Case Report

A Stepwise Diagnostic Approach to Treacher Collins Syndrome Presenting as Refractory Otitis Media with Effusion: A Case Report

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ABSTRACT

Introduction: Treacher Collins syndrome (TCS) is a rare genetic disorder of craniofacial development. Otologic manifestations, including refractory otitis media secondary to Eustachian tube (ET) dysfunction, are hallmark features of TCS. Here, we present a case illustrating the diagnostic challenges in TCS and the paramount importance of a meticulous clinical evaluation. We also highlight the profound life decisions patients with TCS may face.

Case presentation: A 32-year-old female presented with recurrent right-sided otitis media with effusion (OME), which was persistent despite previous tympanocentesis. Our evaluation extended beyond the tympanic membrane to include a comprehensive physical examination and nasoendoscopy. Physical examination revealed classic TCS stigmata, including bilateral down-slanting palpebral fissures, malar hypoplasia, micrognathia, and low-set ears with a pre-auricular tag. She reported a family history and prior *TCOF1* variant diagnosis; variant details and the report were unavailable for review. She also revealed that to prevent genetic transmission, she had chosen to remain unmarried and childless. Nasoendoscopy unveiled a structurally abnormal and inflamed nasopharynx with purulent discharge pooling in a lateral recess. The culture yielded *Staphylococcus aureus*. Management evolved from empirical therapy with cefaclor and corticosteroids to targeted clarithromycin therapy based on culture susceptibilities.

Results: Treatment resulted in complete resolution with no adverse events; no recurrence occurred by the 12-month telephone follow-up.

Discussion: This case underscores that refractory OME may be the sentinel sign of an underlying syndromic diagnosis. The personal decision of the patient regarding reproduction reveals the significant psychosocial and ethical dimensions of managing a heritable condition.

Conclusion: This case highlights the need to integrate genetic counseling and otologic care to provide holistic, patient-centered support.

KEYWORDS

Treacher Collins syndrome, *TCOF1* gene, refractory otitis media, Eustachian tube dysfunction, genetic counseling, bioethics

1 Introduction

Treacher Collins syndrome (TCS; OMIM #154500), an autosomal dominant disorder of craniofacial development stemming from mutations in the *TCOF1*, *POLR1C*, or *POLR1D* genes, has an incidence of approximately 1 in 50,000 live births[1]. The characteristic phenotype, which arises from first and second branchial arch anomalies, includes bilateral symmetrical hypoplasia of the zygomatic bones and mandible, down-slanting palpebral fissures, and external ear abnormalities[2,3]. Otologic sequelae are nearly universal and often debilitating. Conductive hearing loss is common due to malformations of the middle ear ossicles and external auditory canal.

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The skeletal deficiencies narrow the nasopharynx and distort the Eustachian tube (ET), predisposing patients to recurrent and refractory otitis media with effusion (OME)[4,5]. ET dysfunction represents a persistent challenge in management, distinguishing it from isolated OME in the general population.

Here, we report the case of a genetically confirmed young adult with TCS whose primary presentation was refractory OME. This case illustrates the anatomic basis of ET dysfunction in TCS and demonstrates the need for a systematic clinical approach combined with nuanced communication to achieve a syndromic diagnosis. Furthermore, this case reveals the profound life-altering decisions that patients may make as a result of their genetic identity.

2 Case Presentation

A 32-year-old Han Chinese woman, a biotechnology researcher, presented to our otology clinic with a two-month history of recurrent right-sided aural fullness, tinnitus, and hearing loss. She had been diagnosed with right-sided OME at another institution and underwent tympanocentesis, which provided symptomatic relief for only one week before symptom recurrence. On October 10, 2024, the results of Epstein-Barr virus (EBV) viral capsid antigen IgA (VCA-IgA) and EBV early antigen IgA (EA-IgA) performed at another hospital were 0.88 cut-off index (COI) and 0.13 COI (reference values range, 0–1).

