Case Report

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A Patient with a Thoracic Tumefation

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ABSTRACT

Tumors of the chest wall are uncommon lesions that comprise a heterogeneous group of neoplasms. These tumors may arise from osseous structures or soft tissues and may be malignant or benign. We describe the case of a proliferative swelling of uncertain origin that led us to suspect a neuroendocrine origin for the mass we observed and studied. Neuroendocrine tumors arise from neuroendocrine cells, which are peptide- and amine-producing cells dispersed throughout the body. Usually, these tumors occur in various organs as intrathoracic or abdominal masses that become manifest after a variable time, usually after inducing a heterogeneous symptomatology secondary to the secretion of various molecules. The case we describe, on the other hand, develops both exophytically and endophytically, first appearing as an externally developing thoracic mass. Subsequent appropriate investigations revealed bone and muscle involvement in the patient's thoracic cavity. Therefore, we describe our management of a paucisymptomatic patient who presented with a rapidly developing swelling in the intermammary site that progressed equally rapidly.

Introduction

Chest wall neoformations usually do not represent a frequent reason for seeking medical attention, but when there is a case, it is necessary to evaluate it very well [1]. Swellings at this level are represented by elementary dermatological lesions or, in the most unfortunate cases, by squamous cell carcinomas [2,3]. Finally, there is a range of tumors that can affect the chest wall either as the origin of the neoplasms or with involvement of the same. These neoplasms can develop in the chest wall or spread to the chest from a tumor present in another part of the body. Almost half of the tumors of the chest wall are fortunately non-cancerous in nature (therefore they are benign neoformations). A mass that is appreciated at the level of the chest wall may be the only symptom if a tumor occurs in the soft tissues of the chest wall. Some people have a fever. Generally,

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subjects do not experience any pain until the tumor has advanced. Tumors that form in bone or cartilage are often painful [4]. Then there is a range of tumors of endocrine origin that can give a sign of themselves before the mass itself is discovered by the action of the molecules they secreted themselves. Other types of neuroendocrine cancer, on the other hand, show up and attract attention for their rapid growth [5-7]. The treatment of these masses involves either surgery or an integrated strategy with chemotherapy, radiotherapy, and surgery. Most tumors of the chest wall are surgically removed. If necessary, the chest wall is then rebuilt, sometimes with tissues from other parts of the body. In other cases, treatment involves chemotherapy and radiation therapy, alone or in combination. We present a case that has come to our observation [8].

Case Presentation

A 54-year-old woman, a former smoker, slightly overweight, with hypertension for 5 years and in therapy (with amlodipine 5 mg and zofenopril 30 mg), with a recent negative colonoscopy, came to the emergency room due to a swelling of the size of a knot, hard in consistency, movable, without associated erythema, painless nor initially painful, in the inter-mammillary region, that had recently enlarged. The swelling was actually hard to the touch, mobile, not painful or minimally painful, in the inter-mammillary site, without an erythematous halo. The patient initially performed a thorax radiography, which was negative. The formation had recently enlarged (Figure 1, 1A) and the patient performed a sedation sampling with aspiration from the lesion: a few cc of transparent liquid were aspirated, not subject to cytological examination, with reported suspicion of benign lesion (probably of lipomatous nature) with an annexed cystic component [9]. In the following 2 weeks, there was significant enlargement of the lesion (Figure 1, 1B) with considerable erythema and pain of the overlying skin. A small frustule of the lesion was then taken, which showed the following characteristics: the minute scrap of lesion at the level of the xiphoid was reported as to the location of malignancy in small undifferentiated cells. Positivity for CD56 and PAS negative for pan-CK (AE1/AE3), TTF1, CD99, pan-LEU. Proliferative activity (Ki -67 Ab) discrete:15-20%. Total body CT (Figure 2), PET-CT and bone scan showed a massive formation, hyperdense compared to the subcutaneous tissue and iso-hypodense compared with the surrounding musculature, about 5 cm, with hypercaptation, sternal involvement and integrity of the remaining parenchymal tissue/bone segments (Figure 3, A-B). The tumor was considered a NET (neuroendocrine tumor); given the confinement of the lesion, neoadjuvant therapy was initiated (3 cycles of etoposide and cisplatin every 3-day cycle, with a 21-day suspension and continuation of dexamethasone). At reevaluation there were good general conditions, decreased lesion volume, no repetitions. The subsequent surgical approach was evaluated as demolitive intervention (resection of ¾ of the sternum with placement of a titanium stent and demolition of the pectoral muscles) and confirmation by histologic diagnosis of the surgical specimen.

