

A Clinicopathological Study of 15 Patients With Neuroglial Heterotopias and Encephaloceles of the Middle Ear and Mastoid Region

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Objectives/Hypothesis: Heterotopic masses of neuroglial tissue involving non-midline structures, specifically, the middle ear region, are exceptional. The pathogenesis of these lesions and, in particular, their relation to encephaloceles, is uncertain. **Study Design and Methods:** H&E-stained sections from 15 lesions diagnosed as neuroglial heterotopias or encephaloceles involving the middle ear region were reviewed. Radiographic or operative evidence of a central nervous system (CNS) relation and clinical factors possibly related to pathogenesis were analyzed. **Results:** All 15 lesions (from six men and nine women; mean age, 49 y; range, 16–67 y), regardless of their relation to the CNS, were composed of varying proportions of neurons and glia with associated chronic inflammatory cells and reactive gliosis. No significant ependymal or choroid plexus component was present. Operative findings revealed that two lesions had definite CNS connections and two were unrelated to the CNS; this relation could not be determined in the remaining cases. Seven of 10 patients for whom clinical information was available had a history of chronic otitis media or mastoiditis or both; four of these seven patients also had a history of previous trauma or surgery. Three patients, including both patients whose lesions had no demonstrable CNS attachment, had no predisposing factors. **Conclusions:** Most neuroglial heterotopias of the middle ear are probably acquired encephaloceles. These

lesions occur in older patients than do their midline counterparts. Determination of the relation of these lesions to adjacent CNS structures must be done radiographically or using operative findings, because histology alone cannot be reliably used to render an accurate diagnosis. **Key Words:** Neuroglial heterotopia, encephalocele, middle ear, temporal bone, pathogenesis.

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INTRODUCTION

Heterotopic neuroglial tissue is defined as a mass composed of mature brain tissue isolated from the cranial cavity or spinal canal.¹ Most reported examples involve midline structures, including the nose and nasopharynx (so-called nasal glioma)^{2–4} as well as the oropharynx, palate, lips, tongue, and tonsils.^{5–9} Lesions involving non-midline structures, and specifically, the middle ear region, are often not recognized and may be misdiagnosed as neoplasms such as teratomas (when adjacent non-neural tissues are present), gliomas, meningiomas, or schwannomas.

The classification and pathogenesis of these lesions, particularly their relation to encephaloceles, remain unsettled. One commonly accepted theory is that heterotopic neural tissue is a variant of encephalocele in which the central nervous system (CNS) connection has been absorbed or become vestigial.¹ Contributing to the uncertainty regarding these lesions are the multitude of entities to which the term “neuroglial heterotopia” has been applied, as well as the number of terms used previously to refer to them, including ectopic neurons in intracerebral white matter, leptomeningeal neuroglial lesions, intracranial extradural “accessory brains,” sequestered encephaloceles, glial choristomas, hamartomas, monodermal teratomas, extracranial gliomas, “brain fungus,” and distal lesions involving the lung and endometrium thought to result from fetal remnants of a previous pregnancy.^{10–15} In the middle ear and mastoid region, most previously reported cases describe an association with previous trauma, surgery, or infectious or inflammatory processes.^{10,13,14,16–20} However,

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patients with no significant predisposing factors or obvious relation to CNS structures have also been described,^{1,11,15,21-24} leaving the pathogenesis unresolved. We evaluated the clinicopathological features of neuroglial heterotopias and encephaloceles involving the middle ear region to assist in the clarification of these issues.

MATERIALS AND METHODS

All lesions diagnosed as neuroglial heterotopias or encephaloceles of the middle ear or mastoid region accessioned at the Armed Forces Institute of Pathology between 1950 and 1996 in which H&E-stained microscopic slide sections were available for review were evaluated. Fifteen lesions were identified in a review of 117 cases of heterotopic CNS tissue or encephalocele of the head and neck seen in consultation during the same period. All identified cases were obtained from civilian sources. This clinical investigation was conducted in accordance and compliance with all statutes, directives, and guidelines of the Code of Federal Regulations, Title 45, Part 46, and the Department of Defense Directive 3216.2 relating to human subjects in research.

All of the available slides, including those additionally stained with Masson trichrome, phosphotungstic acid-hematoxylin (PTAH), or Nissl stains or with antibodies to glial fibrillary acidic protein (GFAP, rabbit polyclonal, dilution 1:500, Dako, Carpinteria, CA), S-100 protein (rabbit polyclonal, dilution 1:800, Dako), or neurofilament protein (mouse monoclonal [clone 2F11], dilution 1:300, Dako), were examined. Appropriate standard positive and negative (serum) controls were used throughout. Specific histological features assessed included the types of neuroglial elements present, the presence or absence and type of associated non-neural tissues, and the presence or absence of inflammatory cells or other reactive changes.