During our initial consultation, we conducted a detailed and thorough physical examination. Beyond the otologic complaint, we observed distinctive craniofacial features: bilateral down-slanting palpebral fissures, hypoplastic zygomatic arches (giving a prominent forehead appearance), significant mandibular hypoplasia with retrusion, and low-set ears with characteristic crumpled helices. A small, benign skin tag was noted between the left tragus and the oral commissure (Figure 1). Otoscopy confirmed a retracted, amber-colored right tympanic membrane with an air-fluid level. Pure-tone audiometry showed a mild right-sided conductive hearing loss. Air conduction thresholds at 500 Hz, 1000 Hz, and 2000 Hz were 40, 40, and 35 dB HL; bone conduction thresholds were 20, 15, and 20 dB HL, with an average air-bone gap of 20 dB. The left ear was normal. Speech discrimination scores were not available.

Given the recurrent OME and the suggestive physical stigmata, flexible nasoendoscopy was performed. This procedure revealed a severely narrowed nasopharynx with markedly swollen and erythematous mucosa covered in thick, purulent secretions. Nasoendoscopy also revealed a deep lateral wall recess that was actively draining pus, obscuring the view of the ipsilateral ET orifice (Figure 2a). A sample of the pus was collected for culture and sensitivity testing. A temporal bone computed tomography (CT) scan showed significant thickening of the nasopharyngeal soft tissues and dysplastic changes in the temporal bones (Figure 3), corroborating the

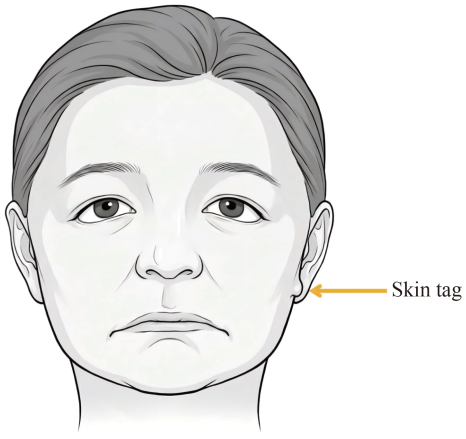


Fig. 1 Clinical findings. Schematic illustration of the patient's facial features, which include down-slanting palpebral fissures, malar hypoplasia, micrognathia, low-set ears, and a pre-auricular skin tag (arrow).

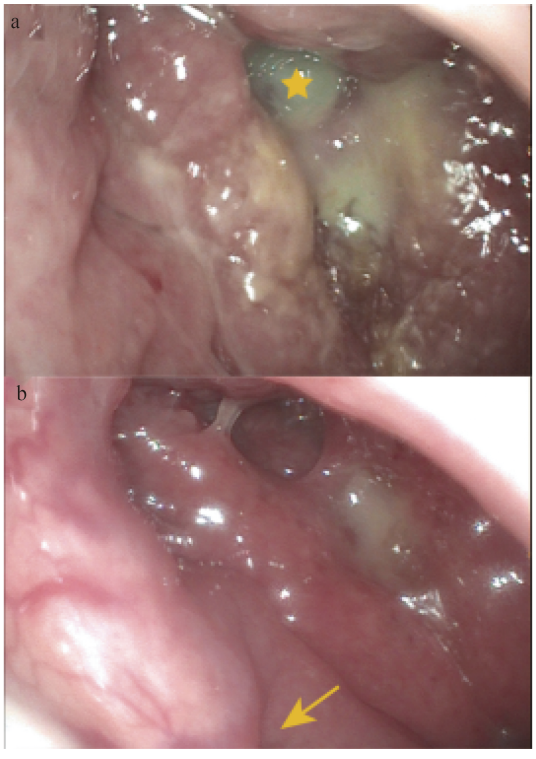


Fig. 2 Endoscopic findings. (a) Initial nasoendoscopic view showing severe inflammation, purulent discharge (star), and anatomical narrowing of the nasopharynx. The ET orifice is not visible due to obstruction. (b) Follow-up nasoendoscopic view after targeted therapy showing resolution of inflammation, a patent nasopharyngeal lumen, and a now-visible ET orifice (arrow).

