



# Periorbital cholesterol granulomas/cysts – two clinical cases presentation

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## Abstract

Cholesterol granulomas and cysts represent uncommon pathological findings in the paranasal cavities; however, they have also been documented in other areas, including the orbit, the petrous part of the temporal bone, and the nasal septum, among others. Histologically, they are composed of granulation tissue and a significant quantity of cholesterol crystals. The etiology of the disease is primarily associated with microtraumas in the affected structures, which result in the rupture of small blood vessels. This phenomenon leads to the accumulation of formed elements and cholesterol in the affected regions, resulting in the formation of a foreign-body-type granuloma that gradually increases in size. The process is both expansive and destructive, characterized by gradual and painless development.

The primary objective of this study was to direct the attention of attending physicians to this rare but existing pathology. The following two clinical cases are presented: they pertain to patients with histologically confirmed cholesterol granuloma, which initially manifested with complaints related to an affected orbit. Patient 1 underwent endoscopic endonasal surgery, yet the disease persisted. Conversely, patient 2 underwent a combined approach, yielding excellent results.

Cholesterol granulomas are a rare pathological entity with a poorly understood etiology. The diagnosis is confirmed through pathological verification. Surgical intervention remains the most effective treatment for cholesterol granulomas in the paranasal cavity region. An accurate diagnosis and effective collaboration among different medical units—including the surgical team, imaging diagnostics, and pathology—are essential for comprehensive treatment.

## Keywords

cholesterol granuloma, cholesterol cyst, combined surgical approach

## Introduction

Cholesterol cysts are histological entities composed of granulation tissue and a large number of cholesterol crystals. These crystals trigger a foreign body-type giant cell reaction, resulting in an osteolytic lesion with an expansive

growth pattern. They are primarily found in the temporal bone but can also develop in the paranasal sinuses—most commonly in the maxillary and frontal sinuses. Additionally, there is evidence of cholesterol granulomas involving the nasal septum.<sup>[1]</sup> This condition predominantly affects middle-aged men.

The primary pathogenic factor contributing to their formation is impaired aeration and drainage of the affected pneumatized structures. Other contributing factors include traumatic injuries (including microtraumas), spontaneous bleeding due to coagulation abnormalities (such as the use of antiplatelet agents or anticoagulants and underlying coagulopathies), and other related conditions.<sup>[2]</sup>

According to the literature, the formation of cholesterol granulomas within the walls of cystic structures leads to their more aggressive expansion, often following an initial inflammatory reaction. It has also been suggested that perlecan—one of the key components of heparan sulfate proteoglycan and low-density lipoprotein (LDL)—plays a role in this process. Perlecan is localized in the cyst capsule of newly formed lesions while simultaneously stimulating their growth. LDL undergoes oxidation in the extracellular space and is subsequently phagocytosed by mast cells. This process disrupts mast cell integrity, leading to the release of free cholesterol into the extracellular space, where it crystallizes and triggers inflammation. As granulation tissue continues to grow, this cycle repeats itself, perpetuating the expansion of the lesion.<sup>[3]</sup>

The clinical presentation of cholesterol granulomas largely depends on their location. Symptoms may include orbital manifestations (the most common form of the pathology), headache, nasal obstruction, rhinorrhea, and epistaxis. In many cases, cyst growth can remain asymptomatic for a long time.<sup>[4]</sup>

Cholesterol granulomas are diagnosed using computed tomography (CT) and magnetic resonance imaging (MRI); however, due to their strong resemblance to other formations in these areas—such as polyps, mycetomas, dermoid cysts, and benign or malignant diseases of the lacrimal gland—definitive diagnosis requires histological examination of the excised material.

