Surgical outcomes after endoscopic management of cholesterol granulomas of the petrous apex: a systematic review

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Object. Endoscopic endonasal treatment of petrous apex cholesterol granulomas allows for a natural drainage pathway into the nasopharynx. Because of the limited number of case series in the literature, there is limited evidence of recurrence rates and outcomes following endoscopic endonasal management. The purpose of this study was to determine the surgical outcomes of endoscopic endonasal approaches in the treatment of cholesterol granulomas of the petrous apex.

Methods. A systematic literature review was performed using PubMed for articles published from January 1980 to April 2014 to identify all studies reporting outcomes for endoscopic endonasal surgical management of cholesterol granulomas of the petrous apex. Operative approach, use of a stent, symptom outcome, restenosis, cyst recurrence, reoperation, and complications were extracted from included studies.

Results. A total of 53 patient cases were included from 22 relevant studies. The mean age was 41 years, and 26 patients (49%) were female. Stents were used in 45.1% of cases. Symptom resolution or improvement was seen in 98.6% of cases at follow-up (mean follow-up 20 months). Complications were reported in 13.2% of cases, with the most common complication being epistaxis. Restenosis on follow-up office endoscopic examination occurred in 9 of 45 cases (20.0%). Only 4 of these restenosis cases resulted in symptomatic cyst recurrence, resulting in an overall recurrence rate of 7.5%. The mean time from surgery to cyst recurrence was 13.5 months. The rate of symptomatic cyst recurrence was 10.7% in cases without the use of a stent compared with 4.3% in cases with stent placement ($p = 0.6$).

Conclusions. Based on current literature, endoscopic endonasal approaches result in a high rate of symptom improvement or resolution. Complication rates are lower than prior case series that have utilized open approaches. Asymptomatic restenosis can be managed conservatively, since it is associated with symptomatic cyst recurrence less than half of the time. This study revealed a nonsignificant trend toward a decrease in symptomatic cyst recurrence when a stent was used, but further work is needed to clarify its impact.
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KEY WORDS • cholesterol granuloma • petrous apex • petrous bone •
endoscopic • endonasal

CHOLESTEROL granulomas are uncommon cystic lesions that can present anywhere in the body, including the petrous apex. Although the exact etiology is unclear, they are thought to form when the air cells of the petrous apex are obstructed, thereby creating a vacuum into which blood is drawn and trapped.^{1,11,16,27} Another theory has more recently been proposed, which contends that exuberant pneumatization of the temporal bone leads to exposure of bone marrow-filled spaces in the petrous apex.²⁰ This leads to a propensity for hemorrhage, and as hemorrhage and clotting occur, the petrous apex outflow tract is obstructed.²⁰ Regardless of the incit-

ing event, the end result is the same; hemoglobin degradation products accumulate, cholesterol crystals form, and a granulomatous inflammatory reaction ensues.^{16,20}

While cholesterol granulomas are benign lesions, their location in the petrous apex can produce local mass effect resulting in headaches, hearing loss, diplopia, and vertigo. A variety of treatment approaches have been described to decompress the mass effect caused by the lesion and establish a conduit for drainage of the air cells. Transcranial approaches include the middle cranial fossa, transcanal infracochlear, infralabyrinthine, transotic, and suboccipital approaches.³ More recently, endoscopic endonasal approaches have been used because the surgical approach itself reestablishes a natural drainage pathway into the nasopharynx with the potential benefits of faster

Abbreviations used in this paper: ICA = internal carotid artery; OCEBM = Oxford Centre for Evidence Based Medicine.

recovery time and ease of office-based endoscopic follow-up.²⁹

Because of the limited number of case series in the literature, there is limited evidence of recurrence rates following treatment. The purpose of this study was to systematically review the outcomes of endoscopic treatment of cholesterol granulomas of the petrous apex.