Histological evaluation was supplemented by a review of the clinical information submitted with each case including patient demographics, symptoms at presentation, location of the lesion, history of previous trauma or surgery, associated abnormalities or malformations, evidence of cerebrospinal fluid leakage, and

radiographic or operative relation of the lesion to adjacent CNS structures. The contributing pathologist's diagnosis was also recorded for each case.

RESULTS

Clinical

Lesions in six men and nine women with a mean age of 49 years (range, 16–67 y) were evaluated (Table I). Nearly half of the patients, including 7 of 10 for whom detailed clinical information was available, presented with symptoms of chronic otitis media or mastoiditis. Other presenting symptoms included hearing loss or deafness, dizziness, and traumatic perforation of the tympanic membrane. Three patients had a history of prior surgery and an additional patient had a history of trauma. Specific information regarding the relation of the lesions to the CNS was documented in only a few cases. There was no radiographic evidence of a bony abnormality in two patients. At the time of surgery, a cerebrospinal fluid leak or evidence of bone erosion was noted in two patients (including one of the above patients whose radiographic studies were interpreted as normal). One additional patient had no evidence of a CNS connection at the time of operation. In summary, 8 of 10 patients in whom clinical information was available had either a history of chronic infection, previous surgery, trauma, or surgical evidence of a CNS connection.

Pathology

Seven lesions involved only the middle ear, four involved the mastoid cavity alone, and four involved the middle ear and mastoid regions. All cases, regardless of their relation to the CNS, were composed of varying pro-

TABLE I.
Clinical Findings of Middle Ear Region Neuroglial Heterotopia and Encephalocele.

Patient No.	Age (y)/ Sex	Location of Lesion	Presenting Symptoms	Past Medical History	Relation of Lesion to CNS
1	16 M	R mastoid	Chronic mastoiditis	Previous mastoidectomy	NR
2	29 F	Middle ear/mastoid	Chronic mastoiditis	NR	No CSF leakage
3	30 F	L middle ear/mastoid	NR	NR	NR
4	37 F	L middle ear	Chronic otitis/mastoiditis	Multiple previous surgeries	NR
5	43 M	Middle ear	NR	NR	NR
6	44 F	R middle ear	Chronic otitis/mastoiditis	NR	NR
7	51 M	L middle ear	Chronic otitis/mastoiditis, deafness	Perforation of ear drum after trauma	NR
8	52 M	R mastoid	Chronic otitis, deafness, dizziness	Multiple previous surgeries	NR
9	56 M	L middle ear	NR	NR	NR
10	57 F	Mastoid	NR	NR	NR
11	58 F	R middle ear	Deafness	NR	No bone erosion on radiograph
12	62 F	R middle ear	NR	NR	NR
13	64 F	R middle ear/mastoid	Chronic middle ear/mastoid problems	NR	No radiographic abnormality but CSF leak at surgery
14	66 F	L mastoid	NR	NR	Bone intact at surgery
15	67 M	R middle ear/mastoid	Infection, hearing loss	Tympanic perforation	CSF leak at surgery

CNS = central nervous system; CSF = cerebrospinal fluid; NR = not reported.

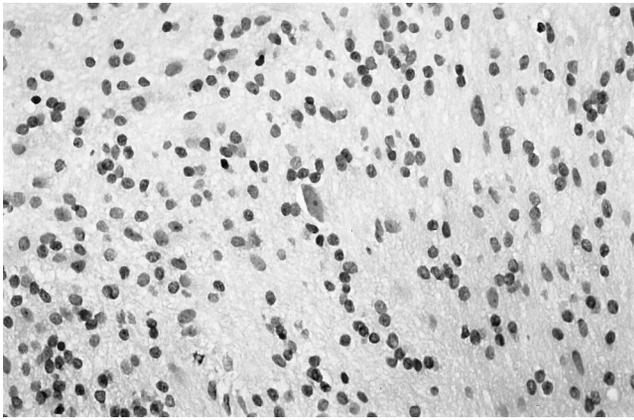


Fig. 1. All middle ear or mastoid region neuroglial heterotopias and encephaloceles were composed of mature brain tissue containing both neurons and glial cells (H&E stain, original magnification $\times 400$).

portions of neurons and glia without a significant ependymal, choroid plexus, or leptomeningeal component (Fig. 1). The glial components were highlighted by the PTAH stain and the GFAP and S-100 protein immunohistochemical antibodies, when performed. Similarly, neuronal elements were Nissl stain- and neurofilament protein-positive. Chronic inflammatory cells, including lymphocytes and macrophages (Fig. 2), and reactive gliosis (Fig. 3) were present in all cases. A flattened to cuboidal epithelial lining (Fig. 4) and associated glandular elements (Fig. 5) were admixed in most cases ($n = 9$). Segments of skin ($n = 1$) and bone ($n = 2$) were associated histological findings in a few cases.

