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Case Report

111In-Octreoscan SPECT/CT hybrid imaging and 68Ga-DOTANOC PET/CT in neuroendocrine adenoma of the middle ear (NAME)

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Abstract

Neuroendocrine adenoma of the middle ear (NAME) represents a rare tumour consisting of an adenoma with mixed neuroendocrine differentiation. A 40-year-old woman was referred to our attention to further investigate the occurrence of a pathological tissue located in the mastoid process of the left temporal bone depicted by head CT and MRI scans. Histopathological examination revealed an epithelial neoplasm with neuroendocrine differentiation features, consistent with the diagnosis of NAME. In order to obtain an accurate differential diagnosis and confirmation of this rare disease, 111In-Octreoscan single photon emission computed tomography (SPECT)/CT and 68Ga-DOTANOC positron emission tomography (PET)/CT were performed, both showing overexpression of somatostatin receptors and thus corroborating the histopathological findings.

Key words: 111In-Octreoscan SPECT; 68Ga-DOTANOC PET/CT; carcinoid; hybrid SPECT/CT imaging; middle ear adenoma; NAME; NET

Introduction

Mainly, the most common sites of neuroendocrine tumours (NET) are the gastrointestinal tract and the lungs but infrequently they could develop in the head and neck region; in this region, an area in which rarely NETs could occur is the middle ear.

Neuroendocrine adenoma of the middle ear (NAME) is a rare benign tumour arising from the middle ear epithelium. It represents less than 2% of all ear tumours, even if the incidence of this tumour is difficult to establish since it may be confused with other entities, such as adenomatous tumours and paragangliomas.[1]

The diagnostic work-up of this kind of neoplasm is commonly very difficult to set because no CT or MRI specific findings are known to date and despite showing various grades of neuroendocrine differentiation, it is difficult to

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achieve clear evidence of its neuroendocrine behaviour based on clinical or laboratory findings.

Somatostatin receptors (SSTRs), expressed in the majority of NETs are the best target for radiotracers used for diagnostic purposes. In light of the above, receptor imaging with 111In-Pentetreotide (Octreoscan®) single photon emission computed tomography (SPECT) and even better with 68Ga-DOTANOC positron emission tomography (PET-CT) represent decisive nuclear medicine diagnostic tools in patients with this kind of tumours.

Case History

A 40-year-old woman was referred to our institution to further investigate the occurrence of a pathological tissue involving diffusely the left mastoid air cells and extending to the middle ear cavity depicted by the head CT scan.

The patient has complained for about 3 years the presence of unilateral left-sided hearing loss, dizziness, otalgia and hearing fullness sensation, resistant to anti-inflammatory and antibiotic therapies administered as the standard of care. No previous clinical issues on patient's medical history were reported nor previous exposure to occupational hearing hazards by work-related conditions.

The audiometric assessment showed minor conductive hearing loss of 35 dB in the left ear and normal hearing in the right ear. Otoscopic examination revealed a mild retro-tympanic tumefaction.

The head CT scan showed a mass with soft tissue density and heterogeneous postcontrast enhancement in the left mastoid process of the temporal bone, diffusely obliterating the mastoid air cells and the tympanic airspace and surrounding the ossicular chain but without any clear sign of bony structures erosion.

The head magnetic resonance imaging (MRI) exam showed a solid tissue (17 × 8 mm), heterogeneously hyperintense on T2-weighted sequences, with marked and inhomogeneous contrast enhancement, located in the left mastoid process, widely involving the left superior mastoid air cells and the tympanic cavity.

Subsequently, a biopsy of the reported pathologic tissue was performed and histopathological examination revealed an epithelial neoplasm with neuroendocrine differentiation features [Figure 1]. Immunohistochemically, the cells excessively expressed synaptophysin and partially chromogranin A, specific markers for neuroendocrine cell differentiation. The proliferation rate (Ki67) was found to be less than 5%. According to the morphological and immunohistochemical features, the diagnosis of NAME was finally given.

