Middle ear adenomatous tumor: A not so rare glomus tympanicum-mimicking lesion

Les tumeurs adénomateuses de l'oreille moyenne : un diagnostic différentiel du glomus tympanique

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Summary
Background and purpose. — Middle ear adenomatous tumors (MEAT) are rare tumors which can be benign or malignant and can present a neuroendocrine differentiation. Their radiological aspect is very similar to glomus tympanicum (GT) which are the most common tumoral lesions of the middle ear. We present several radiological and clinical findings that could help radiologists to accurately identify MEAT.

Material and methods. — We retrospectively reviewed the radiological and clinical findings of three patients with MEAT and of eight patients with GT. Diagnostic was obtained after surgical resection in all cases. All patients had high resolution CT and MR of the middle ear associated with a subtracted digital carotid angiography. Tumor location, size, extension, signal intensity, and enhancement were analysed. From the medical records of the patients, clinical manifestations (hearing loss, tinnitus), evolution length and recurrences were noted.

Results. — MEAT and GT appeared as tissular lesion with significant enhancement on CT and MR. A vascular blush was present on angiography in all cases of GT and absent from all cases of MEAT. A close relationship between the tumor and the Jacobson’s nerve or its branches was identified in all cases of GT. Pulsatile tinnitus was present in all patients with GT and absent in all patients with MEAT.

Conclusion. — A middle ear tissular lesion clearly separated from the Jacobson nerve or its branches, showing significant enhancement after contrast medium injection but with a normal angiography, should make one suspicious for MEAT.

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Introduction

Tissular lesions inside the middle ear have to be separated in the ones arising in the middle ear and the others extending from their original area to the middle ear. In the first group,
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From GT.

findings that will help the radiologist to discriminate MEAT.

of significant enhancement after gadolinium administration (arrow).

C. Axial T1-weighted MR sequence. Tissular lesion of the middle ear (arrow) located on the promontory, clearly distinct from the Jacobson nerve canal (arrowhead) showing up a significant enhancement.

D. Axial gadolinium enhanced T1-weighted MR sequence. Presence of significant enhancement after gadolinium administration (arrow).

Methods

We retrospectively reviewed the radiological and clinical findings of 11 patients with middle ear tumors followed in the radiological and in the ENT departments of our institution: eight patients presented GT and three patients MEAT. The histologic diagnosis had been established after surgical excision in all patients.

We compared the clinical presentation, evolution and radiological findings of these two tumors types. Contrast-enhanced high resolution CT, unenhanced and contrast-enhanced MR imaging and subtracted digital carotid angiography had been performed in all patients. Following clinical characteristics were collected from the medical records: age of patient, presence of a pulsatile tinnitus, presence of a red-blue tympanic appearance, and general evolution (recurrences). High resolution CT examinations of the ears were realized after intravenous administration of contrast medium in axial and coronal planes with three different CT units (Sensation 16, Siemens Medical Systems, Erlangen, Germany; Vision, Siemens Medical Systems, Erlangen, Germany). We evaluated T1-weighted images before and after intravenous administration of gadolinium, and T2-weighted images. Two radiologists (G.B., F.V.) evaluated, in consensus, the T1 and T2 intensity of the tumors, and their enhancement after intravenous gadolinium administration. On T1 and T2-weighted signal MR images, tumoral signal was quoted as iso-, hypo-, or hyperintense to the cerebral grey matter. On gadolinium enhanced T1-weighted images; enhancement was qualitatively evaluated as significant or not. Subtracted digital carotid angiography was considered as abnormal in case of a typical vascular blush aspect.

Results

Radiological findings

On contrast enhanced CT examinations, GT and MEAT appeared as tissular middle ear formations, isodense to brain grey matter (Figs. 1—4). Ossicular involvement was noted in 1/3 MEAT, and in 3/8 GT (Figs. 2—4). Bone erosion was present in 2/3 MEAT, and in 3/8 GT. The mean size of MEAT and GT were, respectively, 6.3 mm (range: 2—10 mm) and 5.8 mm (range 2—15 mm).

