Introduciton:
Cholesterol granulomas (CGs) are expansile, round or ovoid cysts containing cholesterol crystals surrounded by foreign body giant cells and chronic inflammation.

- **Petrous apex**: truncated pyramid forming the medial portion of the temporal bone.
  - Base: bony labyrinth and the internal carotid artery (ICA) anteriorly
  - Superior surface: middle cranial fossa, Meckel’s cave, and the ascending ICA.
  - Posterior surface: posterior cranial fossa and Dorello’s canal (CN VI)
  - Inferior surface: jugular bulb and the inferior petrosal sinus.

- Marrow-filled in 84%, pneumatized in 9%, and sclerotic in 7% of temporal bones.
- CGs in this region: 10 times as often as cholesteatomas, 40 times more common than mucocles.

Incidence:
- Cholesterol granuloma of the petrous apex: one for every 30 acoustic neuromas, an incidence of less than 0.6 cases per million population per year.
- Found in as many as 12-20% of temporal bones with chronic otitis media.
  - (12% of COM patients with intact tympanic membranes and in 21% of a group with perforation).
- Friedmann (biopsies taken during mastoidectomy procedures): primary pathological process in 5.5% of cases and also noted that it occurred only in uninfected ears.
- Can occur in isolation, without any previous history of infection.

History:
- First reported by Manasse in 1894 (external and middle ear)
- In 1982, House & Brackmann: two cases of CGs of the petrous apex

Experimental cholesterol granuloma
- In 1957, Ojala introduced cholesterol granuloma in chick humeri by obstructing the ventilation.
- In 1959, Friedmann injected sterile suspensions of cholesterol into bullae of guinea pigs; he found that cholesterol granulomas developed, but that cholesteatomas did not.
- In 1963, Dota et al. produced cholesterol granulomas in the tympanic cavity of the
rabbit by repeated injections of 1% oxalic acid solution.

- In 1966, Beaumont induced cholesterol granuloma following the experimental exclusion of air from pneumatized bones using the pneumatized humerus of the domestic fowl (Gallus domesticus).
- In 1970, Main et al. created experimental cholesterol granulomas in squirrel monkeys by obstructing the Eustachian tubes for 6-12 months.
- In 1979, Goycoolea et al. produced cholesterol granulomas in cats. In the same year, Kuiper et al. experimentally induced middle ear effusions and cholesterol granulomas 20 months after tubal obstruction in germ-free rats.
- In 1980, Hiraide et al. produced cholesterol granulomas experimentally in the middle ear of the guinea pig by injecting only one dose, transtympanically, of a saturated solution of cholesterol in absolute alcohol.
- In 1982, Heumann et al. produced experimental cholesterol granulomas in chicken humerus. In the same year,
  - Hiraide et al. experimentally induced middle ear effusions and cholesterol granulomas >=1 month after Eustachian tube obstruction in squirrel monkeys and
  - Paparella et al. created cholesterol granulomas from long-term Eustachian tube obstruction in cats, monkeys, guinea pigs and chinchillas.

→Hypoventilation, deprivation of oxygen and the presence of fluid in the middle ear space appeared to be prerequisites for the formation of cholesterol granulomas.

**Pathology:**

*Gross pathology*

Macroscopically, the lesion has a round, ovoid or more irregular appearance with a brownish or yellow color and a glistening surface.

*Histopathology*

Composed of a large number of cholesterol crystals surrounded and engulfed by multinucleated, foreign-body giant cells and embedded in fibrous granulation tissue with histiocytes, round cell infiltration, macrophages and many accompanying capillary-sized blood vessels.

Additional findings may include the presence of areas of old and recent hemorrhage with numerous macrophages and hemosiderin.
Electron microscopy

Giant cells display large numbers of mitochondria and smooth endoplasmic reticulum surrounding the small needle or dart-shaped cholesterol crystals. Large numbers of lysosomes are present.

Pathogenesis:

The obstruction-vacuum theory:
The exposed marrow theory
Diagnosis:
Terao et al. reviewed the findings for 92 patients from 1990 to 2001

Table 2. Summary of Preoperative Symptoms of 92 Patients

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No. of cases* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing loss</td>
<td>34 (37.0)</td>
</tr>
<tr>
<td>Vertigo</td>
<td>27 (28.3)</td>
</tr>
<tr>
<td>Headache</td>
<td>25 (27.2)</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>17 (18.5)</td>
</tr>
<tr>
<td>Disturbance of facial sense</td>
<td>15 (16.3)</td>
</tr>
<tr>
<td>Aural pressure</td>
<td>12 (13.0)</td>
</tr>
<tr>
<td>Otolgia</td>
<td>7 (7.6)</td>
</tr>
<tr>
<td>Trigeminal neuralgia</td>
<td>5 (5.4)</td>
</tr>
<tr>
<td>Diplopia</td>
<td>5 (5.4)</td>
</tr>
<tr>
<td>Facial spasm</td>
<td>3 (3.3)</td>
</tr>
<tr>
<td>Nausea</td>
<td>3 (3.3)</td>
</tr>
<tr>
<td>Seizure</td>
<td>3 (3.3)</td>
</tr>
<tr>
<td>Visual disturbance</td>
<td>3 (3.3)</td>
</tr>
</tbody>
</table>

*Each patient has some symptoms.

