors is not studied because of their rarity, but studies on GIT NETs limit the use of this therapy to patients with functioning tumors or to those with nonresectable bulky disease [14]. Our case received multiple doses of Sandostatin with no detected radiological response. Chemotherapy whether neoadjuvant or adjuvant has only a modest response in the treatment of these tumors and no overall survival benefit has ever been demonstrated [15]. Three cycles of cisplatinum-based neoadjuvant chemotherapy was also given to our patient with a stationary course (based on RECIST criteria).

NET varies significantly in prognosis depending on the mitotic index, Ki-67, and differentiation. WHO incorporated these variants in classifying NET into three categories: well-differentiated low grade, well-differentiated intermediate grade, and poorly differentiated high grade [16].

Conclusion

The origin and behavior of primary soft-tissue NETs are still not well understood. They appear to have an indolent course, show no response to chemotherapy, and are generally nonfunctioning. Distant metastasis can be the first presentation, although this should not change the plan for surgical resection with a curative intent.

The limitation of our study is that occult GIT NETs could not be completely excluded without somatostatin imaging, which is not available in Egypt to our knowledge. Also, we can assume that we superseded this limitation by the long-term follow-up of the patient for nearly one and half years with CT imaging, with no evidence of GIT lesion.

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Conflicts of interest

There are no conflicts of interest.

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