All GT were located at the level of the promontory, in close relationship with the Jacobson nerve (Fig. 4). In two patients, MEAT was located at the level of the promontory (Figs. 1 and 2). One was distinctly separated from the Jacobson nerve, but the size of the second was so huge that it fulfilled the whole middle ear and contacted the Jacobson nerve (Fig. 2). In the third case, the MEAT was located in the posterior attic (Fig. 3). GT and MEAT presented a similar aspect on MR: tissular lesion showing iso- or hypointense signal to brain grey matter on T1-weighted images and hyperintense signal on T2-weighted images (Figs. 1—3).
A significant contrast enhancement was present in both GT and MEAT after gadolinium contrast medium injection (Figs. 1—3).

Arteriography was abnormal in all the GT with the typical blush aspect present in all cases (Fig. 4C). At the opposite, arteriography was normal in all of the MEAT (Fig. 1E).

**Clinical and histopathological findings**

The mean age of patients with MEAT and GT were, respectively, 38.7 (± 10.1) and 62.3 (± 17.3) years. Pulsatile tinnitus was present in all patients with GT and absent in all patients with MEAT. The aspect of the tympanum was

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**Figure 1**  Adenomatous tumor in a 42-year old patient. A. Axial contrast-enhanced high resolution CT examination of the right ear. Presence of a tissular lesion (white arrow) fulfilling the middle ear from the retrotympanum to the Eustachian tube, with a subsequent serous otitis media (black arrow). The Jacobson nerve canal is visible in the inner wall of the middle ear (black arrowhead). Note ossicular involvement (white arrowhead). B. Gadolinium enhanced T1-weighted MR image. Presence of a significant enhancement of the tissular lesion (arrow). Lower enhancement of otitis media in the mastoid cells (arrowhead).

**Figure 2**  Adenomatous tumor in a 42-year old patient. A. Axial contrast-enhanced high resolution CT examination of the right ear. The tumor (arrow) is located in the external attic; this finding excludes the diagnostic of glomus tympanicum. Note ossicular involvement (arrowhead). B. Gadolinium enhanced T1-weighted MR image. Presence of a tissular lesion with significant enhancement in the external attic (arrow).

**Figure 3**  Adenomatous tumor in a 48-year-old patient. A. Coronal contrast-enhanced high resolution CT examination of the right ear. The tumor (arrow) is located in the external attic; this finding excludes the diagnostic of glomus tympanicum. Note ossicular involvement (arrowhead). B. Gadolinium enhanced T1-weighted MR image. Presence of a tissular lesion with significant enhancement in the external attic (arrow).

**Figure 4**  Glomus tympanicum (GT) in a 56 year-old patient. A. Axial contrast-enhanced high resolution CT examination. A tissular lesion of the middle ear is visible on the promontory (arrow). The canal of the Jacobson nerve could be identified beneath the tumor (black arrowhead). Note ossicular involvement (white arrowhead). B. Gadolinium enhanced T1-weighted image of a GT. The tumor is located on the promontory and presents an important enhancement after gadolinium administration (arrow). C. Digital subtraction carotid angiography. Presence of the characteristic hypervascular blush of the GT (arrow).
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Classical treatment is surgery, tympanomastoidectomy with complete resection of the neoplasm, ossicles have to be removed if involved. Recurrence rate is significant (25% of patients) and is in general secondary to tumoral regrowth after incomplete resection, rather than to a former tumoral aggressiveness.

GT are three to four times more frequent in women than in men, and a hormonal (oestrogen) influence has been suggested. GT arise from paraganglia, which are specialized organelles distributed along the course of autonomic nerves. In the middle ear, they arise from the Jacobson nerve, which is a tympanic branch of the glossopharyngeal nerve (CN IX). It enters the tympanic cavity along with the tympanic artery by the inferior tympanic canaliculus. Jacobson’s nerve is in charge of collecting sensation from the middle ear and the bony Eustachian tube, and providing parasympathetic fibers to the parotid gland. In general, GT are found at the level of the cochlear promontory, but they can be present anyway long the Jacobson nerve branches.