Treatment involves surgical removal of the granuloma from the affected anatomical area, followed by bone treatment if the localization permits. Surgical intervention can be performed either via an external approach or endoscopically. Regardless of the approach, recurrence may occur within 12–18 months postoperatively.<sup>[5]</sup>

To decompress the lesion and reduce intra-cystic pressure, preoperative fenestration is recommended in certain cases. This technique has been shown to be effective in reducing the size of various cystic lesions, including unicystic ameloblastoma and odontogenic keratocysts. Both fenestration and marsupialization are considered effective conservative surgical techniques.<sup>[6,7]</sup>

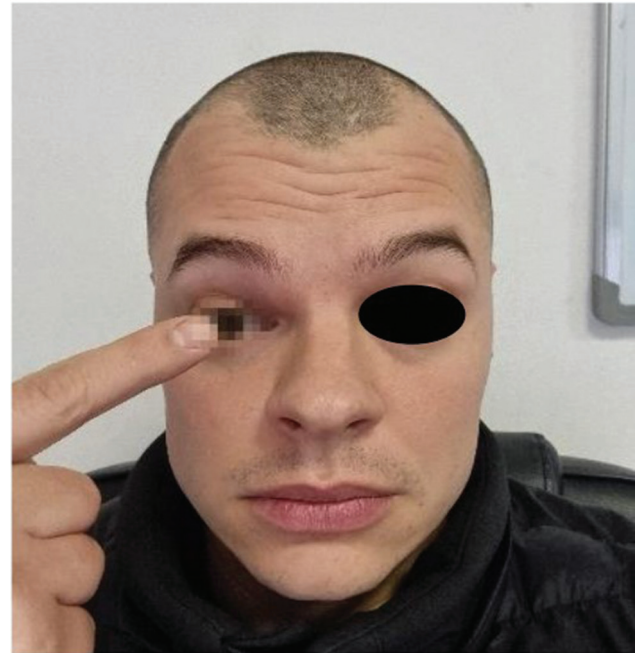
## Aim

The primary aim of this study was to draw the attention of attending physicians to this rare but existing pathology.

## Case report

### Case 1

A 33-year-old man presented with a longstanding swelling in the forehead area above the right eyebrow, accompanied by periodic nasal congestion. He reported no associated pain, history of traumatic injury to the area, or any systemic diseases (Fig. 1).



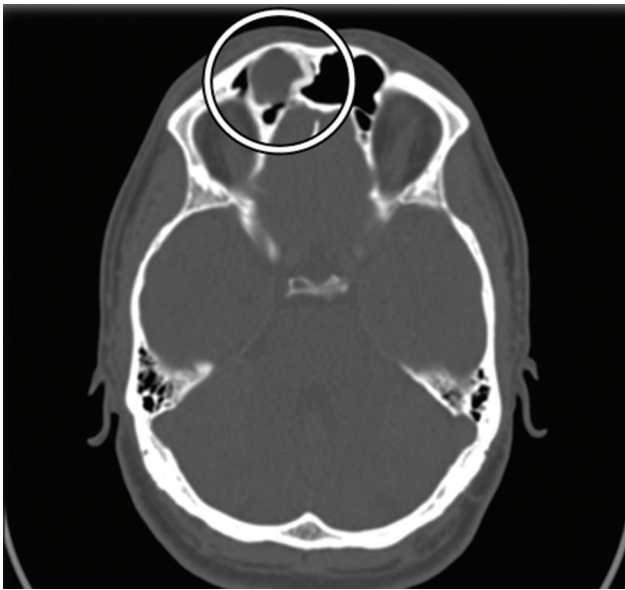
**Figure 1.** Pronounced facial asymmetry with swelling in the right periorbital region, painless on palpation with firm, elastic consistency.

Endoscopic examination of the nasal cavity revealed a deviated nasal septum with a bony spur and a convexity toward the right in the posterior third. The nasal mucosa appeared bluish and edematous.