Methods

A PubMed search was performed using the term “cholesterol granuloma,” which returned 722 results (Fig. 1—PRISMA flow diagram²⁵). Resulting titles and abstracts were screened for relevant articles, resulting in 102 articles. Articles were included if they presented surgical outcomes related to endoscopic treatment of petrous apex cholesterol granulomas. Technical notes not presenting surgical outcome and radiographic studies were excluded. Cholesterol granulomas not primarily involving the petrous apex were excluded. Additional exclusion criteria included non-English-language articles; studies prior to 1980; and animal, cadaveric, and in vitro studies. There were no restrictions on publication status. Full text was assessed for eligibility criteria in the resulting 102 articles. For clinical studies using duplicate data, only the study with the most recent results were included. References of full-text articles were searched for any additional

references not identified in the original search. The search period ended April 1, 2014.

Assessment of full-text articles resulted in 22 articles that met eligibility criteria and were included in the final systematic review. Data extraction from the 22 articles was independently conducted by 2 reviewers (D.F.E. and V.R.K.), and results were consistent. Strength of evidence of the included articles were assessed and assigned a score using the Oxford Centre for Evidence Based Medicine (OCEBM) Level of Evidence 2 classification system.¹⁸ Because none of the included studies were case-control or cohort studies, we could not apply the Newcastle-Ottawa Scale for nonrandomized studies.⁴⁰

The association of use of a stent and recurrence of the cholesterol granuloma was evaluated using a 2-sided Fisher's exact test. A p value < 0.05 was considered significant.

Results

The systematic review resulted in a total of 53 cases of endoscopic endonasal surgery for the treatment of petrous apex cholesterol granulomas (Table 1). There were 9 case series^{8,10,13,17,19,29,31,33,38} and 13 case reports.^{2,6,7,12,21,23,24,28,30,32,34,36,39} Since the first reported case in 1994, publications on the endoscopic endonasal approach to cholesterol granulomas of the petrous apex have in-

Fig. 1. Study selection process.

TABLE 1: Reported cases of petrous apex cholesterol granulomas managed endoscopically*

Authors & Year	No. of Cases	Surgical Approach	Stenting	Outcome	Cyst Recurrence	Restenosis	Additional Procedures	Mean Follow-Up in Mos (range)	Complications
Griffith & Terrell, 1996	2	EETS/EETC	no	Sx resolution (2/2, 100%)	no	2/2 (100%)	endoscopic reopening (1/2)	15 (12–18)	intermittent epistaxis on Day 6, resolved w/ anterior nasal packing (n = 1)
Georgalas et al., 2008	4	EETS/EETC	no	Sx resolution (4/4, 100%)	no	2/4 (50%)	none	55 (4–120)	none
Edkins et al., 2010	2	EETS/EETC	yes (2/2)	—	no	no	none	—	none
Jaberoo et al., 2010	2	EETS/EETC (1/2), EETP (1/2)	no	Sx resolution (2/2, 100%)	no	no	none	21 (18–24)	none
Prabhu et al., 2010	2	EETS/TC	—	Sx resolution (2/2, 100%)	no	—	none	6 (only specified for 1 patient)	none
Paluzzi et al., 2012	17	EETS/EETC (4/17), EETC + ICA lateralization (5/17), EETC/infrapetrous (8/17)	yes; Silastic stent (11/17), isolated mini-flap (3/17)	Sx improvement (13/17, 76%), partial improvement (3/17, 18%), asymptomatic at start (1/17, 6%)	2/17 (12%) at 11 & 32 mos postop in pts w/o stents	2/17 (12%)	redrainage & stent placement (2/17), stent removal in office (9/17), stent removal under GA (2/17)	20 (3–67)	epistaxis requiring bilat internal maxillary artery embo (n = 1), eye dryness & chronic serous otitis media requiring tympanostomy (n = 1), transient CN VI palsy (n = 1)
Sade et al., 2012	3	EETS/EETC	yes (2/3)	Sx resolution (1/3, 33%), Sx improvement (2/3, 66%)	1/3 (33%) at 7 mos	2/3 (66%)	stent removal in office (2/3), widening of opening (1/3)	25 (10–36)	chronic sphenoid sinusitis (n = 1)
Emanuelli et al., 2013	4	EETC/infrapetrous	no	successful drainage (Sx resolution not specifically mentioned)	no	no	none	27 (12–50)	none
Tomazic et al., 2013	4	EETS/EETC	no	Sx resolution (4/4, 100%)	no	no	none	6	none
case reports	13	EETS/EETC (11/13), EETC + ICA lateralization (1/13), EETC/infrapetrous (1/13)	yes (5/13)†	Sx resolution (10/12, 83%), Sx improvement (1/12, 8%), no change (1/12, 8%), not specified (1/13, 8%)	1/11 (9%) at 4 mos; 2/13 not specified	1/7 (14%); 6/13 not specified	redrainage & Doyle splint placement, then removal (1/13), Berkowitz drain removal (1/13)	28 (3–48)	delayed epistaxis (n = 1); hemorrhage, pneumocephalus & CSF leak resulting in severe headache, nystagmus, diplopia, Horner's, unilat leg weakness (n = 1)