Because of reduced symptoms, diagnosis of MEAT is frequently delayed, and often made only after years.

On pathologic examinations, MEAT are avascular, fibrous tumors with a pale reddish appearance composed by small cells with regular nucleus and heterogeneous chromatin. Involvement of the ossicular chain is frequent, but, at the opposite, destruction or invasion of the surrounding bone is rare. Tympanic perforation with external canal involvement is possible. Tumors size can range from 0.2 to 3 cm and all of the cases in our series were in this range. Immunohistochemical analysis could demonstrate the neuroendocrine differentiation with positive staining of synaptophysin, chromogranin, serotonin, neuron-specific enolase which are markers of neuroendocrine and neuronal neoplasms. Classical treatment

Discussion

MEAT arises from the lining of the middle ear. They can develop at any age, without gender predilection. Middle ear carcinoïd neoplasms are thought to be a kind of adenomatous tumors and the difference between the two entities is still in debate among pathologists. Some authors report immunohistochemical evidence of neuroendocrine differentiation to be efficient for the diagnosis of carcinoïd tumor over adenoma. Others consider neuroendocrine differentiation as part of the spectrum of middle ear adenoma, and the two entities merge depending on the extent of neuroendocrine differentiation. In a purpose of simplification and in regard to their clinical and radiological presentations, carcinoïd tumors and others adenomatous tumors could be apprehended by radiologists as a unique entity. Therefore, we decide in our study to include carcinoïd and non carcinoïd tumors under the term of MEAT.

On pathologic examinations, MEAT are avascular, fibrous tumors with a pale reddish appearance composed by small cells with regular nucleus and heterogeneous chromatin. Involvement of the ossicular chain is frequent, but, at the opposite, destruction or invasion of the surrounding bone is rare. Tympanic perforation with external canal involvement is possible. Tumors size can range from 0.2 to 3 cm and all of the cases in our series were in this range. Immunohistochemical analysis could demonstrate the neuroendocrine differentiation with positive staining of synaptophysin, chromogranin, serotonin, neuron-specific enolase which are markers of neuroendocrine and neuronal neoplasms. Classical treatment

red-blue or red in all patients with GT. In patients with MEAT, the tympanum was normal in one case and had a reddish, inflammatory appearance in two cases. All patients were treated by surgical ablation of the tumor. Recurrences occurred in two patients with MEAT and in three patients with GT, after a mean period of, respectively, 16 (± 10) and 22 (± 9) months. Two of our cases of MEAT presented significant neuroendocrine differentiation on immunohistochemical analysis (Fig. 5A and B).

Figure 5  Histopathologic and immunohistochemical examinations of a middle ear adenomatous tumor. A. Photomicrograph (hematoxylin eosin stain; original magnification, x40). Tumoral proliferation of small cells with regular nucleus presenting a granular chromatin. No evident signs of mitosis are noted. B. Photomicrograph (synaptophysin stain, polyclonal antibody; original magnification, x40). Important staining of the cytoplasms indicating neuroendocrine peptides secretion (arrow).
tumor in our series, as it was present in one of our cases of MEAT, but in several cases of GT too. Ossicular involvement and destruction may occur in both and could be well depicted on CT [1,36]. Bone involvement, often described as absent in adenomatous tumour, is possible but rare and, if present, could be consistent in erosion or in invasion. Bone erosion could be found in the two pathologies, but as paragangliomas are earlier clinically symptomatic, this finding is more rare in paragangliomas [3]. GT are poorly destructive, and grow along pathways of least resistance. In our series, ossicular involvement and bone erosion were present, respectively, in 3/8 and 3/8 cases of GT, and in 1/3 and 2/3 cases of MEAT. Nevertheless, the presence of massive bone destruction should evoke differential diagnosis like adenocarcinomas, endolymphatic sac low-grade adenocarcinomas, metastatic tumors or cholesteatomas [34,37]. GT and MEAT are not discernable by their size, as their mean diameters were close in our series, respectively, 5.8 and 6.3 mm.