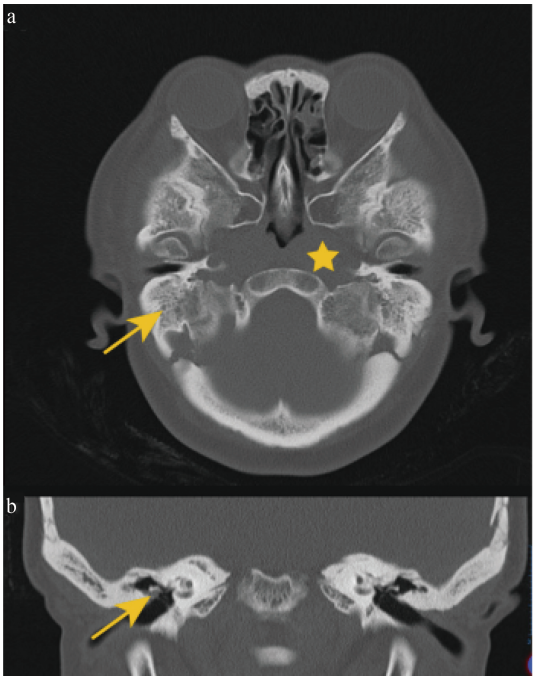


Fig. 3 Axial and coronal views of temporal bone CT scan. (a) Axial bone window view at the level of the nasopharynx, demonstrating significant thickening of the soft tissue (star), leading to nasopharyngeal stenosis. The ET orifices are obscured. Note the dysplastic and sclerotic changes of the temporal bones (arrow). (b) Coronal bone window view revealing opacification of the right epitympanum (arrow) and sclerotic, poorly pneumatized (diploic) mastoid cells with thickened septa in the bilateral direction.

endoscopy findings.

The patient's facial features—bilateral down-slanting palpebral fissures, malar hypoplasia, micrognathia, low-set crumpled ears, and a left pre-auricular tag—strongly suggested an underlying syndromic disorder. We therefore considered the main differential diagnoses (Table 1).

Nager and Miller syndromes were unlikely because she had no limb abnormalities (no thumb defects, no postaxial deficiencies). Goldenhar syndrome was ruled out due to symmetric facial involvement and the absence of epibulbar dermoids or vertebral anomalies. Pierre Robin sequence did not explain the zygomatic hypoplasia or ear malformations seen here. Otodental syndrome was not supported by any dental findings. The combination of symmetric malar hypoplasia, down-slanting palpebral fissures, and external ear deformities pointed us to TCS.

When approached with these objective findings as a contextual foundation, the patient was receptive to discussing her craniofacial history. She disclosed a maternal history of similar facial features; she also revealed that, prompted by her own observations and professional background, she had undergone clinical genetic testing, which identified a pathogenic heterozygous variant in the *TCOF1* gene. She did not provide the exact nucleotide-level details of the variant. In a subsequent, more profound disclosure, she shared that her awareness of this autosomal-dominant inheritance pattern had led her to choose to forgo marriage and childbearing as an act of responsibility to prevent the transmission of TCS to future generations.

3 Clinical Course and Patient Perspective

3.1 Diagnoses

The final diagnoses were as follows:

(1) TCS (confirmed by *TCOF1* mutation);

(2) Acute suppurative nasopharyngitis with structural abnormalities;

(3) Right-sided recurrent OME, secondary to the above two diagnoses.

3.2 Treatment

Management was undertaken in two phases.

Phase 1 (empirical anti-inflammatory and antimicrobial therapy): The patient was started on a course of oral methylprednisolone (20 mg/day for 5 days) to reduce mucosal edema, intranasal corticosteroid spray, and saline nasal irrigations. Empirical antibiotic therapy with cefaclor (375 mg twice daily) was initiated. After one week, symptoms and otoscopic findings had improved significantly, but nasoendoscopy revealed only a slight improvement in inflammation.