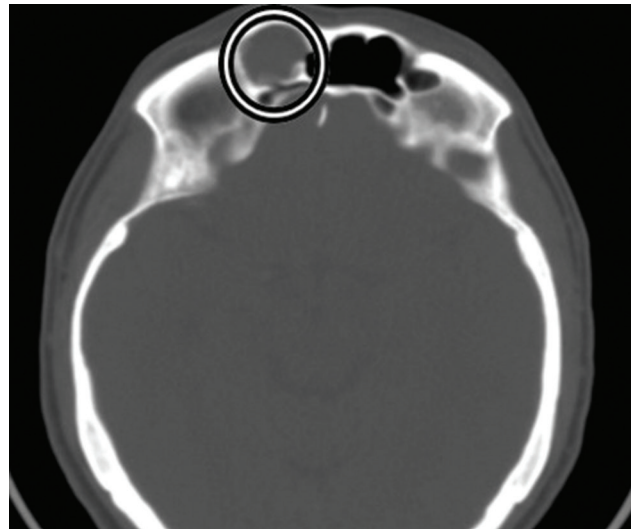
CT and MRI imaging studies revealed a mass in the right frontal sinus with features suggestive of a mucocele, polypoid mucosal hypertrophy, or a mucoretention cyst (Figs 2, 3).

Endonasal endoscopic sinus surgery (Draf IIB) with marsupialization of the suspected mucocele was performed. Intraoperatively, the formation contained atypical material with a type and consistency inconsistent with the initial working diagnosis. A tissue sample was collected for histological examination. Histological analysis revealed necrosis, cholesterol crystals, and areas of chronic inflammation with peripheral purulence. The postoperative period was uneventful, and the patient was discharged from the clinic four days after surgery.

A follow-up CT scan six months after surgery revealed a persistent mucocele in the right frontal sinus, with a density ranging from 25 to 50 HU (Hounsfield Units). The lesion pro-



**Figure 2.** Patient 1: initial CT (axial view).



**Figure 4.** Axial CT image confirming the persistence of the formation.



**Figure 3.** Patient 1: initial CT (coronal view).



**Figure 5.** Coronal CT image confirming the persistence of the formation.

lapsed into the medial orbital wall and the frontoethmoidal recess, measuring 2.4 cm (transverse), 2.4 cm (sagittal), and 2.2 cm (craniocaudal) (Figs 4-6).

Due to imaging findings indicating a relapse, an endoscopic revision was performed with a Draf III procedure (Fig. 7). Histological analysis of the collected material again revealed necrosis, cholesterol crystals, areas of chronic inflammation, and pus.

Despite the revision surgery, a few months later, a follow-up imaging study revealed the persistence of the pathological finding in the right frontal sinus.

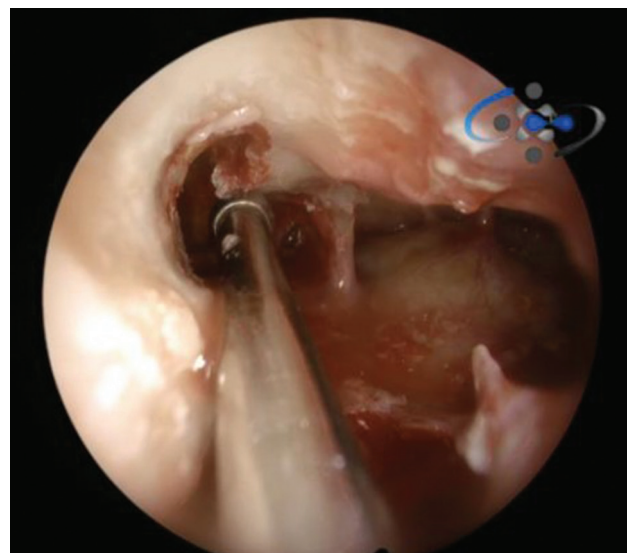
## Case 2

A 59-year-old patient presented with symptoms similar to the first clinical case, including a decreased sense of smell over several months, impaired nasal breathing, intermittent diplopia in the right eye, ptosis of the upper eyelid, facial asymmetry, and right-sided exophthalmos (Fig. 8).

