CASE REPORT

Rare Case Report of Neuroendocrine Tumor in Axilla-Metastasis from Unknown Primary or De Novo?

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Abstract Neuroendocrine tumors (NET) are the neoplasm arising from neuroendocrine cells which are present throughout the body. It can be benign, being more common or malignant. Gut is the most common site, but they can be seen in any part of the body. We had a case of grade III NET in axilla presented with a fungating lesion with unknown primary. Clinical behavior of such tumor is predicted by tumor grade or differentiation. We treated this patient by surgery and adjuvant chemotherapy.

Keywords Neuroendocrine tumour · Neuroendocrine carcinoma · NEC of axilla

Case Report

A 65-year-old male patient presented with left axillary swelling since 6 months. It was gradually increasing in size, and for 15 days, he had an ulcer over swelling. On examination, 10.9-cm-sized well-defined solid partially fixed swelling in the left axilla felt like matted lymph nodal mass with a 4.3-cm-sized ulcer swelling with serous discharge and crusting (Fig. 1a). There was no history of flushing, diarrhea, breathlessness, or

generalized lymphadenopathy. Tru-cut biopsy was suggestive of round cell neoplasm and IHC was positive for synaptophysin (Fig 1c) and negative for chromogranin, HMB45, CK7, CK20 with Ki67 index (Fig 1d) approximately 80%. The report was in favor of WHO grade III (high grade) neuroendocrine carcinoma (NEC). CECT scan showed a lobulated heterogeneously enhancing lesion measuring 82.65 mm in the left axilla with abutment of the axillary vessels and adjacent muscles. PET scan was normal except for axillary lesion. So, we kept a diagnosis of metastatic NEC from unknown primary or de novo NEC in axilla. In view of fungation and skin ulceration, surgery was planned. On exploration, axillary vein was compressed and parts of latissimus dorsi and subscapularis muscles were infiltrated by tumor. Axillary artery and brachial plexus were normal (Fig 1b). All major neurovascular structures were preserved and the wound was closed primarily. Postoperative course was uneventful. Final report showed NEC (grade III) with negative margin and two identified lymph nodes showed hyperplasia only. In view of NEC, adjuvant treatment in form of 6 cycles of cisplatin and etoposide was given. The patient was doing well on first follow-up at 3 months after completion of chemotherapy.

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Discussion

Neuroendocrine tumors (NETs) originate from neuroendocrine cells throughout the body and most commonly found in the appendix, rectum, ileum, lungs, and bronchi. NETs arising in soft tissues are very rare [1]. NEC of unknown primary site is very rare, usually arises from an occult primary site like bronchus, pancreas, stomach, colon, rectum [2]. The incidence of lymph node metastasis from an unknown primary NETs is less than 5% of all carcinoma arising from

Fig 1 10.9-cm-sized well-defined solid partially fixed swelling in the left axilla felt like matted lymph nodal mass with a 4.3-cm-sized ulcer swelling with serous discharge and crusting

unknown primaries [3]. Eusebi et al. reported eight cases of neuroendocrine tumors in lymph nodes with unknown primary and described the possibility of a lymph node-origin tumor on the basis of epithelial inclusions or anomalous carcinomatous differentiation of stem cells of the lymphoreticular system [4]. So, in our case, it could be lymph node metastasis from unknown primary NET or de novo from axillary lymphatic tissue or soft tissue.

The diagnosis of a NET is based on histopathology, circulating biomarkers, and imaging. Computerized tomography, magnetic resonance imaging, somatostatin receptor scintigraphy, and positron emission tomography with specific isotopes such as (68)Ga-DOTA-octreotate, F18-dopamine, or FDG are commonly used for staging workup [5]. In the novel WHO 2010 classification for NETs Table 1, tumor grade is based on proliferation (i.e., the Ki-67 index) and the mitotic count. Well-

differentiated tumors are called G1 or G2 NET (Ki-67 < 20) and poorly differentiated are called G3 NECs (Ki-67 > 20) [6].

Management of these patients is dependent on tumor grade/differentiation. Low-grade or well-differentiated tumors are frequently indolent and are managed surgically [2]. Poorly differentiated NETs are chemosensitive to the etoposide plus cisplatin combination, but prognosis remains poor with a 2-year survival less than 20% [2, 7]. Our case was grade III NEC. Usually, grade III tumors are considered as small cell carcinoma and not managed by surgery but by chemotherapy because of extremely poor prognosis. Our case had local complication like fungation and ulceration so we did surgery on him. Biology and prognosis of NEC with unknown primary are mainly dependent on the histological grade of the tumor [8].

So, neuroendocrine tumor with grade III histology usually has poor prognosis because it behaves like a small cell carcinoma. With known or unknown primary, standard treatment is to give cisplatin- and etoposide-based chemotherapy. Palliative surgery can be considered for symptomatic relief.

Table 1 WHO 2010 classification for NETs

Low grade	Neuroendocrine tumor, grade 1	2 mitosis/10hpf and < 3% Ki67 index
Intermediate grade	Neuroendocrine tumor, grade 2	2–20 mitosis/10hpf or 3–20% Ki67 index
High grade	Neuroendocrine carcinoma, grade 3 (small cell, large cell NEC)	> 20 mitosis/10hpf or > 20% Ki67 index

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