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CASE REPORT

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Efficacy of tezepelumab in chronic rhinosinusitis with nasal polyps (CRSwNP) in non-type 2 patient: a case report from the Middle East*

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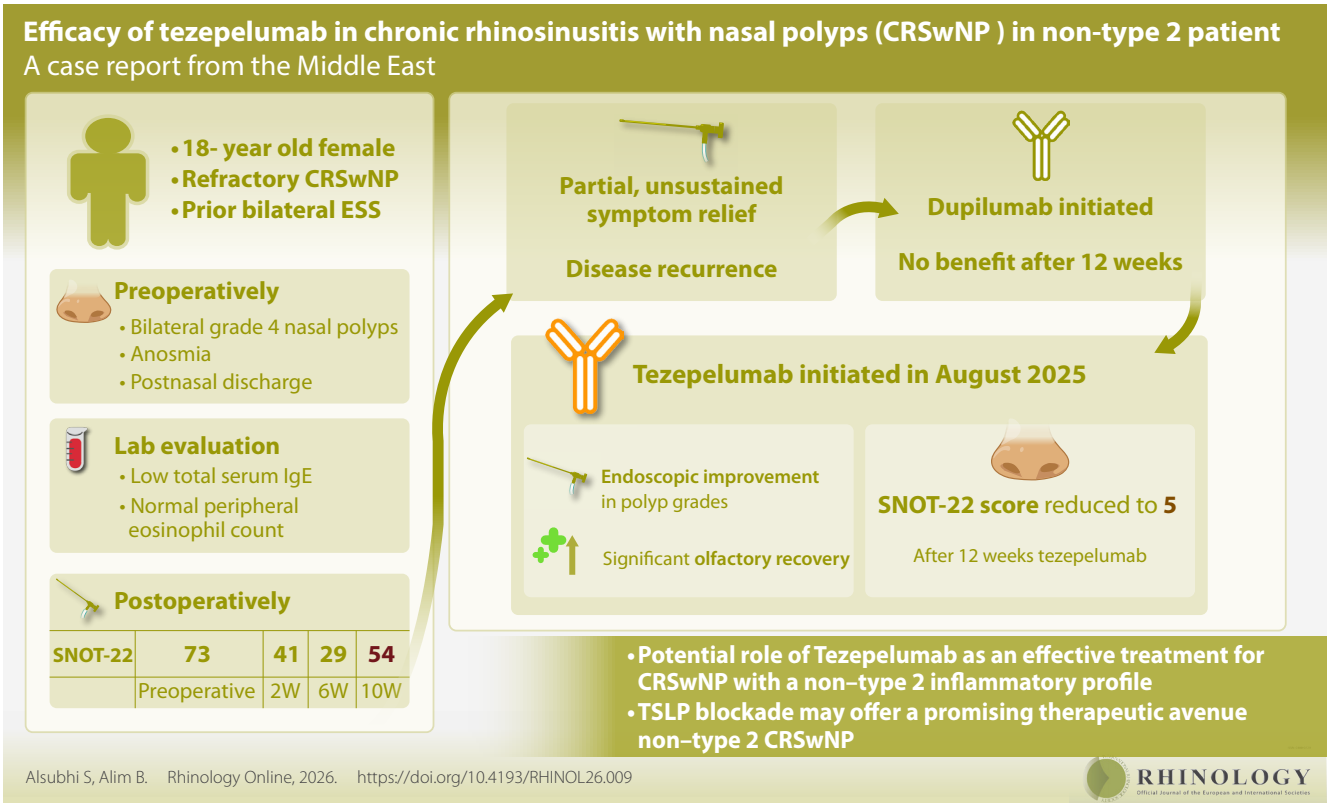

Abstract

Background: Chronic rhino-sinusitis with nasal polyps presents with non–type 2 inflammatory profiles and often show a poor response to corticosteroids and biologics targeting type 2 inflammatory pathways. Tezepelumab, against thymic stromal lymphopoietin (TSLP), inhibits an upstream epithelial cytokine that can modulate both type 2 and non–type 2 immune responses.

