Open Journal of
Clinical & Medical
Case Reports

Volume 8 (2022)
Issue 07

Clinical Image ISSN: 2379-1039

Neuroendocrine carcinoma and cushing's syndrome: Radiologic-pathologic correlation

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Clinical Presentation

A Twenty-three-year-old African American male with past medical history of recently diagnosed Cushing syndrome and Type 2 diabetes mellitus presented to the emergency room for worsening bilateral lower extremity edema and abdominal swelling. Patient reported that the swelling started 3 months ago, initiated from trunk, spreading to the whole body, accompanied with swelling face and significant weight gain. Patient also reported fatigue, orthopnea and difficulty swallowing. Physical exam was pertinent for moon face, buffalo hump, abdominal distention, diffuse striae and lower extremity edema. Laboratory results demonstrated hypokalemia and increased ACTH. Chest X ray was unremarkable and computed tomography of the chest revealed an anterior mediastinal mass with focal calcifications and moderate amount of pericardial effusion (Figure 1). Patient was admitted for ectopic ACTH and Cushing Syndrome work-up by endocrinology. Cardiothoracic surgery was consulted and performed an anterior mediastinotomy with incisional biopsy of the anterior mediastinal mass and drainage of pericardial effusion. Several large incisional biopsies were obtained and sent to Pathology. Positron emission computed tomography (PETCT) was requested and revealed moderate increase of FDG avidity within the anterior mediastinal soft tissue mass (Figure 2). Immunohistochemical stains showed tumor cells positive for CD56, AE1/AE3, Synaptophysin, ACTH (focal), Chromagranin, TTF-1 and CAM5-2 and negative for CD99 and CK5/6 (Figure 3). Final diagnosis was Malignant Small Blue cell tumor with neuroendocrine differentiation. Radio-pathological findings correlation was consistent with Neuroendocrine carcinoma involving the mediastinum. Oncology was consulted and suggested chemo-radiation therapy as outpatient. Patient was stable to be discharged and follow up appointment with endocrine, hematology-oncology, radiation oncology and cardiothoracic surgery were ordered.

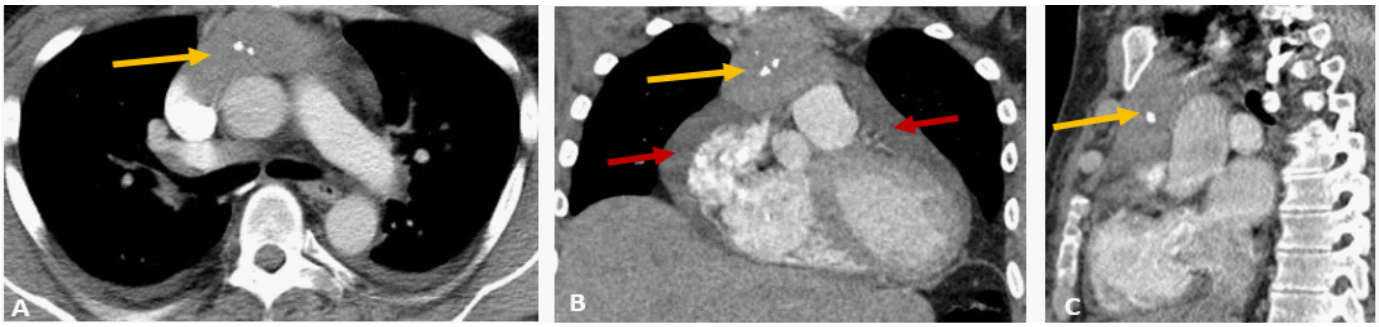

Figure 1: Computed tomography of the chest with contrast. **(A)** axial, **(B)** coronal and **(C)** sagittal images demonstrated an anterior mediastinal soft tissue density mass measuring approximately 7 x 3 cm with punctate calcifications (yellow arrows). A moderate amount of pericardial effusion is also noted (red arrows).