Phase 2 (targeted antimicrobial therapy): The microbiological culture was positive for *Staphylococcus aureus*, and susceptibility testing indicated sensitivity to clarithromycin. Accordingly, the antibiotic was promptly switched to clarithromycin (250 mg twice daily) for a two-week course, while continuing topical nasal therapy.

3.3 Outcomes

Upon completion of targeted therapy, the patient reported complete resolution of her otologic symptoms. A follow-up nasoendoscopic examination demonstrated dramatic improvement, with normalized nasopharyngeal mucosa, no evidence of purulent discharge, and clear visualization of the anatomical landmarks, including the previously obscured ET orifice (Figure 2b). No adverse events were observed during or after the treatment, including drug-related side effects, related complications (such as otorrhea, tympanic membrane perforation), or hearing worsening. The timeline of the clinical course is summarized in Figure 4.

3.4 Patient perspective

The patient worked in biotechnology. She had noticed her

Table 1 Differential diagnosis of TCS.

Feature/syndrome	TCS	Nager syndrome	Miller syndrome	Goldenhar syndrome (OAVS)	Pierre Robin sequence	Otodental syndrome
Genetics	*TCOF1*, *POLR1D*, *POLR1C*	*SF3B4*	*DHODH*	Sporadic; heterogeneous	Sporadic; *SOX9*-associated	*FGF3* deletion
Facial symmetry	Bilateral, symmetric	Symmetric	Symmetric	Unilateral/asymmetric	Symmetric	Symmetric
Malar hypoplasia	Present	Present (severe)	Present (severe)	May be present	Absent	Absent
Mandibular hypoplasia	Present	Present (severe)	Present (severe)	May be present (unilateral)	Present (isolated)	Absent
Down-slanting palpebral fissures	Present	Present	Present	May be present	Absent	Absent
Lower eyelid coloboma	Characteristic	Rare	Rare	May be present	Absent	Absent
External ear anomalies	Present	Present	Present	Present (asymmetric)	Absent	Absent
Hearing loss	Conductive	Mixed/conductive	Sensorineural	Conductive	May occur	Sensorineural
Limb anomalies	None	Thumb anomalies (hypoplasia/absence, radial defects, radioulnar fusion)	Postaxial defects (5th digit absence/hypoplasia of all four limbs)	Occasional	None	None
Cleft palate	Occasional (about 30%)	Common	Common	Occasional	Core feature (U-shaped)	Absent
Glossoptosis	Absent	May be present	May be present	Absent	Present	Absent
Dental anomalies	Absent	Absent	Absent	Absent	Absent	Globodontia
Epibulbar dermoids	Absent	Absent	Absent	Characteristic	Absent	Absent
Vertebral/rib anomalies	Absent	Absent	Absent	Vertebral anomalies	Absent	Absent
Intellectual disability	Normal	Normal	Normal	Normal	Normal	Normal

Note: OAVS, oculo-auriculo-vertebral spectrum; TCS, Treacher Collins syndrome.