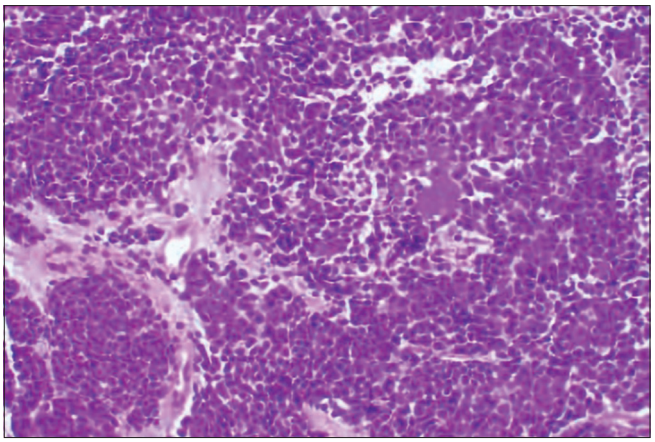

Figure 1: Neuroendocrine adenoma of the middle ear with mixed epithelial and neuroendocrine tumour, prominent clusters of small to medium-sized cells with minimal cytoplasm, hyperchromatic nucleoli and frequent mitotic figures

Four and 24 h after i.v. injection of 121.9 MBq of 111In-DTPA-octreotide (111In-Pentetreotide, Octreoscan®), planar whole body (double energy window set at 172 and 245 keV ±20%; 1024 ×256 matrix; scan speed 8 cm/min) and head SPECT images (64 projections, 128 × 128 matrix; 50 s acquisition time per projection) were obtained, using a dual-headed gamma camera equipped with medium-energy high resolution (MEHR) collimators. SPECT images were reconstructed using the iterative OSEM algorithm (8 iterations, 8 subsets) with a post-processing low-pass Butterworth filter, and the obtained images were transferred to the workstation and fused semi-automatically with the CT scan, by using dedicated software (Volumetrix tool, Xeleris Workstation 2.1, GE Healthcare).

111In-Octreoscan planar and particularly SPECT images showed a focal area of increased uptake of the SSTRs tracer in the left mastoid region, apparently in correspondence of the mastoid air cells and of the middle ear cavity, more clearly evident in the delayed 24 h images. Fused 111In-Octreoscan SPECT/CT images proved that the focal pathologic uptake matched correctly with the soft tissue density mass detected on CT and MRI scans in the same area [Figure 2].

PET/CT scan, from the upper thighs to the base of the skull, was performed 60 min after i.v. injection of 204 MBq of 68Ga-DOTANOC (Siemens Biograph 6 PET/CT) in the patient having fasted for 6 h. PET scan emission images were acquired for 4 min per bed position. CT low dose scan was used for non-uniform attenuation correction and anatomic localization (140 kV, 90 mA, 0.8 s tube rotation, 5 mm thickness). All images were reconstructed using the iterative OSEM algorithm with 2 iterations and 21 subsets followed by a post-reconstruction smoothing with a Gaussian filter (4.0 mm FWHM). A dedicated software (Hermes Hybrid Viewer) was applied to assess the fused PET/CT

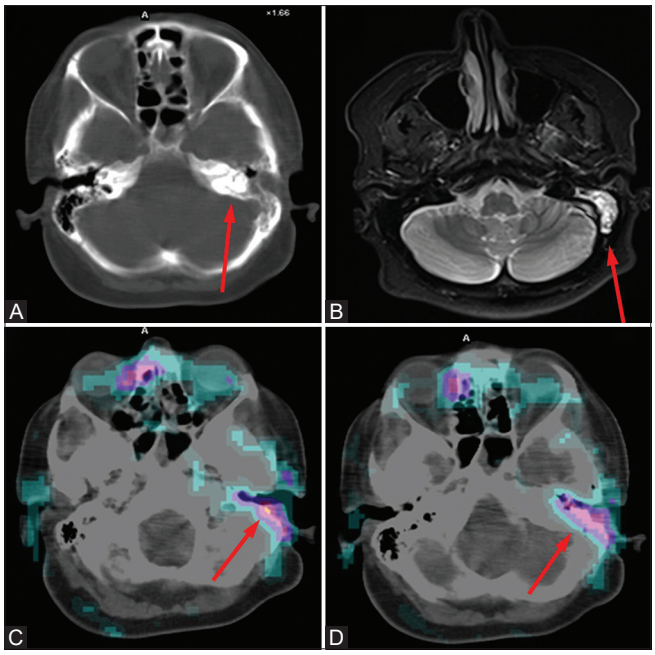

Figure 2 (A-D): CT scan (A) and T2-weighted STIR sequence on MRI exam (B) of the head showed a pathologic tissue obliterating the left mastoid cells and middle ear cavity. Fused 111In-Octreoscan SPECT/CT hybrid images on transaxial plane (C and D) demonstrating the clear correspondence between the morpho-structural alterations and the SSTR receptorial imaging findings