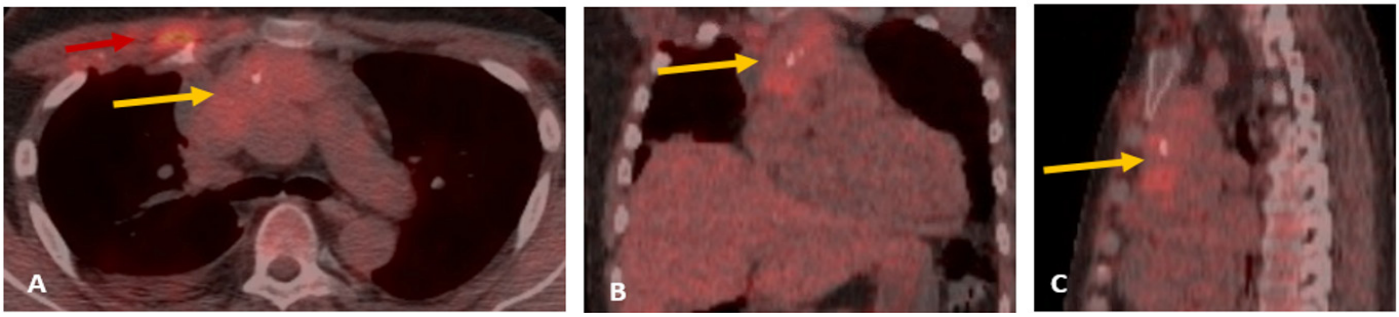

Figure 2: Positron emission computed tomography-CT fusion. **(A)** axial, **(B)** coronal and **(C)** sagittal images show moderate increase of FDG avidity within the anterior mediastinal soft tissue mass (yellow arrows). Red arrow within the axial view represents postsurgical changes.

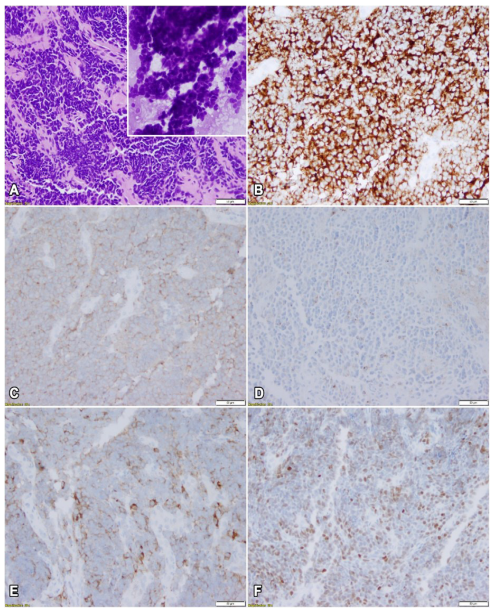

Figure 3: Permanent tissue sections represent nests and sheets of small tumor cells **(A)** with high nucleus to cytoplasmic ration, focally dark coarsely stipple ("salt and pepper") chromatin with inconspicuous nucleoli, nuclear molding, overlapping, and crush artifacts (insert touch preparation, H&E, 20x). Immunohistochemically, tumor cells show strong and diffuse membranous positivity for CD56 **(B)**, weak and diffuse granular cytoplasmic positivity for synaptophysin **(C)**, focal and weak cytoplasmic positivity for chromogranin **(D)**, and strong and patchy cytoplasmic positivity for ACTH (E) (CD56, synaptophysin, chromogranin, and ACTH immunostaining, respectively, 20x). Diffuse and strong nuclear positivity for TTF1 (F) supports the lung origin of tumor cells (TTF1 immunostaining, 20x).

