

Primary Small Cell Neuroendocrine Carcinoma of the Petrous Apex: A Report of an Atypical Case

Jules-Joel Bakhos^{1,*}, Evelyne El Helou², Elias Rizk² and Nabil Moukarzel²

¹*Faculty of Medicine, Saint Joseph University, Beirut, Lebanon*

²*Sacred-Heart Hospital, Lebanese University, Beirut, Lebanon*

*Corresponding author: jules-j.bakhos@live.co.uk

Abstract.

Introduction

Small cell neuroendocrine carcinomas (SCNEC) are extremely rare in the head and neck region, known to be highly aggressive with poor prognosis.

We report the second case in the literature of a poorly differentiated SCNEC involving the petrous apex of the temporal bone, and we present its management.

Case Summary

A 42-year-old white male smoker, without personal or familial significant history, presented with right-sided otalgia.

A transnasal endoscopic biopsy of the right apical petrous bone was performed and the histopathological analysis was consistent with poorly differentiated SCNEC.

The patient received four cycles of systemic chemotherapy followed by thirty radiotherapy sessions. Brain MRI, PET-scan, and whole-body CT-scan images confirmed the absence of metastatic focus.

Discussion

Treatment regimens for head and neck SCNECs are poorly documented in the literature. Few reports recommend a combination of chemotherapy and radiotherapy with the exclusion of surgery, representing the main challenge for our management.

Keywords: Neuroendocrine Carcinoma; Small Cell Neuroendocrine Carcinoma; Petrous Apex; Temporal Bone.

Background

Neuroendocrine cells are part of the diffuse neuroendocrine system spread throughout the body: they share structural characteristics with neurons and secrete hormones like endocrine cells.¹ Abnormal changes can occur, resulting in neuroendocrine tumors that could become cancerous and then be called neuroendocrine carcinomas. These neoplasms are mainly found in the gastrointestinal and pulmonary systems.¹

Based on the 2017 World Health Organization classification of neuroendocrine neoplasms, small cell neuroendocrine carcinomas (SCNEC) are classified as poorly differentiated and high grade carcinomas (grade 3).²

Known for its highly aggressive neoplastic actions and poor prognosis, SCNEC are extremely rare in the head and neck.³

We report the case of a SCNEC involving the petrous apex of the temporal bone of a 42-year-old man and we present its management. This is the second documented case in the literature to be described in this region of the skull.⁴

Case Presentation

A 42-year-old white male smoker (0.5 pack-year) without personal nor familial significant history presented for