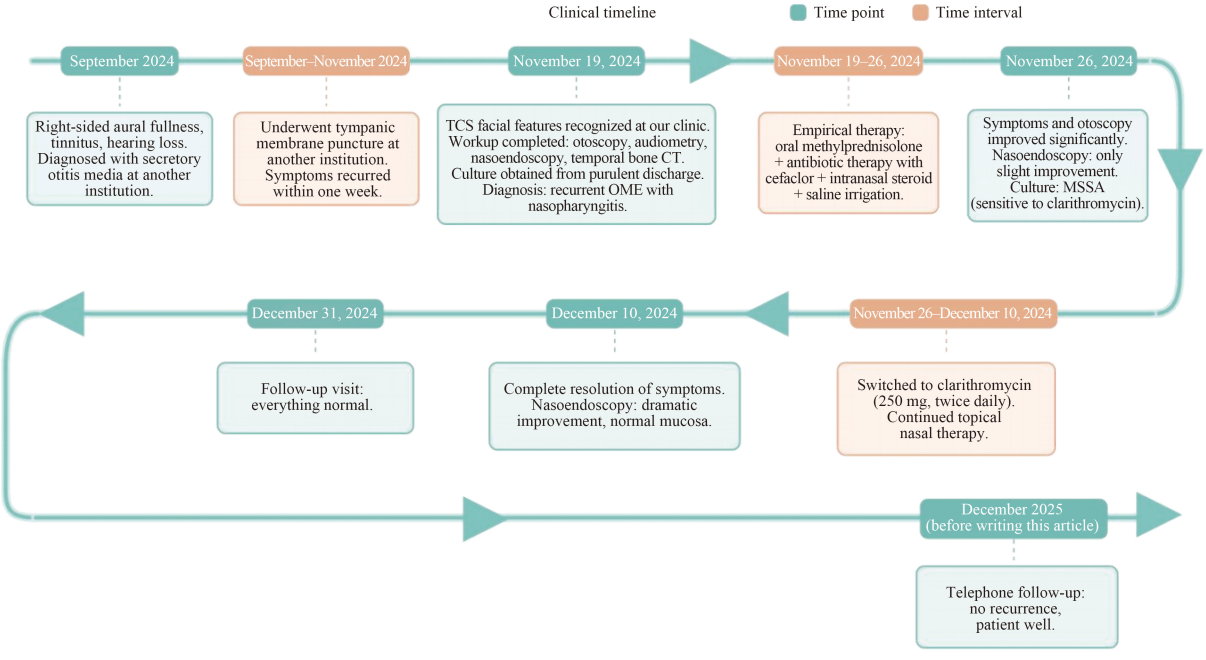


Fig. 4 Timeline of the patient's clinical course. Key events spanning an approximately 15-month period from symptom onset through diagnosis, treatment, and 12-month telephone follow-up are shown. MSSA, methicillin-susceptible *Staphylococcus aureus*.

facial differences since adolescence but never received a clear diagnosis. Her professional background made genetic testing accessible, so she arranged it on her own. The result showed a *TCOF1* mutation. When we asked how that information affected her, she said she was relieved to finally have an answer. She knew about preimplantation genetic testing for monogenic disorders (PGT-M). However, she told us she had decided not to marry or have children. She described the decision as personal and deliberate, not impulsive. She added that the

ear infections, while annoying, did not compare to the lifelong social burden of looking different. We report her choice as part of her story, not as a recommendation. Her decision was personal. It was shaped by her values, not by medical options alone.

4 Discussion

This case offers several profound learning points for practicing otolaryngologists. First and foremost, it reinforces that recurrent or refractory OME should prompt a search for an underlying etiology. The initial failure to recognize the patient's syndromic features likely stemmed from a common clinical dilemma: the hesitation to directly inquire about a patient's distinctive physical appearance, particularly in a young adult, for fear of causing offense. This case demonstrates that such inquiries are not only justified but also clinically necessary when guided by objective findings. Using the refractory nature of the OME and the nasoendoscopic abnormalities as a starting point allows the clinician to broach the subject professionally and collaboratively. In the present case, this approach led to the pivotal disclosure of the genetic diagnosis.

The otologic presentation in this case directly reflects the characteristic pathoanatomy of TCS. Craniofacial hypoplasia compromises ET function through two deterministic and synergistic mechanisms. The first mechanism is a fixed structural stenosis: a congenitally narrowed nasopharyngeal cavity, confirmed in this patient by both imaging and endoscopy, creates a persistent mechanical obstruction at the ET orifice, fundamentally impairing middle-ear ventilation and clearance. The second, functionally more consequential mechanism is failure of active tubal dilation. The malformed craniofacial framework alters the origin, vector, and mechanical advantage of the tensor veli palatini (TVP) muscle[6].