DISCUSSION

Since the initial description of glial heterotopias over the dorsal surface of the cervical spinal cord in 1907,²⁵ various different types of neuroglial heterotopias have been described. These lesions may be classified based on their location and possible pathogenic mechanisms as follows: 1) intraparenchymal CNS lesions; 2) dural and lep-

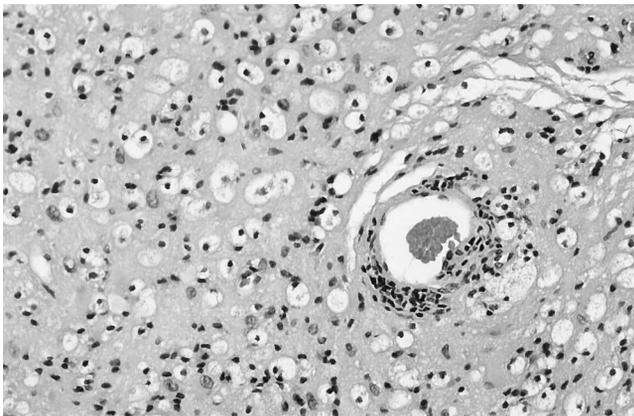


Fig. 2. Chronic inflammation, including lymphocytes and macrophages, was prominent in this lesion (H&E stain, original magnification $\times 400$).

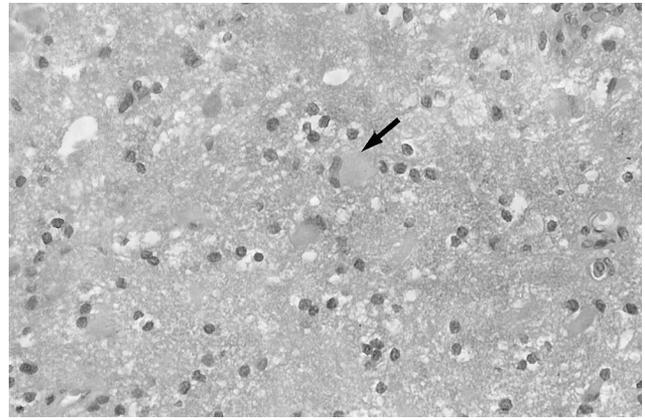


Fig. 3. Reactive astrocytes with prominent gemistocytic cytoplasm (arrow) were observed in all cases (H&E stain, original magnification $\times 400$).

tomeningeal lesions; 3) intracranial extracerebral lesions; 4) distal lesions thought to result from a previous pregnancy; 5) midline “nasal gliomas,” thought to originate as encephaloceles; and 6) non-midline lesions of the head and neck.^{12,26}

Non-midline neuroglial heterotopias are rare. Cases have been reported to involve the eye and orbit,²⁷ the face and neck,^{28,29} the skin and soft tissue,^{30,31} and the middle ear region.^{1,10,11,13–24} Most of the case reports or limited series have emphasized the clinical diagnosis and treatment of patients with these lesions; only a handful of studies have evaluated the histopathological features and differential diagnosis of neuroglial heterotopias and encephaloceles.^{1,14,19}

Unlike their midline counterparts, most middle ear region neuroglial heterotopias and encephaloceles are diagnosed in adult patients. In our series, most patients presented with signs and symptoms of chronic infection or inflammation. Other authors have reported cerebrospinal fluid otorrhea and symptoms of a mass lesion as the most common presenting symptoms.^{16,18} Chronic infection or inflammation, previous trauma, or surgical procedures have been described in the literature as predisposing fac-

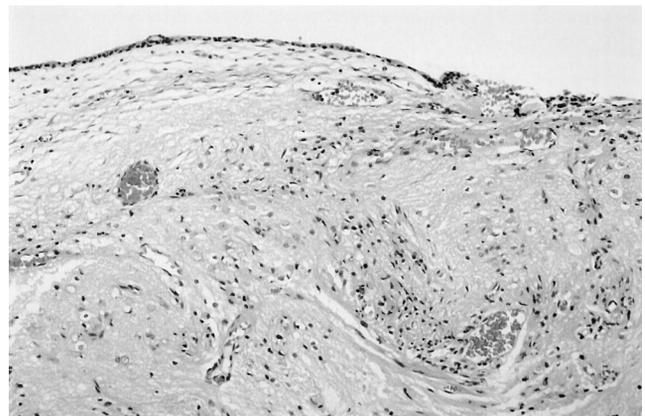


Fig. 4. The surface of this lesion was covered by a cuboidal epithelium (H&E stain, original magnification $\times 250$).