* bilat = bilateral; CN = cranial nerve; EETC = endoscopic endonasal transcranial; EETP = endoscopic endonasal transpharyngeal; EETS = endoscopic endonasal transsphenoidal; embo = embolization; GA = general anesthesia; ICA = internal carotid artery; pts = patients; Sx = symptom; — = not specified.

† Type of stents used in the 5 cases are as follows: 1 Doyle splint, 1 Berkowitz drain, 2 T-shaped, 1 silicone tube.

creased (Fig. 2). All included studies were case series or reports, and as such, all were Level 4 or 5 evidence based on the OCEBM classification system. Of the patients in these cases, 27 were male and 26 were female, with an age range of 13–78 years (mean 41 years, median 38 years). The follow-up duration ranged from 3 to 120 months (mean 20 months, median 11 months).

The petrous apex was most commonly approached via an endoscopic endonasal transsphenoidal transclival approach in 33 (62.3%) of 53 cases, which includes cases in which the lesion eroded through the clivus into the sphenoid sinus. Endoscopic endonasal transclival with lateralization of the internal carotid artery (ICA) and a combined transclival/intrapetrous approach were used in 6 (11.3%) and 13 (24.5%) of the remaining cases, respectively, with the least common approach being the endoscopic endonasal transpharyngeal approach. Of the 51 cases in which it was stated that stenting was performed, stents were placed in 23 (45.1%) and varied greatly across institutions and specific patient characteristics. Included in this group were 4 cases in which a vascularized nasoseptal mini-flap was used as a stent ($n = 3$) or in addition to a stent ($n = 1$) to prevent contraction of the fibrous cyst walls.²⁹

Clinical outcome, with regard to symptomatology, was reported in 45 cases. The majority of patients postoperatively reported symptom resolution (84.4%) or improvement (13.3%). Of the 45 cases in which the degree of patency of the outflow track on follow-up endoscopic examination was noted, restenosis was observed in 9 cases (20.0%). However, only 4 of these restenosis cases were associated with symptomatic cyst recurrence that required redrainage, resulting in an overall recurrence rate of 7.5%. When stratifying by stent use, there was a 10.7% recurrence rate without the use of stents and 4.3% when they were used, which was not a statistically significant difference ($p = 0.6$).

There were 7 patients (13.2%) with reported complications. These included epistaxis ($n = 3$), chronic otitis media requiring tympanostomy ($n = 1$), chronic sphenoid sinusitis ($n = 1$), and transient sixth nerve palsy ($n = 1$). For 1 case serious complications were reported, with significant hemorrhage from the clival venous plexus requiring transfusion, a CSF leak, and tension pneumocephalus anterior to the frontal lobes, resulting in severe headache,

nystagmus, diplopia, and unilateral leg weakness.³⁰ This patient was treated conservatively with 100% oxygen and bed rest in the supine position until the pneumocephalus and associated symptoms gradually resolved.

