

METHODS

Primary small cell neuroendocrine carcinoma of the petrous apex: a report of an atypical case

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Introduction: The head and neck region is a very uncommon location for small cell neuroendocrine carcinomas (SCNEC), which are notoriously aggressive and have a terrible prognosis. We describe the second case of a poorly differentiated SCNEC involving the petrous apex of the temporal bone in the literature and discuss its therapy.

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 4 cycles of systemic chemotherapy followed by 30 radiotherapy sessions. Brain magnetic resonance imaging, positron emission tomography scan, and whole-body computed tomography scan images confirmed the absence of metastatic focus.

Discussion: The literature lacks enough documentation of treatment regimens for head and neck SCNECs. The biggest difficulty in our management is that few studies advise combining radiotherapy and chemotherapy without surgery.

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 change 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).

Small cell neuroendocrine carcinomas (SCNEC) are categorized as poorly differentiated and high-grade carcinomas in the 2017 World Health Organization classification of neuroendocrine neoplasms (grade 3) (2). SCNEC is known for its highly aggressive neoplastic actions and poor prognosis. SCNEC is extremely rare in the head and neck (3).

We describe the care of an SCNEC that affected a 42-year-old man's petrous apex of the temporal bone. 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 per year) without personal or familial significant history presented for right-sided otalgia with one reported episode of right ear blood discharge from a few months ago.

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.

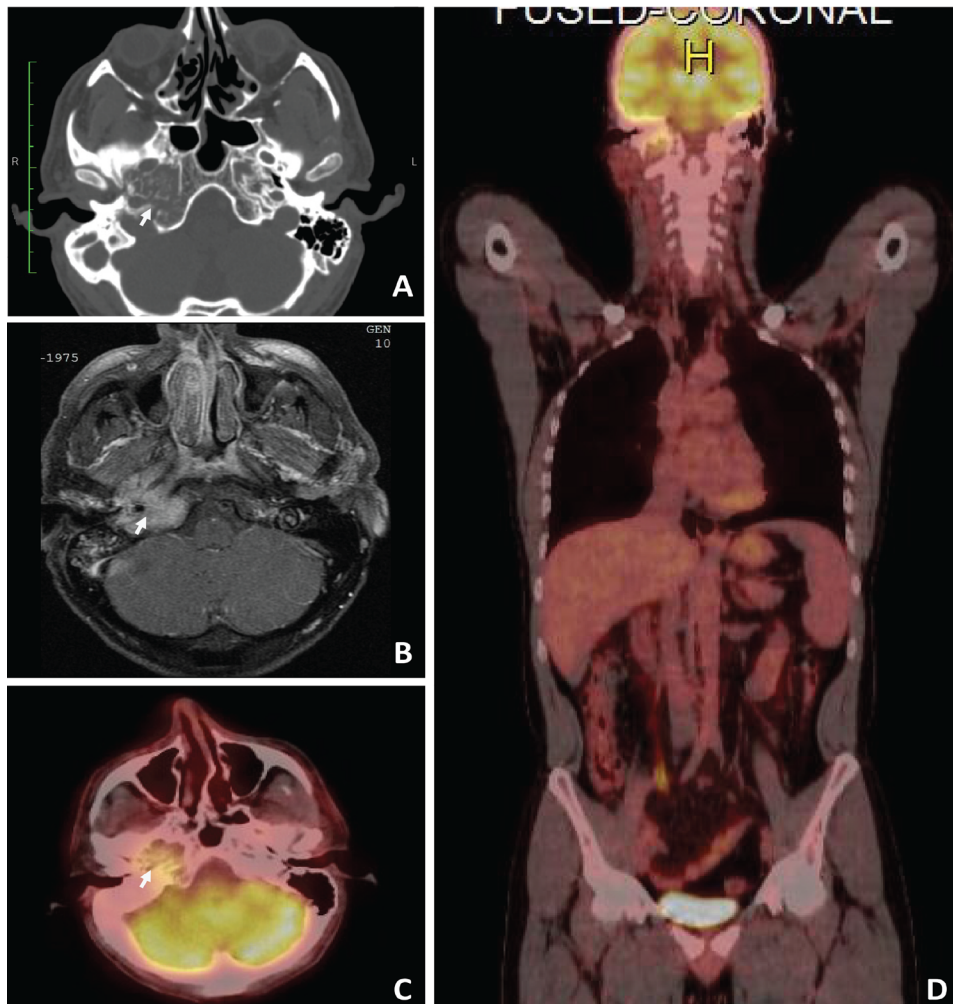


FIGURE 1 | Imaging studies. **(A)** Axial CT scan image of the right temporal bone showing the mass process (arrow). **(B)** Axial MRI confirming the mass in the right temporal bone (arrow). **(C)** Axial PET scan image indicating the mass process in the right temporal bone (arrow). **(D)** Full body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