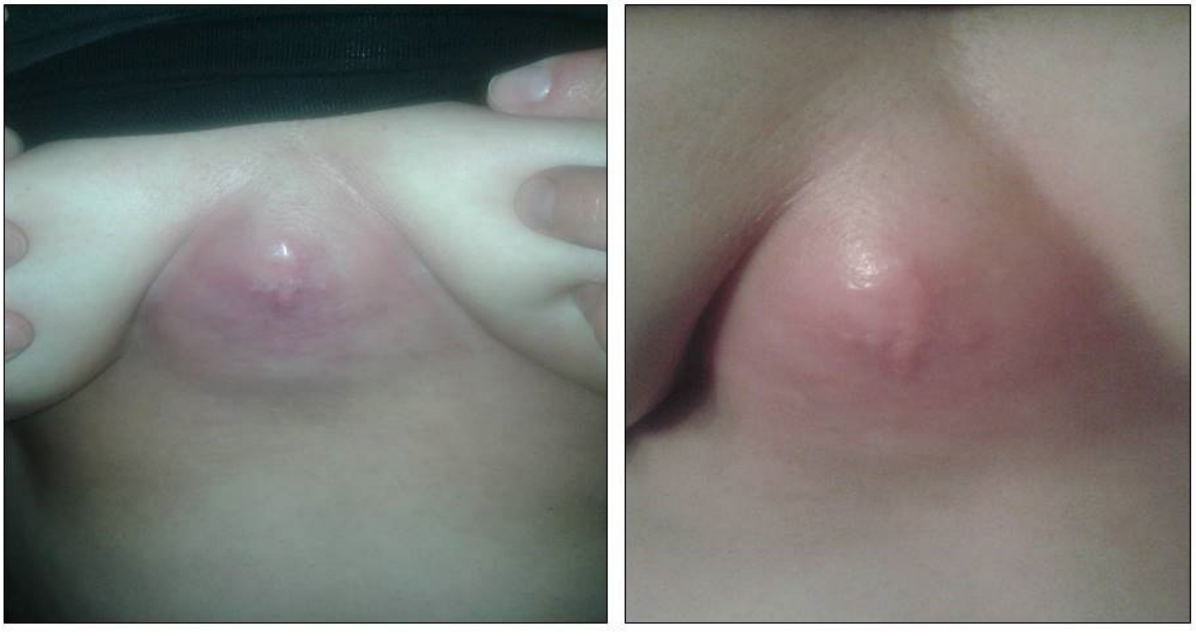

Fig. 1. Presence of swelling in the intermammilar site (Figure 1A, on the left side). Macroscopic picture, reassessed after about 2 weeks (Figure 1B, on the right side).

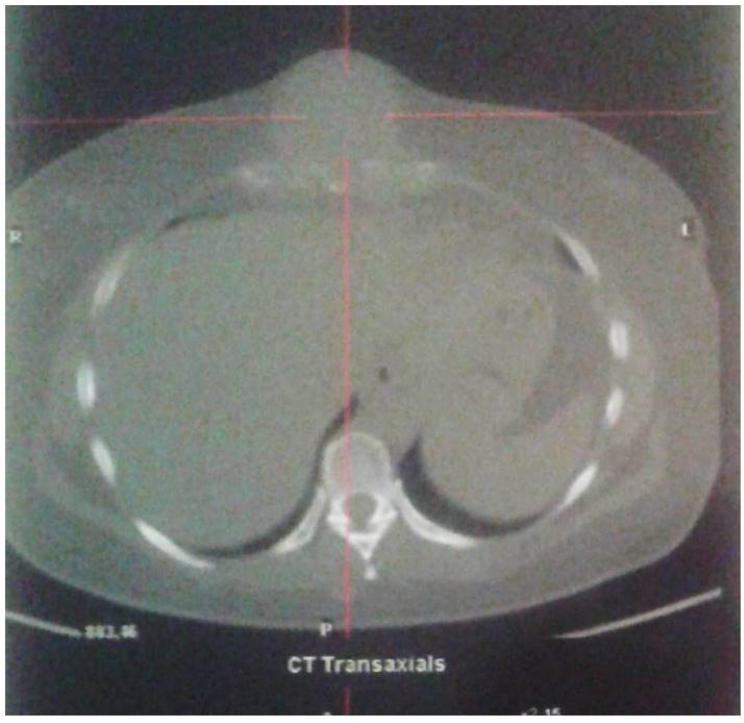

Fig. 2. CT picture of the lesion. Formation in the size of 3 x 3.6 x 4 cm. In the deep planes, close contact of the formation with the distal end of the body of the sternum and of the xiphoid process, which appear reworked. At the superficial level, the formation determines the ejection of the skin planes.