Discussion

Fucci et al. first reported the use of the endoscopic endonasal approach to treat a cholesterol granuloma of the petrous apex in 1994.¹² Since then, endoscopic management has become increasingly used to treat these lesions. Because these lesions are relatively uncommon, evidence of outcomes after treatment with endoscopic approaches has been limited. The largest case series to date was of 17 patients reported by Paluzzi et al.²⁹ In this study, we reviewed the collective evidence from 53 cases of endoscopic endonasal management of petrous apex cholesterol granulomas. The outcomes tallied from the 13 case reports were similar to those in the 9 case series identified; therefore, we included the case reports and felt they did not unfairly bias the results. Meaningful statistical evaluation for publication bias (e.g., funnel plot) was not feasible because of the limited number of series and small sample size per series. However, the possibility of publication bias, in regard to success rates and complications, remains a significant limitation of this study.

Irrespective of the approach used to drain the cholesterol granuloma, the commonly accepted definition of successful treatment is the absence of continuous growth in combination with an improvement in symptoms. In this study, we found that nearly all patients had at least some degree of symptom improvement and were thus successfully treated by an endoscopic approach. Reported success rates with open surgical approaches have been similar, with the largest published series reporting an 82% improvement of symptoms,³ but most smaller series reporting 90%–100% improvement.^{4,5,9,26}

Because of the concern for recurrences, the use of stents has been proposed, although their true benefit has not been well established in the literature. Stenting remains at the discretion of the surgeon and can be based on multiple factors, including the size of the cyst opening, loss of mucosa, and proximity to the ICA.³³ In this study, we found that approximately 45% of patients had stents placed. Those patients largely did well, with only 1 (4.3%) of 23 developing a symptomatic cyst recurrence, compared with 10.7% in the nonstented group. While this may reflect a trend toward superiority of stent use in preventing recurrence, this difference was not statistically significant. In addition, there is likely significant selection and institutional bias in determining which patients received stents. One might imagine that cysts that have a narrow corridor into the cyst might be more likely to have a stent placed, whereas cysts with significant extension into the sphenoid sinus may not require a stent after wide marsupialization of the cyst. However, one might expect the cholesterol granulomas with a narrow opening to have a higher recurrence rate regardless of stent placement, which would underestimate the true benefit of stenting. As additional cases of cholesterol granuloma of the petrous apex are performed endoscopically, the true

Fig. 2. Mean number of publications per year on the endoscopic endonasal management of petrous apex cholesterol granulomas.

TABLE 2: Reported cases of petrous apex cholesterol granulomas treated by an open approach*

Authors & Year	No. of Cases	Surgical Approach	Stenting	Outcome	Cyst Recurrence	Mean FU (range)	Complications
Gherini et al., 1985	9	infralabyrinthine, middle cranial fossa, translabyrinthine	9/9 silicone	8/9 (89%) Sx improvement	1/9 (11%)	—	hearing loss (83%)
Graham et al., 1985	4	transmastoid, middle cranial fossa	3/4 silicone	—	—	—	hearing loss (25%)
Thedinger et al., 1989	10	infralabyrinthine, transotic, trans-sphenoidal, suboccipital	10/10 silicone	—	6/10 (60%)	47	—
Goldsfky et al., 1991	9	infralabyrinthine, translabyrinthine, suboccipital	—	—	1/9 (11%)	—	—
Brodkey et al., 1996	10	infralabyrinthine, infracochlear, translabyrinthine	—	9/10 (90%) Sx improvement	—	29.5	hearing loss, CSF leak/meningitis, labyrinth sacrifice (60%)
Eisenberg et al., 1997	10	middle fossa, petrosal	—	10/10 (100%) Sx improvement	0	46	CSF leak, seizures 2 yrs postop (20%)
Cristante & Puchner, 2000	8	middle fossa	—	8/8 (100%) Sx improvement	0	60	subgaleal hematoma, transient facial palsy (25%)
Brackmann & Toh, 2002	34	infracochlear, infralabyrinthine, middle fossa, translabyrinthine, transotic	—	28/34 (82%) Sx improvement	5/34 (15%)	62.9	hearing loss (3%), minor complications (8.8%)
Mosnier et al., 2002	8	infracochlear, infralabyrinthine, transotic	—	8/8 (100%) Sx improvement	0	18	0
Sanna et al., 2009	15	infralabyrinthine, transotic, infra-temporal	—	—	1/15 (7%)	56.7 (15–112)	53%; ICA bleeding (n = 1), CN VII palsy (n = 4), hearing loss (n = 1), CSF leak (n = 2)
Kusumi et al., 2013	17	middle fossa, infralabyrinthine	2/17 silicone	—	1/17 (6%)	47.6 (2–132)	ICA occlusion & death (n = 1), epidural infection (n = 1)