This confluence of mechanisms creates a self-perpetuating pathophysiological state. The resulting persistent middle-ear effusion produces a stagnant, nutrient-rich microenvironment that is inherently susceptible to secondary bacterial colonization[7]. The clinical manifestation in this case—purulent nasopharyngitis with culture-confirmed *Staphylococcus aureus*—is therefore an anticipated microbiological outcome of the compromised anatomy rather than a coincidental finding.

We considered nasopharyngeal carcinoma (NPC) because the patient was a young adult of East Asian descent with unilateral OME. As described above, EBV serology was negative; this lowered the risk of NPC[8], but does not completely rule it out. Her symptoms recurred, so we performed nasoendoscopy at our center. Nasoendoscopy revealed no mass; instead, a narrow nasopharynx and a deep lateral recess containing pus were observed, findings not suggestive of malignancy.

These pathophysiological insights necessitate a structured clinical approach. For OME cases that recur, persist beyond three months, present unilaterally, or exhibit atypical features, we recommend a sequential diagnostic and management pathway:

1. Anatomical/endoscopic evaluation (perform diagnostic nasoendoscopy)

In this context, nasoendoscopy becomes essential rather than discretionary. It provides definitive visual confirmation of the anatomical obstruction (stenosis) and allows identification of active purulent discharge. These findings establish the need for microbiological evaluation. If purulent secretions or structural abnormalities are detected, microbial culture and susceptibility testing should be performed to initiate or adjust antibiotic therapy accordingly; if no purulent secretions or structural abnormalities are detected, alternative underlying etiologies should be explored.

2. Microbiological evaluation (pursue microbiologically-guided therapy)

When endoscopy confirms purulence, both culture and antimicrobial susceptibility testing are essential. Empirical antibiotic therapy may offer short-term coverage but should not be continued without microbiological justification; doing so increases the risk of therapeutic failure and conflicts with established antimicrobial stewardship principles[9,10]. The clinical resolution achieved in this case followed targeted therapy (specifically, clarithromycin selected on the basis of susceptibility data), illustrating the value of a rational, de-escalated treatment approach.

3. Genetic/syndromic evaluation (conduct directed physical exam and history)

A systematic assessment of craniofacial features such as retrognathia, malar hypoplasia, and auricular dysplasia should be integrated into every evaluation. Patients with no concerning findings continue routine management and follow-up. When such stigmata are present, or when family history is suggestive, formal genetic assessment and counseling are warranted. This step transcends symptomatic treatment by establishing a definitive etiological diagnosis, clarifying familial recurrence risk, and initiating the coordinated, multidisciplinary care required for lifelong management[11].

In summary, this case demonstrates that refractory OME may be the first clinical indication of an underlying syndromic disorder. Accordingly, a management framework that integrates anatomical visualization, microbiological diagnostics, and genetic evaluation can fundamentally reshape clinical practice. Such an approach transforms the treatment of what appears to be a localized infection into the key opportunity for definitive syndromic diagnosis and the initiation of personalized long-term care (Figure 5).

Finally, and perhaps most significantly, this case compels us to look beyond the otologic sequelae. The patient's conscious decision to remain childless to halt the transmission of TCS is a powerful testament to the profound psychosocial and ethical burdens carried by individuals with heritable conditions. This disclosure moves the narrative from a purely clinical success to a human story that underscores that medical intervention alone cannot resolve all long-term disease-related challenges. It highlights a critical aspect of comprehensive care: the imperative for proactive and sensitive genetic counseling. As clinicians, we must be prepared not only to manage the physical symptoms, but also to recognize, acknowledge, and provide resources for guiding patients and their families through these complex decisions, ensuring that they feel supported in all dimensions of their well-being[12].