Case presentation: 18-year-old female with refractory CRSwNP despite prior bilateral endoscopic sinus surgery. Preoperatively, she presented with bilateral grade 4 nasal polyps, anosmia, and postnasal discharge. Laboratory evaluation revealed low total serum IgE, and normal peripheral eosinophil count, consistent with a non–type 2 inflammatory pattern. Postoperatively, her SNOT-22 score improved from 73 preoperatively to 41 at two weeks follow-up and 29 at six weeks, but subsequently increased to 54 at ten weeks post op, indicating partial but unsustained symptom relief. Despite surgical and topical medical therapy, disease recurrence became evident. Dupilumab, was initiated but demonstrated no clinical benefit after 12+ weeks of use.

Tezepelumab, was started in August 2025. 12 weeks later, her SNOT-22 score decreased markedly to 5, accompanied by endoscopic improvement in polyp grades, along with significant olfactory recovery.
Conclusion: This case highlights the potential role of Tezepelumab as an effective treatment for CRSwNP with a non–type 2 inflammatory profile. The patient demonstrated improvement in symptom burden, nasal patency, and olfactory, suggesting that TSLP blockade may offer a promising therapeutic avenue non–type 2 CRSwNP phenotypes.

Key words: chronic rhino-sinusitis, Tezepelumab, non–type 2 inflammation, biologic therapy

Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a persistent inflammatory disorder of the sinonasal mucosa that affects approximately 2–4% of the general population and is associated with significant impairment in quality of life [1]. The majority of CRSwNP cases are characterized by type 2 inflammation, distinguished by elevated eosinophil counts, increased serum IgE levels, and overexpression of interleukins IL-4, IL-5, and IL-13 [2]. However, a substantial subset of patients exhibits non–type 2 CRSwNP, which is frequently associated with neutrophilic or paucigranulocytic inflammation, bacterial biofilms, obesity, or odontogenic sinus infections. These patients typically demonstrate poor responsiveness to conventional corticosteroid therapy [3].

Thymic stromal lymphopoietin (TSLP), an epithelial-derived cytokine (alarmin), thereby bridging both type 2 and non–type 2 inflammatory responses. Inhibiting this upstream signal can down-regulate multiple downstream pathways, including those that drive neutrophilic inflammation, thereby offering a broader therapeutic effect than current type 2-specific biologics [4]. Tezepelumab, a fully human monoclonal antibody against TSLP, has demonstrated efficacy in severe asthma irrespective of baseline eosinophil counts or serum IgE levels [5].

Here, we report a unique case of a patient with non–type 2 CRSwNP, low IgE, normal eosinophils, and no comorbid asthma, who responded favorably to tezepelumab after failure of surgical, topical medical rinses, and type 2-targeted biologic therapy.

Case report

An 18-year-old female presented to the office with a one-year history of progressive bilateral nasal obstruction, anosmia, postnasal discharge, and foul-smelling nasal secretions. SNOT22 was 73. Her past medical history was notable for dental procedures involving the left upper molars done a year back, with no history of asthma, allergic rhinitis, or aspirin sensitivity.

Initial evaluation

Nasal endoscopy revealed bilateral grade 4 polyps, bilateral purulent nasal discharge, left-sided septal deviation, and hypertrophied inferior turbinates. CT imaging of the paranasal sinuses revealed a Lund-Mackay score (LMS 20/24), with diffuse mucosal thickening and near-complete opacification

Surgical management

Due to failure of medical therapy, the patient underwent Bilateral Computer-Assisted Sinus Surgery (BiCASS) on 9 November 2024, Postoperative management consisted of a tapering course of oral steroids and budesonide saline irrigations.

Postoperative course

The postoperative course was initially favorable, with improvement in symptoms and reduction in SNOT-22 scores (Table 1). However, ten weeks post-surgery, the patient reported recurrence of nasal obstruction, anosmia, and postnasal discharge. Endoscopic evaluation revealed recurrent grade 3 nasal polyps with purulent nasal discharge bilaterally, and a follow-up CT showed LMS (24/24).