From the outset, the differential diagnosis for this patient was broadened. Based on a review of the literature, a new pathological entity—cholesterol granuloma—was added to the initial working diagnosis of mucocele.



**Figure 6.** Sagittal CT image confirming the persistence of the formation.



**Figure 7.** Second surgery intraoperative endoscopic view.



**Figure 8.** Patient 2: preoperative images.

The physical examination of the nasal cavity did not reveal any significant pathology. CT imaging described a soft tissue formation with a density of 33 HU in the upper part of the right orbit. The lesion measured 32 mm and displaced the eye bulb ventrally. The orbital roof showed areas of discontinuous contour, and the lesion did not encapsulate the contrast medium (Figs 9-11).

A combined surgical approach was performed, utilizing both an endoscopic endonasal technique (Draf IIB frontal sinusotomy) and an external approach. Septal deformities were gradually corrected. An infundibulotomy was performed on the right side, followed by an ethmoidectomy, exposing the skull base and localizing the sphenoid sinus, which was subsequently expanded. A retrograde approach was used to remove the remaining ethmoid cells, reaching and probing the frontal recess. No tumor formation was encountered during the initial examination, and inflamed tissue was removed.

The surgery proceeded with an external latero-superior orbital approach – skin incision and layer-by-layer soft tissue

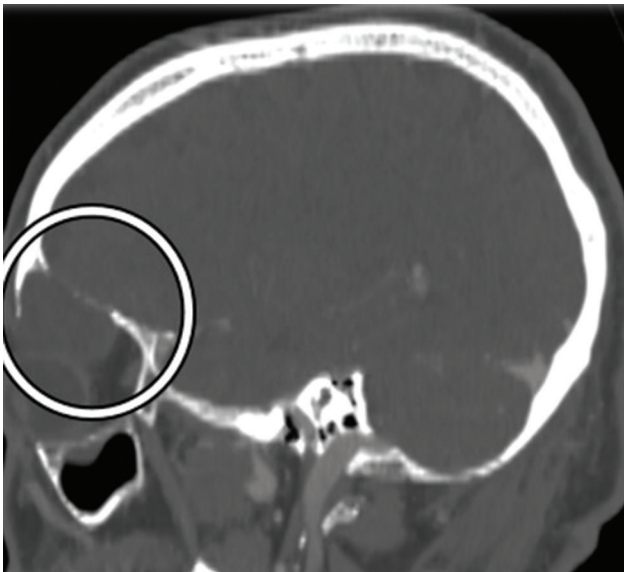
dissection. The cystic lesion was identified. A puncture and aspiration were performed, revealing an atypical “chocolate” content inconsistent with a mucocele. A radical excision of the lesion was carried out, as it had partially lysed the posterior wall of the frontal sinus (Figs 12-16). The affected area was treated with a diamond bur, followed by irrigation of the cavity with Braunol. Two hemostatic sponges were placed, along with a drain. Suturing and dressing of the operative wound.

Histological results—a cyst surrounded by fibrous tissue with chronic inflammation and the presence of cholesterol granulomas, which were also found within the cavity.

Follow-up CT imaging showed no evidence of residual formation (Figs 17, 18).

## Discussion

There are two main theories regarding the development of cholesterol granulomas: the obstruction-vacuum the-



**Figure 9.** Patient 2: preoperative CT image (sagittal view) revealing a cystic tumor formation in the area of the right frontal sinus, causing lysis of its floor and extending into the periorbital space.



**Figure 11.** Patient 2: preoperative CT image (coronal view) revealing a cystic tumor formation in the area of the right frontal sinus, causing lysis of its floor and extending into the periorbital space.



**Figure 10.** Patient 2: preoperative CT image (axial view) revealing a cystic tumor formation in the area of the right frontal sinus, causing lysis of its floor and extending into the periorbital space.