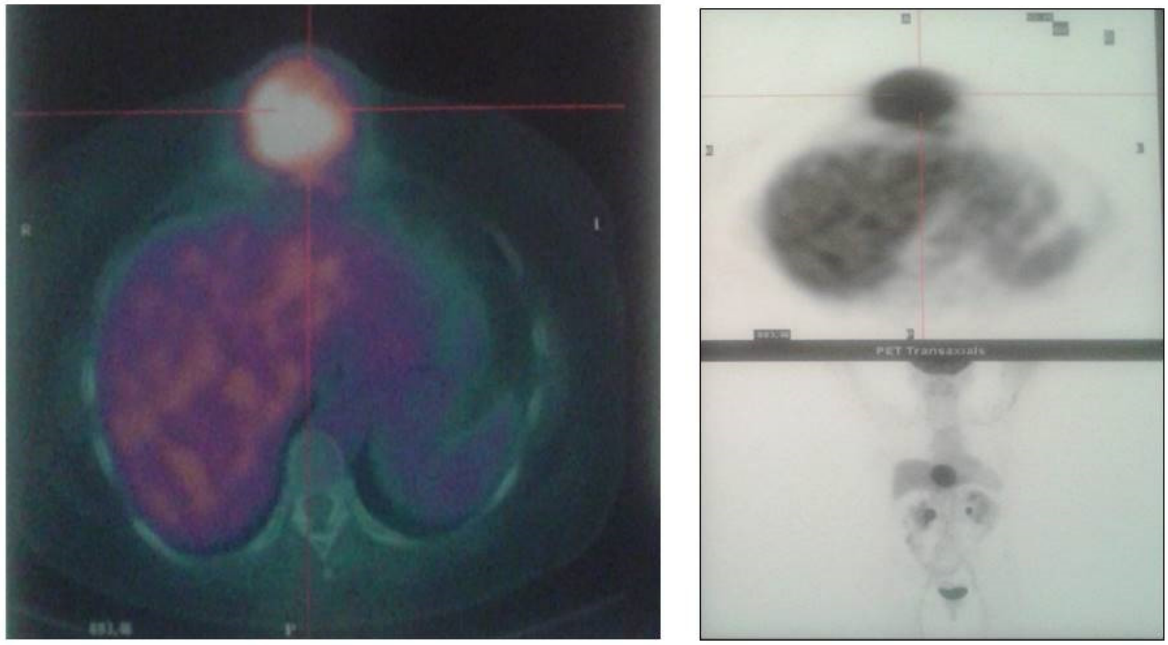

Fig. 3. PET-CT picture with 18F-FDG (378 MBq iv). Hyperfixation of the radiocomposed at the voluminous lesion formation (Figure 3A, on the left side). There are no documented areas of pathological hyperaccumulation of the radiocomposite in the remaining body segments examined (Figure 3B, on the right side).

Discussion

The neuroendocrine system consists of cells with typical characteristics of both endocrine and nerve cells. Neuroendocrine cells are present throughout the body and in various organs, performing specific functions in them, such as regulating the flow of air in

the lungs and the speed of food in the gastrointestinal tract [10-13]. Neuroendocrine tumors (NET) are rare, with a low incidence of about 3-4 new cases per 100 thousand subjects/year [14]. Based on their origin, they can originate from different body sites and therefore affect various organs and systems: the most frequent concern the gastroenteropancreatic tract [15], the lungs [16], the respiratory tract, the skin [17, 18], the thyroid [19], the parathyroid glands, and the adrenals. They are therefore very numerous in type and heterogeneous: NET of the gastrointestinal tract, pulmonary, thymic NET, pheochromocytoma, Merkel cell tumor. Neuroendocrine tumors are rare tumors characterized by heterogeneous clinical manifestations as well as various biological behaviors. Over the years, the incidence of these malignancies has steadily increased, also due to improvements in diagnostic capacity. They remain asymptomatic for a long time.

The diagnosis of NET is complex and, together with anamnesis and objective examination, it makes use of specific blood chemistry tests based on the dosage of non-specific but neuroendocrine production molecules (chromogranin A, PP, Neurono-Specific Enolase) or more specifically from some tumors (insulin, glucagon, 5-hydroxy-tryptamine, 5-HIAA, etc.) [20], as well as the use of diagnostic imaging techniques (CT, MRI) and nuclear medicine (PET, scintigraphy) or hybrid techniques (TC-PET) [21-24]. The biopsy remains the most important exam, but the cytologic diagnosis of NET, both high and low grade, can be difficult so an accurate diagnosis depends on clinical correlation, screening for any neuroendocrine features and cell block morphology. A Ki67 index is mandatory for grading of all neuroendocrine tumors: in our case, the proliferative activity appeared to be not low, making us understand that the therapy had to be as timely as possible [25, 26]. Immunohistochemistry has become an essential ancillary examination for the identification and classification of carcinomas of unknown primary site [27-29]. Pan Cytokeratin [pan-CK AE1/AE3] antibody recognizes the acidic and basic (Type I and II) subfamilies of cytokeratins. In immunohistochemistry studies, this Pan Cytokeratin antibody has proven useful as a screener for the majority of human carcinomas. So, the negativity of cytokeratins leads to the exclusion of a carcinoma (in practice, this is not a tumor of the epithelium) [30, 31]. The positivity of cytokeratins, however, can also come from the presence of tumors derived from the neuroectoderma [32]. CD99 antigen (cluster of differentiation 99) was also studied: it is found on the cell surface of Ewing's sarcoma tumors but its expression is also altered in a cell line of Hodgkin's lymphoma and in non-small cell lung cancer [33-35].