Laboratory findings

Antinuclear Antibody (ANA) and Antineutrophil Cytoplasmic Antibody (ANCA) testing were done to rule out underlying autoimmune or vasculitis processes such as granulomatosis with polyangiitis. ESR and CRP were assessed to evaluate for systemic inflammation or occult infection, while a chest radiograph was ordered to exclude pulmonary involvement that could indicate systemic granulomatous disease or allergic broncho-pulmonary pathology. All results were within normal limits, supporting a localized, non–type 2 inflammatory sino-nasal process, as summarized in Table 2.

Table 1. Serial SNOT-22 scores.

Time point	Date	SNOT-22 score
Preoperative	7 Nov 2024	73
2 weeks post-op	23 Nov 2024	41
6 weeks post-op	21 Dec 2024	29
10 weeks post-op	18 Jan 2025	54
6 weeks after dupilumab	1 July 2025	54
4th week after tezepelumab	16 Sep 2025	4
11 weeks after tezepelumab	4 Nov 2025	5

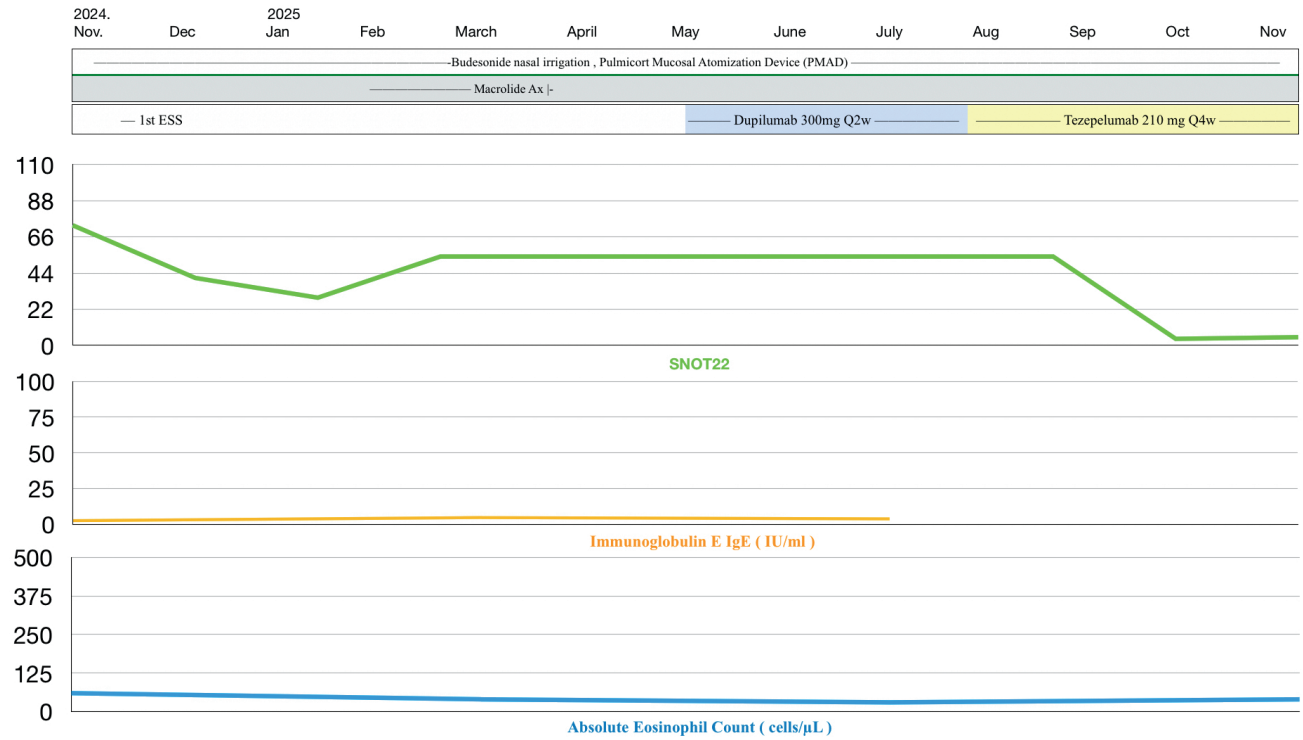

Figure 1. Axial section computed tomography image showing a calcified mass in the left inter-septo-turbinal space (a); histological sections images stained with Gromori Grocott showing numerous agglomerated mycelial filaments, sometimes septate, consisting of large hyphae (b).

Biologic therapy

Dupilumab (300 mg subcutaneously every two weeks) was initiated on 20 May 2025 and continued until 5 August 2025, with no clinical improvement .

Subsequently, tezepelumab (210 mg subcutaneously every four weeks) was initiated on 5 August 2025. Marked clinical improvement was observed after 2nd month into treatment. The patient's SNOT-22 score decreased from 54 pre-treatment to 5, with a reduction in nasal polyp grade to G0 on the left and G1 on the right, with significant olfactory recovery. By the 12-week, a follow-up visit (4 Nov 2025) revealed sustained improvements, with stable endoscopic findings, and no adverse events. The patient remained on budesonide saline irrigations.

Outcome

After 12 weeks, her SNOT-22 scores dropped from 54 to 5, reflecting near-complete symptom relief. Nasal endoscopy scores demonstrated a substantial reduction in polyp burden, improving from Nasal Polyp Score (NPS) of 8 down to one, with improved nasal airflow and a regain of sense of smell. The patient reported better sleep, easier nasal breathing, and improved overall quality of life.