images sets.[2] 68Ga-DOTANOC PET/CT images strongly confirmed the presence of a high density of SSTRs focus right in correspondence of the solid tissue reported in the mastoid and tympanic airspaces, showing a clear and sharp pathologic uptake of the 68-Ga-radiopeptide [Figure 3].

No further findings were reported in remaining body segments by both hybrid SPECT/CT and PET/CT scans.

Discussion

'NAME', a term first proposed by Thompson and Mills in 2002, is a rare benign tumour with mixed patterns of epithelial and neuroendocrine differentiation. The nosologic distinction between middle ear neuroendocrine tumours from adenomatous tumours is not so unequivocal, given that someone keeps considering them two distinct entities while others believe them to represent a spectrum of the same disease.[3] Middle ear glandular neoplasms were classified by Saliba *et al*. in three different types based on the occurrence of immunohistochemical markers and/or metastasis. Type I (*Neuroendocrine Adenoma of the Middle Ear*) shows positive markers and negative metastasis and is the most common type (76% of the cases), followed by Type II (*Middle Ear Adenoma*) showing negative immunohistochemistry and negative metastasis (20%) and the least common being Type III (*Carcinoid Tumour of the Middle Ear*) showing positive immunohistochemistry and positive metastasis (4%).[4] Differential diagnosis includes

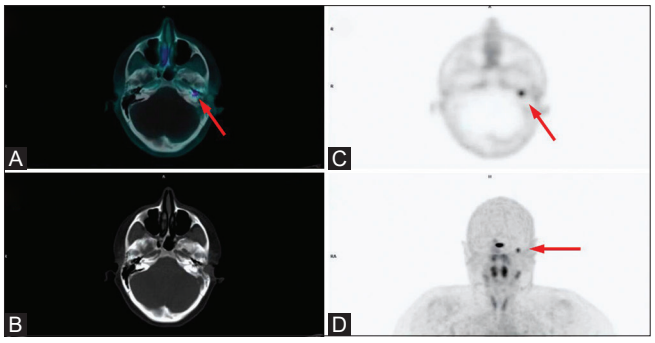

Figure 3 (A-D): 68Ga-DOTANOC PET/CT shows focal pathologic uptake in correspondence of the solid tissue reported in the left mastoid and tympanic airspaces, confirming the occurrence of high density of somatostatin receptors (SSRs 2,3,5) in this region. (A) Fused PET/CT image on axial plane (B) CT image on axial plane (C) 68Ga- DOTANOC PET image on axial plane (D) 68Ga-DOTANOC PET maximum-intensity projection (MIP)

paraganglioma, cholesteatoma, chronic otitis media, schwannoma, squamous cell carcinoma, rhabdomyosarcoma, meningioma, and papillary adenocarcinoma. The most common neoplasms of the middle ear are glomus tympanicum, a type of paraganglioma, and facial nerve schwannoma. The first appears as a soft tissue mass located in the hypotympanum and extending into the middle ear cavity, usually sparing the ossicles chain while schwannoma of the VII cranial nerve shows a predilection for geniculate ganglion region, nonetheless may occur in the tympanic and mastoid region.[5] It usually appears in the 5th decade, without any sex predominance. The cardinal symptom is conductive hearing loss. Other uncommon symptoms are tinnitus, auditory fullness, otalgia, and rarely facial nerve paralysis signs and otorrhoea. Unfortunately, even in the case of a tumour with relevant neuroendocrine differentiation, it is difficult to achieve any clinical or laboratory clear evidence of its neuroendocrine behaviour.

Histologically, NAME shows a dual cell population with different growth patterns ranging from cords and trabeculae to solid sheets and glandular structures. At the histopathological examination, the cells appear with a finely granular eosinophilic cytoplasm and oval pleomorphic nuclei.