Then, the formation would then appear not to originate from the lung (negative TTF1. Although there are certain extremely undifferentiated microcytomas that have negative TTF1) [36,37]. In fact, in these cases, from the immunohistochemical point of view, we study the expression of TTF-1 (transcriptional thyroid factor 1, present in most adenocarcinomas and microcytomas, but only exceptionally in squamous carcinomas), the expression of p63 and p40 (present in squamous carcinomas), and the expression of chromogranin, synaptophysin, and CD56 (present in neuroendocrine carcinomas). In the histological report, positivity to CD56 is reported. CD56 (or NCAM: Neural Cell Adhesion Molecule) is a transmembrane glycoprotein expressed on the surface of neurons, glia, and skeletal muscles. This protein plays a role in the adhesion mechanism between cells, in the growth of axons, in synaptic plasticity, and in the mechanisms of learning and memorization [38]. This protein is used in pathological anatomy to recognize some tumors, but it is normally contained in NK cells, T cells, brain and neuroendocrine tissues [39]. Being that NET is heterogeneous, it is difficult to adopt a unique therapeutic strategy. It is essential to contact a specialized medical center for a multi-disciplinary approach. Among the various therapeutic options, surgery is the most used for potentially curative purposes: in fact, if the NET is completely removed, surgery allows for complete healing in many cases. The surgical approach also allows for the removal of any metastases or reduction of the tumor mass (also for palliative purposes, to reduce symptoms when the disease reaches its terminal stage). Systemic chemotherapy is generally used as polychemotherapy, using different combinations of drugs, including platinum derivatives (doxorubicin, 5-fluoro-uracil and cyclophosphamide).

Conclusion

The diagnosis of NET is complex and involves history, objectivity, dosage of nonspecific neuroendocrine molecules (chromogranin A, PP, NSE) or, more specifically, molecules from certain cancers (insulin, glucagon, 5-OH-tryptamine, 5-HIAA, etc.), imaging methods (CT, MRI), nuclear medicine (PET, scintigraphy), and hybrid techniques (CT-PET). Biopsy is very important but can be incomplete due to the small sample size. A carcinoma was excluded (negative for cytokeratins), and the origin from the lung was probably excluded as well (TTF1 negative), but there was no description of small cells (spindle? Round cells? Lysis/crush artifacts?) nor the pattern of growth (available to the palisade? nests/tubules?). Since NET is heterogeneous, it is difficult to adopt a single therapeutic strategy. We adopted a flow-chart that is similar to the algorithm for diagnostic and therapeutic decisions for managing

patients with Merkel cell carcinoma [40]. The surgical approach is the most used for potentially curative purposes: indeed, if the NET is entirely removed, in many cases there is complete recovery. Surgery allows for the removal of metastases and tumor shrinkage (even for palliation: reduction of symptoms in terminal illness) [41]. Systemic polychemotherapy uses different combinations of drugs, including platinum derivatives [42,43].

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

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Conflict of Interests

The authors state that they have no conflicts of interest.

Learning Points

• The differential diagnosis of chest wall lesions due to neoplasms opens a wide number of hypotheses, making it a challenge for the clinician to investigate other signs and symptoms that allow for a better diagnostic approach.

• Clinicians should remain vigilant for the presence of a NET in each patient with a suspected mass, as these can attenuate prognosis, uncover specific biomarkers, and facilitate tumor-specific management.

• Computed tomography (CT) and CT/PET imaging can facilitate differentiation of neoplasms from normal chest wall structures and fully characterize abnormalities by demonstrating the various internal components of complex lesions.

• Biopsy is very important, and immunohistochemistry is required to confirm their diagnosis. There are several markers of NET, but their sensitivity and specificity are less than optimal.

• The evaluation of a thoracic swelling must never be superficial and must include both more frequent forms of cancer (including metastases) and rare ones, such as neuroendocrine tumors.

• This case is explanatory of how an adequate evaluation of a patient's chest wall mass should be used as markers for treatment feasibility and outcome.

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