- Any focal neurological deficit, especially of cranial nerves V–VIII, should prompt a radiological investigation and raise suspicion for cholesterol granulomas.
Four patterns of clinical presentation can be evidenced:
1) retrocochlear symptoms by the involvement of the internal auditory meatus;
2) headaches, sometimes associated with a trigeminal or an abducens nerve palsy, because of the traction of the posterior or middle fossa dura;
3) serous otitis media by a compression of the eustachian tube;
4) incidental diagnosis in cases of nonaggressive lesions

Image study:
- A CT of a cholesterol granuloma is nonenhancing, well margined, and isodense with brain. Bone erosion is usually present.
- The MRI of a cholesterol granuloma is pathognomonic – there is highsignal intensity on both T1 and T2-weighted images without gadolinium enhancement

<table>
<thead>
<tr>
<th>Features</th>
<th>Cholesterol Granuloma</th>
<th>Cholesteatoma</th>
<th>Mucocele</th>
<th>Retained Mucus</th>
<th>Asymmetric Pneumatization</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT density</td>
<td>Isodense</td>
<td>Hypodense</td>
<td>Hypodense</td>
<td>Hypodense</td>
<td>Hypodense (normal septae)</td>
</tr>
<tr>
<td>Contrast CT</td>
<td>Rim enhancing (occasionally)</td>
<td>Non-enhancing</td>
<td>Non-enhancing</td>
<td>Non-enhancing</td>
<td>Non-enhancing</td>
</tr>
<tr>
<td>T1 MRI</td>
<td>Hyperintense</td>
<td>Hypointense</td>
<td>Hypointense</td>
<td>Hypointense</td>
<td>Hyperintense</td>
</tr>
<tr>
<td>Gadolinium</td>
<td>Non-enhancing</td>
<td>Non-enhancing</td>
<td>Rim enhancing Mass is non-enhancing</td>
<td>Non-enhancing</td>
<td>Non-enhancing</td>
</tr>
<tr>
<td>T2 MRI</td>
<td>Hyperintense</td>
<td>Hyperintense</td>
<td>Hyperintense</td>
<td>Hyperintense</td>
<td>Hyperintense</td>
</tr>
<tr>
<td>Borders of lesion</td>
<td>Smooth</td>
<td>Scalloped</td>
<td>Smooth</td>
<td>Smooth</td>
<td>Smooth or scalloped</td>
</tr>
</tbody>
</table>

CT                           T1                       T2
**Differential diagnosis**

- An expansile lesion of the petrous apex: (i) schwannomas; (ii) meningiomas; (iii) bone and cartilaginous tumors; (iv) cholesteatomas; (v) mucoceles; (vi) other granulomas; (vii) glomus tumors; (viii) carotid aneurysms; (ix) lymphomas; (x) petrositis; and (xi) metastatic tumors.