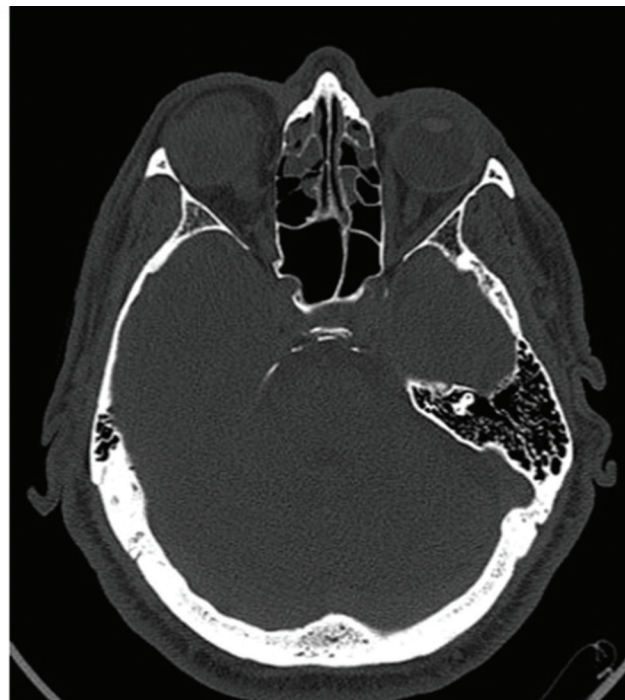
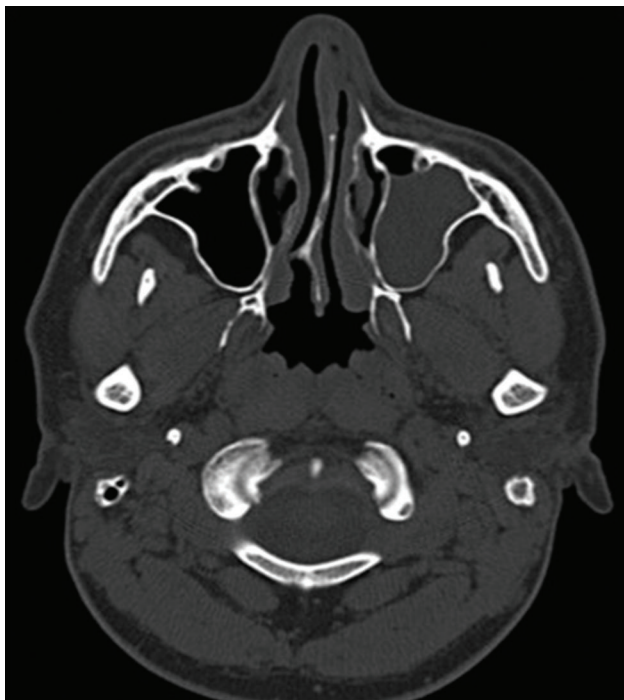


**Figure 12.** Patient 2: preoperative CT image (coronal view) indicating the reason for making the PST.

ory and the expansion theory. According to the obstruction-vacuum theory, mucosal edema leads to impaired aeration of pneumatized cells or structures, resulting in negative pressure within the enclosed space due to air reabsorption. The negative pressure causes extravasation of intravascular fluid and blood components into the free spaces. The erythrocyte destruction leads to the formation of hemosiderin, which contributes to cholesterol accumulation and the formation of cholesterol crystals. The presence

of these crystals triggers a foreign body-type inflammatory reaction, ultimately leading to the erosion of surrounding structures, including bones.<sup>[8]</sup>

According to the expansion theory, the pathophysiological process of cholesterol granuloma formation begins with the obstruction of air cells in the affected bone structures (similar to the obstruction-vacuum theory); this obstruction leads to blood stasis and disruption of the integrity of small blood vessels, resulting in the deposition of cholest-