Discussion

Neuroendocrine carcinomas (NEC) are epithelial neoplasia. The most frequent location for NEC includes the gastrointestinal tract, genitourinary tract, lungs, and thymus. Uncommon locations for NEC are retroperitoneum, mesentery, presacral region, inferior vena cava and mediastinum [1]. The WHO classifies NEC of the lung, pleura, thymus, and heart into low-grade NET (typical carcinoid), intermediate-grade NET (atypical carcinoid) and high-grade tumors (large cell NEC and small cell NEC) [1,2]. Approximately 30% of Neuroendocrine tumors (NETs) present with secretory syndromes. Cushing's syndrome caused by a mediastinal NET is rare, with limited literature [3]. Clinically, patients with ectopic producing adrenocorticotropic hormone (ACTH) neuroendocrine tumors present with Cushing's syndrome symptomatology such as weight gain, fatigue moon face, buffalo hump, abdominal distention, diffuse striae, and lower extremity edema. Laboratory abnormalities include increased ACTH, hyperglycemia, hypokalemia, among others. [4,5]. Radiology imaging findings of NEC include soft tissue mass density with punctuate calcifications on computed tomography. PET-CT revealed a focus of increase FDG avidity within the mass. Definitive diagnosis of NECT is made by pathology. Small round blue cell tumors (SRBCTs), which was the final pathological diagnosis in our case, are neoplasms composed of small, round, basophilic cells on hematoxylin and eosin (H&E) staining. Intrathoracic SRBCTs include small cell lung carcinoma, Ewing sarcoma, extranodal marginal zone B-cell lymphoma, embryonal rhabdomyosarcoma, desmoplastic small round cell tumor, post-transplant lymphoproliferative disorder and NEC [6]. The immunohistochemical markers of NEC are chromogranin, synaptophysin and CD56. NEC arising from lungs/mediastinum are positive for CK7 and TTF-1. ACTH secreting NEC are positive for ACTH stain [1-7]. In our case, diffuse and strong nuclear positivity for TTF1 supports the lung origin of tumor cells instead of thymus origin. Chemotherapy with steroidogenesis inhibitors or glucocorticoid receptor antagonist represents a novel management for NEC secreting ACTH [8,9]. North American Neuroendocrine Tumor Society guidelines suggest surgical resection with mediastinal lymphadenectomy for locoregional disease [1,10].

References

1. Liyas M, Dona D, Devi U, Noorunnisa N. Primary small cell neuroendocrine carcinoma of the anterior mediastinum presenting with trepopnea. BMJ Case Rep. 2018; 11: e225014.

2. Travis WD, Brambilla E, Burke AP, et al. Nicholson AG ed. WHO classification of tumours of the lung, pleura, thymus and heart. 4th edn. Lyon France: IARC Press. World Health Organization Classification of Tumours. 2015.

3. Mokhtar A, Arnason T, Gaston D, Huang WY, MacKenzie H, et al. ACTH-Secreting Neuroendocrine Carcinoma of the Cecum: Case Report and Review of the Literature. Clin Colorectal Cancer. 2019; 18: e163-e170.

4. Di Filippo L, Vitali G, Taccagni G, Pedica F, Guaschino G, Bosi E, Martinenghi S. Cervix neuroendocrine carcinoma presenting with severe hypokalemia and Cushing's syndrome. Endocrine. 2020; 67: 318-320.

5. Montebello A, Zahra Bianco E, Babic D, Delicata NP, Azzopardi N. Large cell neuroendocrine carcinoma arising from the anterior mediastinum. BMJ Case Rep. 2021; 14: e240453.

6. Chang A, Pfeifer K, Chen P, Kalra V, Shin MS. Thoracic Presentations of Small Round Blue Cell Tumors. J Clin Imaging Sci. 2016; 6: 25.

7. Nsour E, Al Khader A, Al-Tarawneh B. Metastatic small cell carcinoma of the lung with prominent spindle cell morphology and hemangiopericytoma-like vascular pattern: A sarcoma mimicker. SAGE Open Med Case Rep. 2020; 8: 2050313X20981177.

8. Zhang HY, Zhao J. Ectopic Cushing syndrome in small cell lung cancer: A case report and literature review. Thorac Cancer. 2017; 8: 114-117.

9. Kanaji N, Watanabe N, Kita N et al. Paraneoplastic syndromes associated with lung cancer. World J Clin Oncol 2014; 5: 197–223.

10. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine Tumors NCCN. 2017.

Manuscript Information: Received: April 15, 2022; Accepted: May 12, 2022; Published: May 16, 2022

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Citation: Gomez JS, Previgliano C, Simoncini A, Sangster G, Aksionau A, Takei H, Cotelingam JD. Neuroendocrine carcinoma and cushing's syndrome: Radiologic-pathologic correlation. Open J Clin Med Case Rep. 2022; 1862.

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