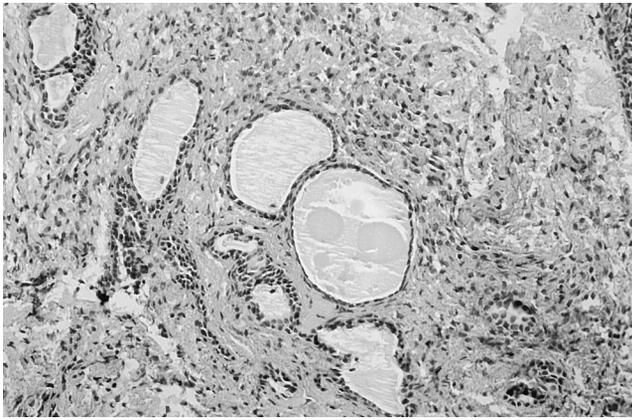


Fig. 5. Admixed glandular elements were present in most middle ear region heterotopias and encephaloceles (H&E stain, original magnification $\times 250$).

tors for the development of middle ear heterotopia or encephalocele,^{10,13,14,16–20} and similar factors were identified in most of our cases. The aggregate of these findings lends support to the concept that middle ear region neuroglial masses are most often acquired encephaloceles. However, a few of our patients had no predisposing factors and no evidence of a connection of their lesions to the CNS. Similar cases have been reported in the literature,^{1,11,15,21–24} suggesting the possibility of a true neuroglial heterotopia or choristoma. Possible explanations for these disparate findings include the possibility of a small congenital defect in the overlying temporal bone, the tegmen tympani. Autopsy studies have documented such defects in up to 20% of cases.^{10,13,23} It is also possible that a remote history of trauma or surgery may not be known at the time of presentation many years later, or that small connections to the CNS may not be detected. As previously stated, in at least one of our cases, there was no radiological evidence of a bony defect, but there was still a cerebrospinal fluid leak at surgery. Again, similar cases have been reported in the literature.^{11,22} In any circumstance, the finding of neuroglial tissue in the middle ear region should prompt a search for a CNS connection to avoid potentially serious complications.^{10,13,19}

Pathologically, middle ear region neuroglial heterotopias and encephaloceles are characterized by varying proportions of neurons and glia, with associated chronic inflammation and gliosis. Although no significant ependymal, choroid plexus, or leptomeningeal component was noted in our cases, choroid plexus tissue can be present.¹¹ Keratinaceous debris, especially when associated with a cholesteatoma, has also been reported.¹⁹ The frequent presence of flattened to cuboidal epithelial lining and glandular elements, most likely representing entrapped tympanic cavity or eustachian tube epithelium, should not be mistaken for teratomatous elements. Communication between the surgeon and pathologist to clarify the relation of the lesion to surrounding structures is helpful to avoid this error. Furthermore, the absence of elements unrelated to normal anatomic structures may be a useful differential diagnostic feature.

In addition to neuroglial heterotopia or encephalocele and teratoma, diagnoses considered by the contributing pathologists in this series included neoplastic lesions such as ganglioglioma, other gliomas, meningioma, neuroma, and schwannoma. Significant overtreatment can result from an incorrect diagnosis. The patient's clinical presentation, as well as the location of the lesion (extra-axial vs. intra-axial) and its relation to surrounding structures (dura, peripheral nerve) are probably the most significant factors in distinguishing neuroglial encephaloceles from these other lesions. In particularly difficult cases with significant obscuring inflammation, immunohistochemistry with antibodies to GFAP may be needed to confirm the neuroglial nature of these lesions.

It should be noted that there are no significant histological differences between lesions with and without demonstrable CNS connections. The accurate diagnosis of heterotopia versus encephalocele therefore requires knowledge of the patient's radiographic and operative findings. Depending on the presence or absence of a CNS connection, which may or may not be known at the time of evaluation, either heterotopia or encephalocele may be appropriate terms for these lesions. However, because most lesions have a predisposing cause, acquired encephalocele is probably the most appropriate term.

CONCLUSION

Neuroglial heterotopias and encephaloceles of the middle ear region occur in older patients than do their midline counterparts and are often associated with a previous history of surgery, trauma, or infection and inflammation. These findings support the concept that they are acquired encephaloceles rather than developmental lesions in most cases. Determination of the relation of these lesions to adjacent CNS structures cannot be reliably done histologically; correlation with the patient's radiographic and operative findings is therefore required for the accurate diagnosis of these lesions. An awareness of these lesions and their typical clinical presentation should allow them to be easily distinguished from teratomas and primary CNS neoplasms in most cases.

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