**Figure 13.** Patient 2: preoperative CT image (axial view) indicating the reason for making the PST.



**Figure 14.** External approach to the cyst.

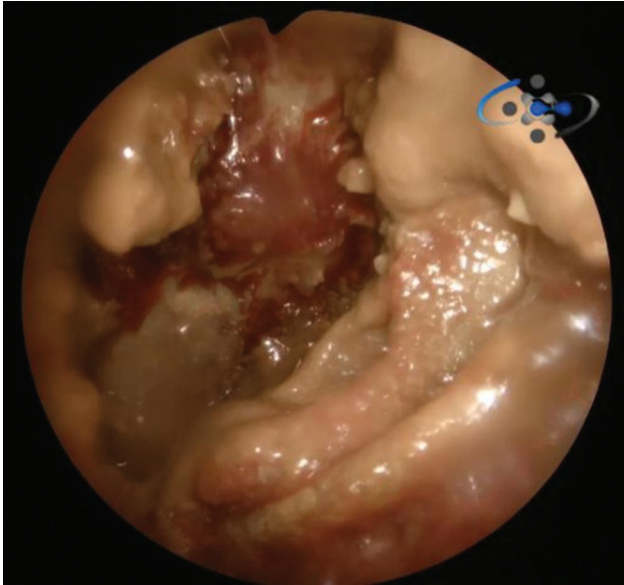
**Figure 15.** Puncture and aspiration of the cyst.

terol crystals, hemosiderin, and other blood components within the tissues. As a result of a foreign body reaction, a cholesterol cyst develops and grows destructively and extensively. This process leads to obstruction, impaired drainage, hemorrhage with hemolysis, and the release of cholesterol products and derivatives into the affected structures, ultimately resulting in cholesterol precipitation. Additionally, the newly formed vessels within the granulation tissue play a crucial role in the progression of the process. Their fragility and tendency to rupture contribute to a vicious cycle of recurrent hemorrhage, further cholesterol deposi-

tion, and continued granuloma growth.

Both the obstruction-vacuum and expansion theories are based on the premise that a certain volume of enclosed blood within a confined space undergoes degenerative processes. The waste products of this process, particularly hemosiderin, trigger the inflammatory factors, leading to the development of a macrophage-mediated foreign body-type granulation response.<sup>[5,9-11]</sup>

According to the hypothesis explaining the presence of bone marrow in cholesterol granulomas, their formation involves the erosion of bone marrow within the affected



**Figure 16.** Internal view of the cyst.

bone structures. This erosion leads to subacute hemorrhage, which then triggers an inflammatory reaction. As the cyst expands, it causes repeated hemorrhages from the bone marrow cavities, perpetuating a self-sustaining cycle of hemorrhage, inflammation, and granuloma growth.

Part of the pathophysiological mechanism of cyst formation involves increased pressure in the affected sinus due to obstruction. This elevated pressure can impair venous and lymphatic drainage, leading to blood vessel rupture and subsequent hemorrhage. In such cases, lymphatic outflow may be insufficient to clear lipid components from erythrocytes, causing their accumulation and the release of cholesterol. The cholesterol molecules then aggregate and form crystals, which grow slowly and contribute to com-

pressive-destructive changes in the surrounding structures. The clinical presentation varies depending on the affected anatomical region.<sup>[13]</sup>