5 Limitations

This is a single case report. A single case cannot establish a general rule. The proposed three-step framework

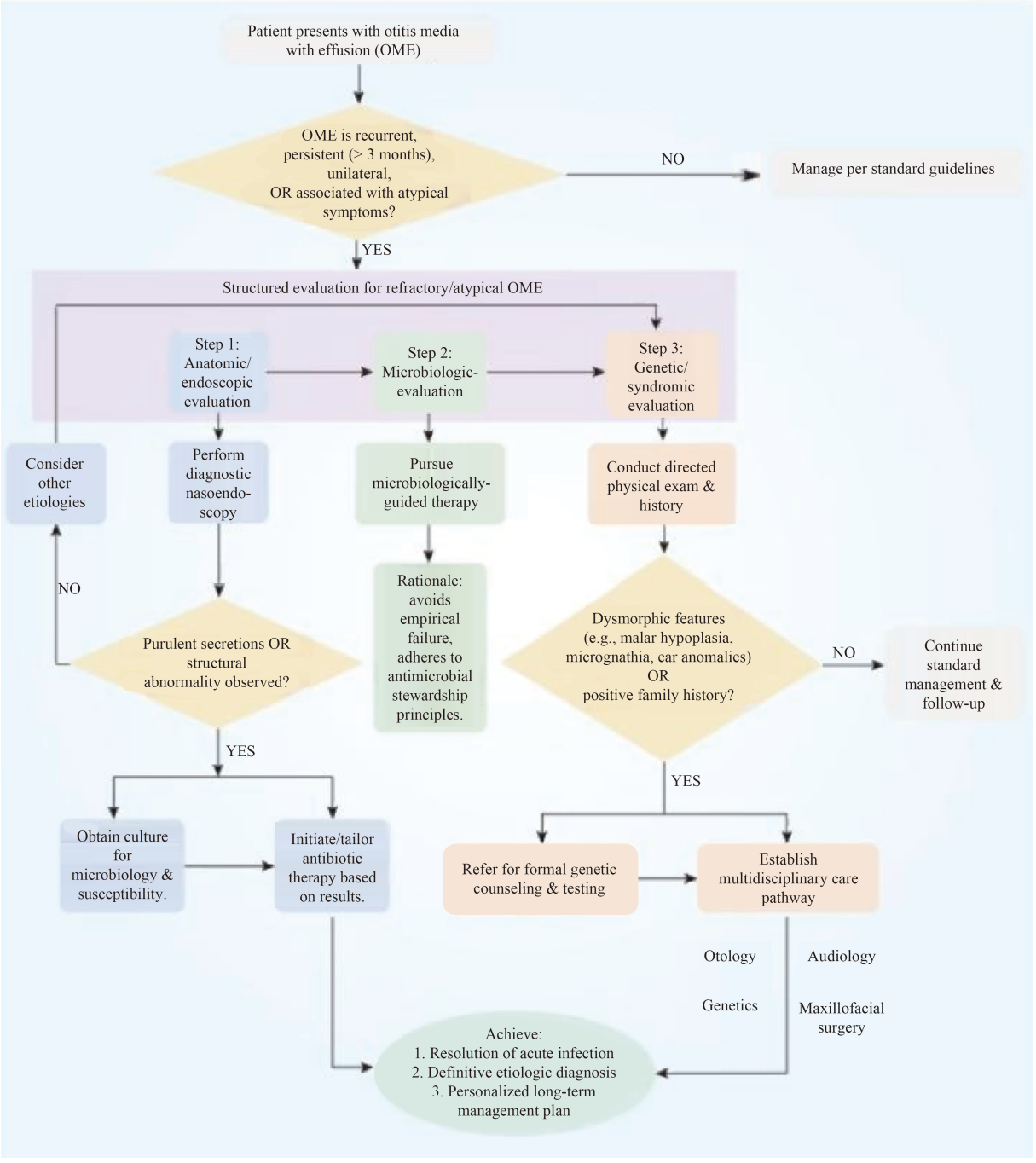


Fig. 5 Proposed diagnostic framework for refractory otitis media with effusion.