Discussion

Chronic rhino-sinusitis with nasal polyps (CRSwNP) is a heterogeneous inflammatory disorder involving both type 2 (T2) and non–type 2 (non-T2) immune pathways. The T2 endotype is marked by eosinophilic infiltration, elevated IgE levels, and cytokine signaling predominantly driven by IL-4, IL-5, and IL-13 [5]. However, a smaller subset of patients display a non-T2 inflammatory profile, characterized by low eosinophil count, normal or reduced IgE levels, and poor responsiveness to corticosteroids. Such patients frequently experience persistent or recurrent disease despite surgical intervention and standard T2-targeted

Table 2. Summary of laboratory investigation.

Parameter	Result range	Reference range	Interpretation
Peripheral eosinophil count	0.03-0.06 *10/L	0.02- 0.5 * 10/L	Normal / Low-normal
Total IgE	2.55-4.75 IU/mL	<100 IU/mL	Low
ANA / ANCA	Negative	-	Normal
ESR / CRP	Within normal limits	-	No systemic inflammation
Chest imaging	Normal	-	No pulmonary involvement

biologic therapy, highlighting a significant unmet clinical need [5,6].

Our patient demonstrates this non-T2 phenotype, with low total IgE (2.55–4.75 IU/mL), normal peripheral eosinophil count ($0.04–0.06 \times 10^9$/L), and absence of asthma or any other atopies. Despite undergoing functional endoscopic sinus surgery (FESS) and receiving extended medical therapies— including oral and topical corticosteroids, macrolide antibiotics, and dupilumab—her inflammation remained uncontrolled. This corticosteroid- and biologic-refractory presentation closely resembles previously reported non-T2 CRSwNP cases that demonstrate poor response to dupilumab or mepolizumab [4].

Tezepelumab, a fully human monoclonal antibody targeting thymic stromal lymphopoietin (TSLP), acts upstream of both T2- and non-T2-mediated inflammatory pathways. TSLP is an epithelial- derived cytokine released in response to allergens and microbial stimuli, triggering dendritic-cell activation and subsequent cytokine cascades. By blocking TSLP, tezepelumab suppresses multiple downstream inflammatory routes, offering a broad-spectrum immunomodulatory approach beyond eosinophilic inflammation [2].