* FU = follow-up.

role of stenting will be more clearly determined. One interesting alternative to stenting is the use of a vascularized pedicle nasoseptal mucoperiosteum “mini-flap,” reported by Paluzzi et al.²⁹ This not only serves the purpose of creating a mechanical barrier but may also promote the formation of mucosal lining along the cyst walls.

It is interesting to note the absence of a definitive association between restenosis of the drainage pathway and symptomatic cyst recurrence. While 20% of cases for which data were available noted restenosis on endoscopic follow-up examination, less than half of these were symptomatic cyst recurrences that required repeat operation. This suggests that a conservative approach is warranted when restenosis is observed on follow-up examination, with reoperation reserved only for cases in which significant symptoms recur.

When comparing overall recurrence rates and complications in the endoscopic cases to those found in previously published series of open approaches to cholesterol granulomas of the petrous apex (Table 2), this study confirms the safety and efficacy of endoscopic management. A literature review revealed 134 reported cases of petrous apex cholesterol granulomas treated by open approaches since 1980.^{3–5,9,14–16,22,26,35,37} Symptom improvement after open surgery appears to be similar to that obtained via endoscopic approaches. Six studies (79 patients) reported symptom outcome after open surgery for petrous apex cholesterol granulomas.^{3–5,9,14,26} Symptom improvement occurred in 71 patients (90%). Nine studies (totaling 120 patients) reported the rate of cyst recurrence, which occurred in 15 patients (or 12.5% overall). The overall recurrence rate for endoscopic approaches found in this study was 7.5%, which compares favorably with reported rates. Importantly, previous studies of open approaches report higher complication rates. Nine studies (115 patients) reported complication rates between 0% and 60%, with a mean of 24.3%.^{3–5,9,14,16,22,26,35} In the present study, we found a lower rate of complications (13.2%) with the endoscopic approaches. Additionally, the difference in the severity of reported complications is important to note. In open approaches, the reported complications have largely been hearing loss and CSF leak, whereas the most common complication in endoscopic cases was epistaxis, although 1 case did report CSF leak as well. While endoscopic endonasal approaches have demonstrated good safety and efficacy, not all petrous apex granulomas are surgically amenable to endonasal approaches. Preoperative imaging must be carefully studied to determine the approximate surgical corridor between the medial wall of the cyst and the lateral wall of the paraclival ICA. Lesions that are completely hidden behind the ICA may be more amenable to an open approach.

Conclusions

Based on current literature, endoscopic endonasal approaches provide a safe and effective approach to treatment of cholesterol granulomas of the petrous apex, with very high rates of symptom improvement or resolution. Complication rates are lower than those reported for prior case series utilizing open approaches. Restenosis on

follow-up endoscopic examination occurs in about 20% of cases, but fewer than half of these cases are associated with symptomatic cyst recurrence. Therefore, asymptomatic stenosis of the drainage track can be managed conservatively. This study revealed a nonsignificant trend toward a decrease in symptomatic cyst recurrence when a stent was used, but further work is needed to clarify its impact.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Kshetry. Acquisition of data: Eytan, Kshetry. Analysis and interpretation of data: Eytan, Kshetry. Drafting the article: Eytan, Kshetry. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Recinos. Statistical analysis: Eytan. Study supervision: Recinos.

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