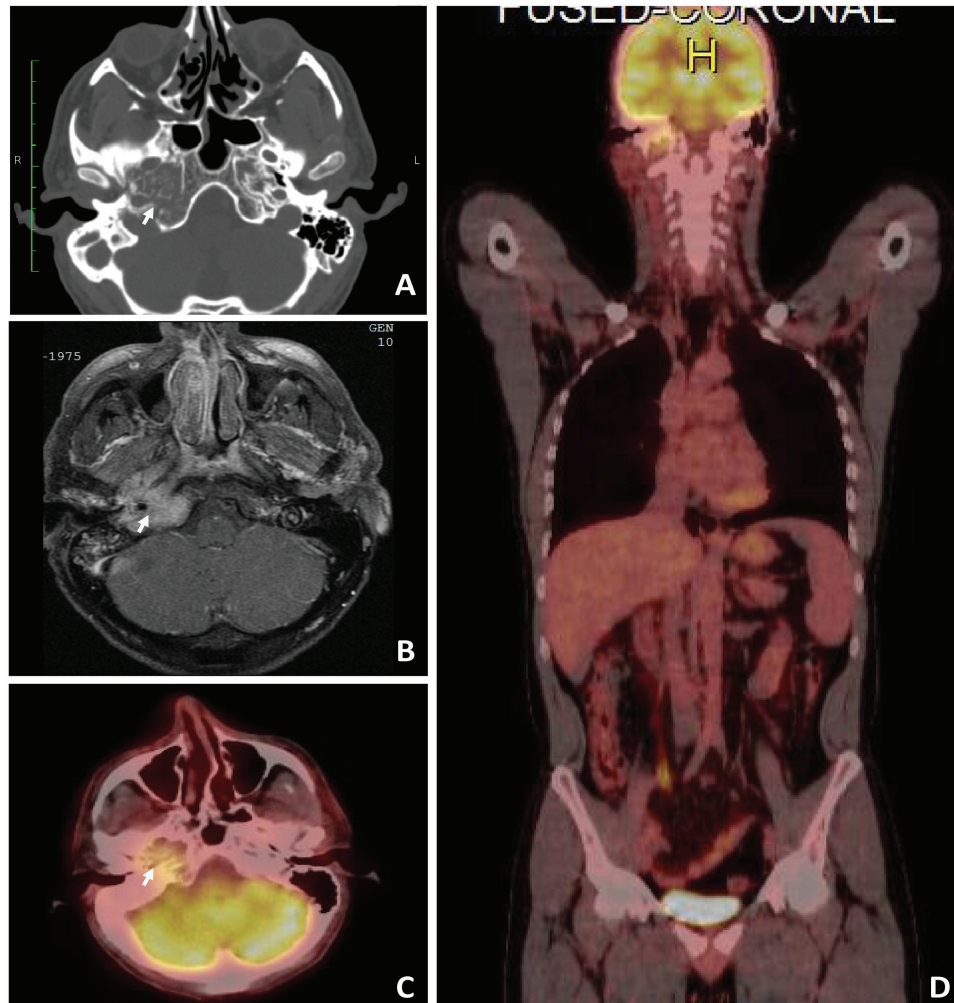


Figure 1. Imaging studies. (A) Axial CT-scan image of the right temporal bone showing the mass process (arrow). (B) Axial MRI confirming the mass in the right temporal bone (arrow). (C) Axial PET-scan image indicating the mass process in the right temporal bone (arrow). (D) Full body coronal PET-scan image indicating the absence of disease outside the petrous apex.

right-sided otalgia with one reported episode of right ear blood discharge from a few months ago.

A multislice spiral computed tomography scan (CT-scan) of the temporal bone showed total opacification of the right middle ear and mastoid air cells while the respective bony labyrinth showed no abnormalities (Figure 1A). Magnetic resonance imaging (MRI) as well as positron-emission tomography scan (PET-scan) confirmed the mass process in the right temporal bone (Figure 1B–C).

A transnasal endoscopic biopsy of the right apical petrous bone was performed and the histopathological analysis was consistent with poorly differentiated SCNEC (to be noted that our histopathological result was confirmed by two pathologists): a dense proliferation of hyperchromatic cells with neuroendocrine differentiation (Figure 2A). The diagnosis was further confirmed by immunohistochemistry: tumor cell immunostaining with adequate controls indicated cytokeratin and synaptophysin expressions (Figure 2B–C) while remaining

TTF-1 and CD45 (Leukocyte Common Antigen) negative (Figure 2D–E). A whole-body PET-scan indicated the absence of disease elsewhere in the body (Figure 1D) with a prior negative 5-HIAA (5-hydroxyindoleacetic acid) urine test realized to assess whether our SCNEC was a serotonin producing tumor.

Consequently, the patient received four cycles of systemic chemotherapy given every 21 days: a combination of Cisplatinum (80 mg/m² administered on day 1) and Etoposide (100 mg/m² administered on days 1, 2, and 3), in analogy with the management of sinonasal and nonsinonasal neuroendocrine carcinomas of the head and neck.^{5,6} The chemotherapy courses were complicated by superficial bilateral thrombophlebitis of the lower limbs, treated with subcutaneous low molecular-weight heparin. Following three cycles of chemotherapy, imaging studies (PET-scan and brain MRI) were performed and evinced a stable disease. After the completion of his chemotherapy treatment, the patient underwent thirty radiotherapy