requires testing in more patients. Follow-up was done by phone at one year; we did not repeat hearing tests or nasal endoscopy at that time; therefore, subclinical middle-ear or nasopharyngeal lesions may be missed, and recurrence status relies solely on patient self-report, introducing recall bias. We cannot fully confirm objective recovery of middle-ear and ET function. Speech discrimination scores were not recorded at the initial evaluation; this omission renders underlying speech-perception deficits difficult to detect and prevents quantitative assessment of speech-communication benefits from intervention and adequate analysis of long-term language prognostic factors. The patient provided her ethnicity and genetic result, but other TCS patients may have different features. She did not give us the specific details of her *TCOF1* variant (although a pathogenic heterozygous variant in the *TCOF1* gene was identified, the patient declined to disclose detailed nucleotide-level information of the variant). EBV serology (VCA-IgA and EA-IgA) done at the outside hospital was negative. That lowers the risk of NPC; however, we did not do a nasopharyngeal biopsy or MRI. We acknowledge this as a limitation. We saw no adverse events, but a single case does not rule out rare side effects of the treatment. We also did not use a structured adverse event assessment tool.

5.1 Expected disease course and recurrence risk

In TCS, the narrow nasopharynx and poor ET function do not change after treatment. Therefore, the risk of recurrent middle-ear effusion or infection remains high, especially after a cold. The patient was told to watch for early signs—ear fullness, hearing changes, nasal congestion—and to come back early. Most episodes can be managed without permanent hearing loss.

5.2 Long-term follow-up and clinical implications

Before the preparation of this manuscript, telephone follow-up was completed in December 2025. The patient reported that she had remained free of otologic symptoms since completing treatment in December 2024 and was doing well overall. Given this favorable outcome, we established a longitudinal surveillance plan for her. The plan consists of annual audiometry to monitor for recurrent conductive hearing loss, clinical evaluation every 6 to 12 months to check for signs of middle-ear effusion, prompt nasoendoscopy if new nasal or aural symptoms emerge, and continued access to genetic counseling to address family planning and potential testing of relatives. The patient was also counseled about her lifelong predisposition to ET dysfunction and advised to seek early evaluation for any upper respiratory infection.

6 Conclusion

This case underscores the critical nature of a meticulous, holistic clinical evaluation, which remains the bedrock of diagnosis, even in the age of genomic medicine. Refractory otitis media should prompt clinicians to look beyond the tympanic membrane for syndromic clues. Because it provides direct insights into pathoanatomy, nasoendoscopic examination is indispensable in this workup. Furthermore, effective management of these complex cases requires a dual strategy: addressing the acute infectious process with targeted therapy while recognizing and managing the underlying, permanent anatomical challenges. Ultimately, this case reminds us that true patient-centered care for those with genetic syndromes must integrate otologic management with compassionate support for the profound personal and ethical ramifications of their diagnosis, with genetic counseling serving as an essential bridge between these domains.

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Ethical statement

This case report was conducted in accordance with the Declaration of Helsinki. This study was approved by the Clinical Research Ethics Committee of Shenzhen Second People's Hospital (Approval No. 2026-068-01PJ).

Conflicts of interest

The authors declare no conflicts of interest.

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Data availability statement

Not applicable.

AI statement

The authors used Deepseek (Version DeepSeek-V4) as a language-editing tool to improve grammar, clarity, and readability. The AI tool was not used for data analysis, data generation, image processing, or scientific content creation. All outputs were carefully reviewed and verified

by the authors, who take full responsibility for the final content.

Author contributions

Yalin Zhang drafted the original manuscript. Yanping Yu contributed to visualization and reviewed and edited the manuscript. Hongsong Dong curated the data. Lu Lu contributed to visualization. Chang Lin contributed to visualization. Guohui Nie conceptualized the study and acquired funding. All authors reviewed, edited, and approved the final version of the manuscript and agree to its publication.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and the accompanying images, including the sensitive personal information regarding her reproductive decisions. The consent form is held by the authors and is available upon request.

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