MRI features are nonspecific. Both MEAT and GT appear as of a soft-tissue tumour of intermediate T1 signal isointense to white matter, and slightly increased T2 signal as compared to grey matter [1,38,39]. Even if less accurate than CT in this purpose, MR could identify ossicular involvement with ossicles appearing as signal void within the lesion [40]. As shown in our cases, significant enhancement is observed after contrast medium injection (iodine or gadolinium) in both tumors, without specific characters [41—43].

In the purpose of distinguishing the two entities, different imaging findings should be recognized. We propose two main criterions that could help differentiate the two kinds of tumors. The first is the tumor location. GT arise from the Jacobson nerve and its branch, and are therefore always connected to a neurological structure. GT are generally found at the level of the cochlear promontory, but not necessarily, and could be present anyway along the Jacobson nerve branches [33]. If a tumor is found to be completely independent from the Jacobson nerve or branches, the diagnostic of paragangliomas should be revoked. Even if the tumour presents an important size, one should carefully identify the origin of the tumoral development. But, in case of too large tumor, when it completely fulfills the middle ear, it is sometimes impossible to determine if the tumor only contacts the Jacobson nerve or arises from it. In our series, one case of MEAT was a huge tumor fulfilling completely the middle ear and it was so impossible to identify its correct relationship with the Jacobson nerve. At the opposite, our third case of MEAT was located in the attic, far away from the Jacobson nerve and its branch, and the diagnostic of GT could have been revoked on this finding. Besides MEAT, the main differential diagnoses of a tissular lesion in such location include meningiomas, neuromas of CN VII or CN VIII, lymphomas, local extension of carcinomas (parotid, pharynx) and metastasis [37,38]. But, at the opposite of MEAT, most of those tumors first arise outside of the middle ear and secondary invade it, and the correct identification of the tumour origin and extension is mandatory to allow an accurate diagnosis.

The second point is the presence of a normal angiography which is a strong argument against the diagnostic of GT. GT present a characteristic angiographic appearance of an early intense and inhomogeneous tumor blush with enlarged feeding arteries, and early-appearing draining veins [44]. The gold standard for the detection of GT is still digital subtraction angiography (DSA) and the presence of an abnormal angiography (presence of a vascular blush) is considered to be sufficient to affirm the diagnostic of paragangliomas [1,44—46]. Avascular paragangliomas are extremely rare and, to our knowledge, this feature has never been reported for tympanicum glomus. Our series found a vascular blush in eight cases of GT which was absent in the three cases of MEAT. We can so assume that the presence of a normal conventional angiography exclude the diagnostic of GT. Thus, in case of middle ear tissular lesion with normal conventional angiography, MEAT should be part of the differential diagnosis.

Nevertheless, the use of conventional angiography to characterize GT can be seen as a limitation of our study. Nowadays, MR or CT angiography is preferred to conventional angiography for the noninvasive exploration of GT, and conventional angiography is only realized in cases which embolization is needed [1,46]. Whether our results can be translated to MR or CT, angiography have to be further investigated.

Conclusion

Even if more rare than GT, MEAT should be evoked in case of middle ear tissular lesion showing significant enhancement after contrast medium injection. The two tumors have similar radiological aspect on CT and MR and are difficult to distinguish. Determination of the type of tumor could be assessed by two findings: the determination of the relationship between the tumor and the Jacobson nerve, GT being always connected to it, at the opposite of MEAT; and the identification of a vascular blush on conventional arteriography, which is characteristic of GT and absent in case of MEAT.

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