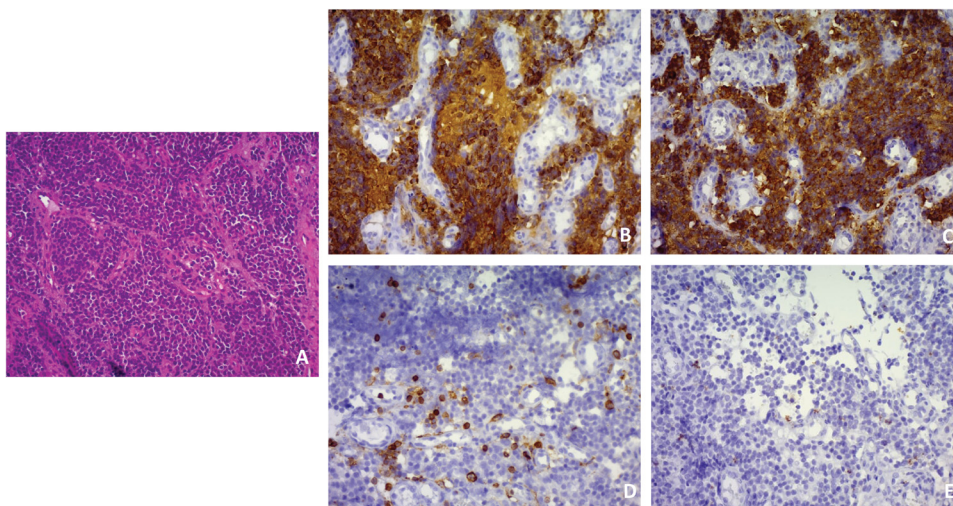


FIGURE 2 | Poorly differentiated SCNEC histopathology with H&E and IHC. **(A)** Dense proliferation of hyperchromatic tumor cells with neuroendocrine differentiation (H&E, 400X). **(B)** Cytokeratin positive tumor cells (IHC, 400X). **(C)** Synaptophysin positive tumor cells (IHC, 400X). **(D)** CD45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

The right middle ear and mastoid air cells were completely opaque on a multislice spiral computed tomography scan (CT scan) of the temporal bone, although the corresponding bony labyrinth had no abnormalities (Figure 1A). The mass process in the right temporal bone was verified by positron emission tomography (PET) and magnetic resonance imaging (MRI) (Figures 1B, C).

A transnasal endoscopic biopsy of the right apical petrous bone was performed and the histopathological analysis was consistent with poorly differentiated SCNEC (it should 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 (Figures 2B, C) while remaining TTF-1 and CD45 (leukocyte common antigen) negative (Figures 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 was performed to assess whether our SCNEC was a serotonin-producing tumor.

Consequently, the patient received 4 cycles of systemic chemotherapy given every 21 days: a combination of cisplatin (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 non-sinonasal 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 exhibited a stable disease. After the completion of his chemotherapy treatment, the patient underwent 30 radiotherapy sessions by intensity-modulated technique, targeting his mass, receiving a total radiation dose of 6,000 cGy (4–6). The brain MRI, repeated after 1 month after completion of radiotherapy, showed a stable tumor.

However, 3 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 a PET scan every 3 months.

Discussion

Treatment regimens for SCNECs outside the gastrointestinal and pulmonary systems are scarcely reported in the literature. Both prospective and retrospective investigations have demonstrated the efficacy of cisplatin and etoposide chemotherapy followed by high-dose proton-photon radiation (5, 6). In fact, in comparison with surgery and radiotherapy alone, the combination of chemotherapy with

radiotherapy has doubled the 2-year overall and disease-free survival rates and cut that 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 damage (5) and cycles of platinum/etoposide as an 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 fluorodeoxyglucose 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 at the petrous apex. After aggressive treatment, the disease was stabilized and the patient is so far asymptomatic, 9 months after diagnosis.

Conclusion

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 cisplatin/etoposide followed by local radiotherapy with 60 Gy) that proved to have controlled the disease for 9 months after initial diagnosis, a treatment regimen to be considered for similar cases.

Ethics approval and consent to participate

Exemption from the Institutional Review Board was received from the Sacred Heart Hospital's Ethics Board (attached).

Consent for publication

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

Author contributions

J-JB: collected and analyzed the data and wrote and revised the manuscript. EH: treated the patient, analyzed the data, and revised the manuscript. ER: followed-up with the patient and revised the manuscript. NM: treated the patient and revised the manuscript. All authors contributed to the article and approved the submitted version.

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