The pivotal WAYPOINT phase 3 trial (NCT04851964) offered the first large-scale, randomized evidence demonstrating tezepelumab's efficacy in severe, uncontrolled CRSwNP. In this trial, tezepelumab significantly reduced nasal polyp scores, nasal congestion severity, and the requirement for systemic corticosteroids or surgery compared with placebo, with benefits seen regardless of baseline eosinophil or IgE levels. These findings establish TSLP inhibition as an effective therapeutic strategy across both T2 and non-T2 CRSwNP endotypes [1].

Post-hoc analyses of the PATHWAY trial and related asthma studies further reinforce the biomarker- independent benefits of TSLP inhibition. In these studies, tezepelumab improved upper-airway symptoms and reduced inflammatory biomarkers, even among patients with low baseline eosinophil count. Similarly, Jacobs et al. demonstrated significant improvements in patient-reported outcomes (PROs), including SNOT-22 and nasal symptom scores, irrespective of inflammatory phenotype [7] — findings that mirror our patient's >90% SNOT-22 reduction [2].

Several published case reports and series have also described favorable outcomes with tezepelumab in CRSwNP. Yamashita reported dramatic improvement in a T2-high patient with aspirin-exacerbated respiratory disease (AERD) and CRSwNP [3]. In contrast, Inoue et al. reported a case series (n = 4) showing improvement in both asthma control and nasal polyp burden [8]. Conversely, Kai et al. and Cristallo et al. documented meaningful benefit even in patients with low eosinophil counts [4,9], similar to our non-T2 case. Collectively, these reports support tezepelumab's utility across the T2–non-T2 spectrum while highlighting variability in treatment response and duration [3,4].

Our case aligns with these findings in demonstrating that tezepelumab can induce a rapid and sustained improvement even in the absence of classical T2 biomarkers. The magnitude of clinical response observed, marked polyp regression and near-complete symptom resolution, mirrors outcomes in the WAYPOINT and PATHWAY analyses. This reinforces the concept that reliance solely on eosinophilic or IgE biomarkers may underestimate candidates who could benefit from TSLP inhibition [1,2].

Nonetheless, several important limitations remain. While WAYPOINT confirms short-term efficacy and safety, long-term durability, relapse risk after discontinuation, and head-to-head comparison with existing CRSwNP biologics (dupilumab, mepolizumab, omalizumab) are still under investigation. Current evidence outside clinical trials is mainly composed of single-patient reports or small series with variable follow-up. With tezepelumab receiving regulatory approval for CRSwNP recently, its optimal placement in treatment algorithms is still evolving, and ongoing data regarding long-term durability and comparative effectiveness will be crucial for guiding patient selection.

In summary, this case, supported by emerging evidence from WAYPOINT, PATHWAY, PROs analyses, and multiple clinical reports, illustrates that TSLP inhibition may offer meaningful benefit in refractory CRSwNP irrespective of inflammatory phenotype. These observations advocate for a more nuanced, endotype-driven approach that incorporates epithelial-alarmin activity alongside classical biomarkers. Future prospective studies should clarify predictors of response and the long-term role of tezepelumab within the biologic treatment landscape for CRSwNP [1,2,5,8].

Conclusion

In this unique case of non–type 2 CRSwNP, tezepelumab induced a robust and sustained clinical response in a patient with low IgE, normal eosinophil count, and no coexistent asthma, who remained refractory to both surgical and type 2-targeted biologic therapy.

This report underscores the importance of personalized, endotype-driven therapy and supports further exploration of tezepelumab in difficult-to-treat CRSwNP, particularly in younger patients. It also suggests that upstream cytokine blockade may broaden therapeutic options beyond current T2- focused strategies, addressing an ongoing unmet clinical need in refractory CRSwNP.

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Authorship contribution

SA: data collection, litriture review, and drafting of the manuscript. BA: Supervision, interpretation, revision, approval.

Conflict of interest

None declared.

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