<table>
<thead>
<tr>
<th>Cholesterol granuloma</th>
<th>Cholesteatoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>Frequent</td>
</tr>
<tr>
<td><strong>Uncommon</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Preferred location</strong></td>
<td><strong>Middle ear</strong></td>
</tr>
<tr>
<td>Petrous apex</td>
<td></td>
</tr>
<tr>
<td><strong>Composed of fibrous tissue in which cholesterol crystals may be seen, surrounded by numerous inflammatory cells and several giant cells of the foreign-body type</strong></td>
<td>Composed of a perimatrix (fibrous tissue) and matrix (stratified squamous epithelium) and always containing horny lamellae in the cystic lumen</td>
</tr>
<tr>
<td><strong>Morphologically, a reactive foreign-body granuloma</strong></td>
<td>Morphologically, an epidermoid cyst</td>
</tr>
<tr>
<td>A “stromal” lesion</td>
<td>Basically an “epithelial” lesion</td>
</tr>
<tr>
<td>Almost always represents a focal response to chronic middle ear infection</td>
<td>May not be connected with a chronic inflammatory process</td>
</tr>
<tr>
<td><strong>CT</strong></td>
<td></td>
</tr>
<tr>
<td>Margins: sharp, smooth</td>
<td>Margins: sharp, smooth</td>
</tr>
<tr>
<td>Density: isodense to brain</td>
<td>Density: isodense to cerebrospinal fluid</td>
</tr>
<tr>
<td>Enhancement: no</td>
<td>Enhancement: no</td>
</tr>
<tr>
<td><strong>MRI</strong></td>
<td></td>
</tr>
<tr>
<td>T1-weighted signal intensity: high</td>
<td>T1-weighted signal intensity: low</td>
</tr>
<tr>
<td>T2-weighted signal intensity: high</td>
<td>T2-weighted signal intensity: high</td>
</tr>
<tr>
<td>Areas of signal void: present</td>
<td>Areas of signal void: absent</td>
</tr>
<tr>
<td>May be associated with adjacent erosion of ossicles and bone</td>
<td>Association with erosion or displacement of the ossicles</td>
</tr>
<tr>
<td>Association with other diseases</td>
<td></td>
</tr>
<tr>
<td>Middle ear adenomatous tumors, endolymphatic sac (Heffner's) tumors, tympanosclerosis</td>
<td>Tympanosclerosis, atelectasis of the ear</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Complete surgical excision</td>
</tr>
<tr>
<td>Drainage and aeration</td>
<td></td>
</tr>
</tbody>
</table>
**Treatment:**

- Small cholesterol granulomas without involvement of the adjacent critical structures usually cause minor symptoms or are asymptomatic. → regular follow-up

- An aggressive cholesterol granuloma requires a surgical procedure to drain the cyst and reestablish an adequate aeration of the evacuated cavity.

- “Aggressiveness in Cholesterol Granuloma of the Temporal Bone May Be Determined by the Vigor of Its Blood Source” eg. sigmoid sinus, carotid artery, a large dural vein, or a rich deposit of vascular marrow in the mastoid tip.

**Surgical approaches:**

1. Transmastoidal-translabyrinthine
2. Transmastoidal infralabyrinthine-subcochlear
3. Transtemporal
4. Suboccipital
5. Transsphenoidal

- Depends first on the status of the patient’s hearing.
- If no serviceable hearing is present, a translabyrinthine approach provides an excellent exposure.
- In case of a giant cholesterol granuloma coming in contact with large areas of middle or posterior fossa dura, a transotic approach with fat obliteration is indicated.
- If the hearing is to be preserved, the infralabyrinthine and the infracochlear approaches are the two main noninvasive routes.

The infralabyrinthine and the infracochlear approaches are usually possible in most...
cases of cholesterol granulomas.

- The surgical treatment is more challenging when transpetrous approaches are unavailable. In such uncommon cases, transsphenoidal and middle cranial fossa approaches are the alternatives.

- The transsphenoidal approach can be used for cysts that abut or prolapse into the sphenoid sinus.

- The middle cranial fossa approach has an indication in uncommon, large cholesterol granulomas that extend into the middle fossa. A complete excision of the cyst is preferred in such cases.

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**Follow-up**

- Based on clinical examination, including audiometric and vestibular evaluation and imaging.
- After surgical drainage, a CT scan can reveal air within the petrous apex, indicating that proper aeration of the cyst has been achieved.
- The cavity is sometimes refilled with serous fluid or scar tissue, which a CT scan cannot distinguish from recurrent cholesterol granuloma.
On MRI scans, the decrease in the signal intensity on T1-weighed images and the reduced size of the lesion confirm its successful evacuation. Moreover, techniques using fat saturation allow postoperative follow-up for cavities filled with fat. MRI is therefore the technique of choice for the follow-up evaluation of cholesterol granuloma after surgical treatment.

**Conclusion**

- Cholesterol granulomas of the petrous apex are relatively rare inflammatory lesions characterized by a granulomatous reaction to the breakdown of blood products.
- Symptoms include a variety of neurological abnormalities, classically involving cranial nerves V–VIII.
- Workup of patients includes CT and MRI imaging and will show pathognomonic hyperintense signals on T1 and T2-weighted MRI with no gadolinium enhancement.
- Nongrowing asymptomatic lesions require no treatment, but should be monitored routinely.
- Symptomatic or growing lesions require surgery to resect and drain the lesion.
- Long-term follow up of postoperative patients is advised.
References
3 Murugasu E, Yong TT, Yoon CP. Invasive middle ear cholesterol granuloma involving the basal turn of the cochlea with profound sensorineural hearing loss. Otol Neurotol 2004; 25:231–235.
15 Thorne MC, Gebarski SS, Telian SA. Rapid expansion in a previously indolent