There are no specific CT and MRI findings, but these imaging modalities are useful for assessing the extent of the disease as well as the presence of erosion of the ossicles chain. Mainly, CT findings of neuroendocrine adenoma consist of a circumscribed soft tissue without evidence of bone erosions occasionally engulfed between ossicles.[6] These tumours rarely show osteolytic destruction of the ossicles, which is, therefore, a helpful radiological sign to make a differential diagnosis from cholesteatoma and adenocarcinoma.[2] The radiological features were very similar to tympanic paraganglioma, which is the most frequent tumoural lesion of the middle ear.[1]

SSTRs, being expressed in the majority of NET are the best target for radiotracers used either for diagnostic and therapeutic purposes, therefore capable to provide high diagnostic accuracy. Although somatostatin analogs scintigraphy has been introduced about three decades ago, it remains the most diffuse radionuclide diagnostic tool in patients with NET, and functional imaging performed by exploiting 111Indium-diethylenetriaminepentaacetic acid-d-phenylalanine-octreotide. (In-DTPA-octreotide) (111In-Pentetreotide, Octreoscan®)could detect either primitive or secondary lesions in presence of a satisfactory lesion/background ratio. Although somatostatin receptor scintigraphy has reported high diagnostic accuracy in literature, in particular for whole-body studies, it has some obvious limitations for the detection of small lesions, due to its sub-optimal spatial resolution. Subsequently, PET imaging has been supported for NETs imaging workup. Because of its lack of specific tropism, 18F- fluorodeoxyglucose (FDG) is not the most effective radio-compound in NET patients' examination, providing the depiction of undifferentiated highly metabolic neoplasms only. In this direction, 18F-dihydroxyphenylalanine (DOPA) and mostly 68Gallium-peptides have shown to constitute excellent alternatives so far.[7]

Thus, currently, this conventional scintigraphic method is followed or sometimes replaced by 68Ga-labeled somatostatin analogs PET/CT, which shows higher sensitivity and a far better resolution in detecting NETs, if compared to SSTR conventional scintigraphy. Moreover, DOTA (1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, also known as Tetraxetan) analogs have a higher affinity to SSTRs (especially SSTR 2, 3, 5) and giving an accurate staging, allows the opportunity to set up a peptide receptor radionuclide therapy or to evaluate a surgical approach and in particular cases, a complete surgical excision with removal of the ossicular chain, if involved, to avoid potential recurrences.[8]

In this case, 111In-Octreoscan SPECT images showed an area of clearly increased uptake in the left mastoid process and in the middle ear region, clearly evident in the delayed 24 h images. After appropriate SPECT images reconstruction and post-processing, fused 111In-Octreoscan SPECT and CT images confirmed that this area matched with soft tissue density mass detected on CT scan and MRI. 111In-Octreoscan SPECT/CT hybrid imaging provided a significant improvement of diagnostic effectiveness and visual assessment confidence in respect of conventional planar and SPECT imaging,[9] through achieving additional anatomic information and consequently a clearer lesion localization, especially when facing minor pathologic uptake foci like the one we described.

68Ga-DOTANOC PET/CT corroborated the occurrence of a small well-circumscribed area of a high density of somatostatin receptors in correspondence of the soft tissue mass described by morpho-structural imaging in the mastoid and tympanic airspaces. It is important to focus on how the higher spatial resolution of PET imaging has allowed an outstanding quality of the images as compared to conventional SPECT imaging.

Substantially, our findings underline the peculiar clinical relevance of nuclear medicine techniques both conventional (Hybrid 111In-Octreoscan SPECT/CT) and PET/CT (68Ga-DOTANOC) in the diagnostic work-up of NETs, even in such rare case of neoplasm in an uncommon localization.

Hybrid 111In-Octreoscan SPECT/CT and mostly PET/CT were crucial to confirm the results of the histopathological examination, to obtain an accurate differential diagnosis of this rare neoplasia. Thus, combined morpho-functional imaging is required primarily to exactly delineate the anatomical extent of the disease, supporting an accurate staging of the disease before further treatments take place. Even considering the rarity of this condition, the occurrence of relapse and metastatic disease was described in the literature,[10] although they represent very rare cases. In this light, we believe it is reasonable and thus we would suggest to apply an accurate follow-up through the aforementioned receptor hybrid imaging techniques for this kind of patients, focusing on their high sensitivity and effectiveness in distinguishing this very peculiar neoplastic condition.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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