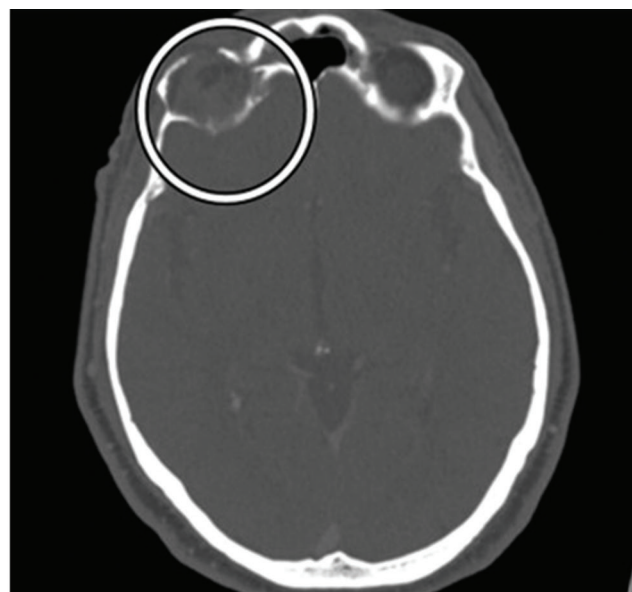
The diagnosis of the disease is established through detailed medical history, clinical examination, imaging studies, and histological verification of the lesion.

According to the literature, primary symptoms of cholesterol granuloma include headache, nasal obstruction, rhinorrhea, epistaxis, and orbital manifestations. In our two cases there was no epistaxis, but the other symptoms were present. The disease often has a prolonged asymptomatic phase (as it was observed in our cases too) and is frequently detected late. Physical examinations usually detect exophthalmos or a soft tissue mass in the orbital or nasal cavities.

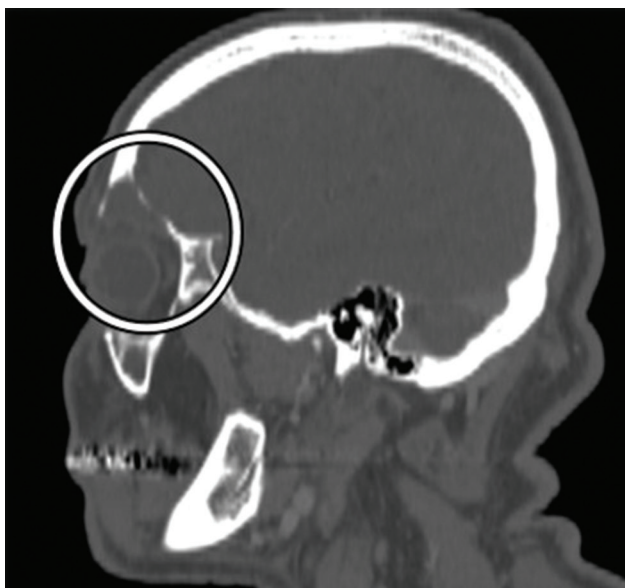
The most popular imaging study in such cases is computed tomography (CT). On it, cholesterol granulomas appear as iso-hypodense lesions, representing non-calcifying masses. Post-contrast imaging does not show contrast enhancement, a key feature that aids in differentiating them from orbital neoplasms.<sup>[12]</sup> In our cases CT was also used as a main diagnostic imaging test and provides all necessary data for tumor size, location, and surrounding tissue damages caused by the pathological process development.

Histological verification of cholesterol granulomas is based on the presence of three key components: granulation tissue, a fibrous capsule, and the hallmark diagnostic feature—cholesterol crystals. Since cholesterol crystals dissolve during tissue processing, hematoxylin-eosin staining reveals characteristic needle-like voids (cholesterol clefts) where the crystals were previously located. Histological pictures of our patients showed all typical features for confirmation of the “cholesterol cyst” diagnosis (**Fig. 19**).

The differential diagnosis of this disease includes mucocele, tumors of the nasal cavities and sinuses, polyps, mycetomas, dermoid cysts, and lacrimal gland tumors, etc.<sup>[13]</sup>



**Figure 17.** Patient 2: postoperative CT (axial view).



**Figure 18.** Patient 2: postoperative CT (sagittal view).

The primary treatment method is surgery (radical removal of the cholesterol granuloma or cyst, along with the cessation of drainage and ventilation in the affected area). Curettage or excision of the surrounding tissue aids in complete removal and helps prevent recurrence. Marsupialization of the cyst using a microdebrider has also been shown to be an effective preventive technique.<sup>[9]</sup>