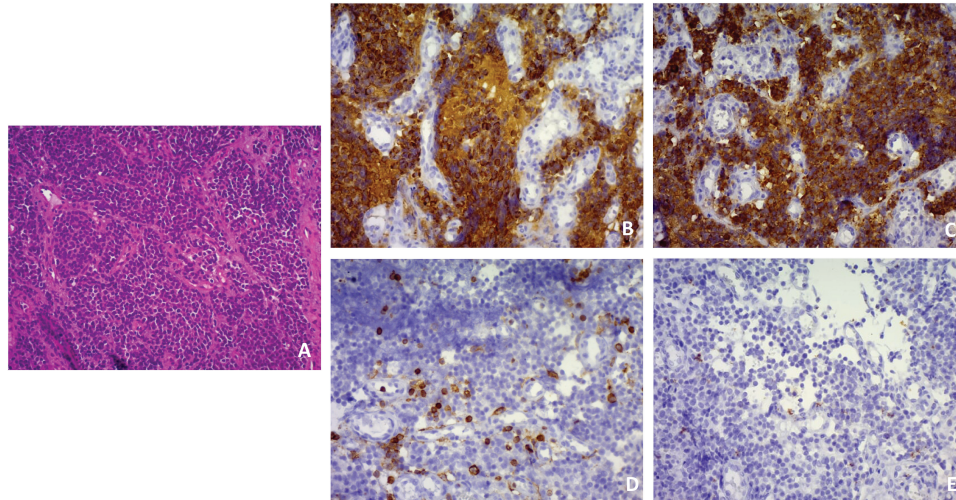


Figure 2. Poorly differentiated SCNEC histopathology with H&E and IHC. (A) Dense proliferation of hyperchromatic tumor cells with neuroendocrine differentiation (H&E, 400×). (B) Cytokeratin positive tumor cells (IHC, 400×). (C) Synaptophysin positive tumor cells (IHC, 400×). (D) CD45 negative tumor cells (IHC, 400×). (E) TTF-1 negative tumor cells (IHC, 400×).

sessions by intensity-modulated technique, targeting his mass, receiving a total radiation dose of 6000 cGy.^{4–6} The brain MRI, repeated one month after completion of radiotherapy showed a stable tumor.

Three months after the previous PET-scan, a whole-body CT-scan was performed and confirmed the absence of metastatic focus.

We plan on following the patient, alternately, with whole-body CT-scan combined with brain MRI, and PET-scan every three months.

Discussion

Treatment regimens for SCNECs outside the gastrointestinal and pulmonary systems are scarcely reported in the literature. Chemotherapy using cisplatin and etoposide followed by high dose proton-photon radiotherapy has been proven by prospective and retrospective studies to be an effective line of treatment.^{5,6} In fact, in comparison with surgery and radiotherapy alone, the combination of chemotherapy with radiotherapy has doubled the two-year overall and disease-free survival rates and cut that of the of distant metastases by half.⁶ Furthermore, besides the better results against surgery, the latter would come with irreversible damage when performed in confined areas such as the petrous apex.⁵ In our case, tumor localization was surgically unapproachable; we used intensity modulated radiotherapy to limit damage⁵ and cycles of platinum/etoposide as induction regimen.⁶

Generally, temporal bone malignancies occur with a grim prognosis of a 20% 5-year survival rate.³ In our case, the risk of an occult malignancy FDG PET negative was considered to be very low because of the urothelial nature of such presentations, the negative 5-HIAA urinary

test, and negative urinary tract symptoms reported by the patient.

This is the case of a high-grade SCNEC of unknown origin presenting in the petrous apex. After aggressive treatment, the disease was stabilized and the patient is so far asymptomatic, nine months after diagnosis.

Conclusions

We report the second case in the literature of a poorly differentiated SCNEC involving the petrous apex of the temporal bone. We describe our therapeutic approach (chemotherapy with Cisplatinum/Etoposide followed by local radiotherapy with 60 Gy) that proved a control of the disease for nine months after initial diagnosis, a treatment regimen to be considered for similar cases.

List of Abbreviations

- SCNEC: small cell neuroendocrine carcinoma;
- CT-scan: computed tomography scan;
- MRI: magnetic resonance imaging;
- PET-scan: positron-emission tomography scan;
- H&E: hematoxylin and eosin stain;
- IHC: immunohistochemistry.

Ethics Approval and Consent to Participate

Institutional Review Board (IRB) exemption obtained from Ethics board of the Sacred Heart Hospital (attached).

Consent for Publication

IRB exemption obtained from Ethics board of the Sacred Heart Hospital (attached).

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Authors' Contributions

- Jules-Joel Bakhos: collected data, analyzed data, wrote article, revised article.
- Evelyne El Helou: treated the patient, analyzed data, revised article.
- Elias Rizk: follow-up with the patient, revised article.
- Nabil Moukarzel: treated the patient, revised article.

Competing Interest

We have no conflicts of interest.

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