Although various surgical approaches can be used depending on the lesion's location<sup>[11,14-16]</sup>, the endoscopic endonasal approach is preferred in many cases, as it allows for precise surgical intervention while minimizing invasiveness. However, using that technique, recurrence may still occur in some patients.<sup>[17]</sup> The open approach, in combination with the endoscopic surgery, has also demonstrated excellent outcomes. Both methods offer advantages for the radical treatment of this pathology.<sup>[18-20]</sup> In case 1, we used an endoscopic approach and experienced a recurrence of the pathological process; in case 2, we used a combined approach, and no recurrence was detected during the follow-up period—our experience confirmed the international opinion that a combined approach gives better results.

## Conclusion

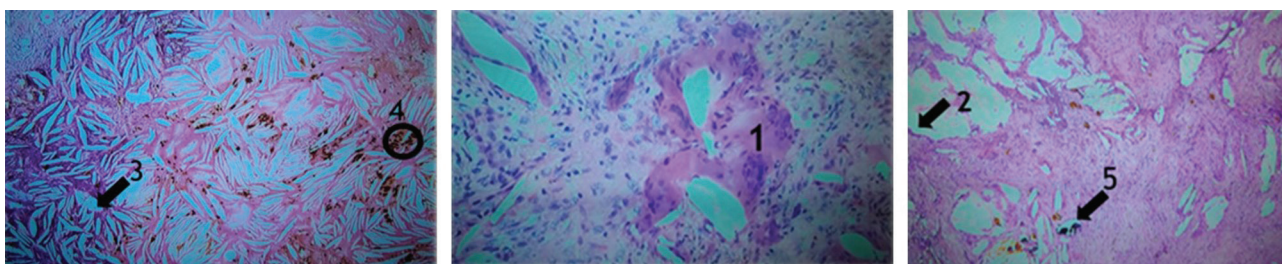
Cholesterol granulomas are a rare pathological entity—1–3% of all tumor cases—affecting pneumatized structures, primarily the temporal bone and paranasal sinuses. They induce an expansile and destructive foreign body-type reaction. The cholesterol cyst formation is attributed to the incomplete clearance of cholesterol crystals and cellular debris due to impaired extracellular drainage. Their expansive-destructive growth pattern contributes to compression symptoms affecting surrounding tissues. Accurate diagnosis and interdisciplinary collaboration between imaging specialists, pathologists, and the surgical team are crucial for effective disease management. The main treatment is surgical lesion removal, radical if possible to minimize the risk of recurrence. According to the literature, the best outcomes are achieved using a combined surgical approach, integrating endoscopic endonasal surgery with an open surgical technique in the orbital region when necessary. When evaluating cystic formations in suspicious areas, cholesterol cysts should be included in the differential diagnosis, as proper identification is essential for determining the most effective treatment.

## Conflict of interest

The authors have declared that no competing interests exist.

## Ethical statements

- The authors declared that no clinical trials were used in the present study.
- The authors declared that no experiments on humans or human tissues were performed for the present study.
- The authors declared that all patients gave signed informed consent for the surgical interventions as well as for the use of the results.
- The authors declared that no experiments on animals were performed for the present study.
- The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.



**Figure 19.** Histological verification of cholesterol granulomas; 1. Granulation tissue; 2. Fibrous capsule; 3. Cholesterol crystals (clefs); 4. Altered roof pigments; 5. Calcifications.

## Use of AI

No AI was used for the preparation of the manuscript.

## Funding

No funding was reported.

## Author contributions

Conceptualization: KD and SM; methodology: GG; software: ED; validation: SM and KD; formal analysis: KG; investigation: SM; resources: GG; data curation: AT and KD; writing—original draft preparation: KD; writing—review and editing: SM and AT; visualization: SM; supervision: AT; project administration: ED; funding acquisition – no funding. All authors have read and agreed to the published version of the manuscript.

## Data availability

Data available on request from the authors.

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