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IL-17 Inhibitor Secukinumab Achieves Remission in Relapsing Polychondritis: A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Female, 23-year-old
Final Diagnosis: Relapsing polychondritis
Symptoms: Auriculas were painful, edematous with severe hyperemia • sparing the earlobes
Clinical Procedure: —
Specialty: Rheumatology

Objective: Diagnostic/therapeutic accidents

Background: Relapsing polychondritis is a rare autoimmune disease of unknown etiology. There are no defined protocols for treatment, and its management depends on the physician's knowledge and empirical experience. Various reports often highlight the insufficient efficacy of conventional disease-modifying anti-rheumatic drugs, and report controversial results associated with the use of different biologic agents.

Case Report: The patient was a 32-year-old woman, previously diagnosed with ankylosing spondylitis. Four years after the initial diagnosis and following her second delivery, the patient presented with a refractory and aggressive relapsing polychondritis, which posed a significant challenge for treatment. Two months prior to the onset of the chondritis, the patient exhibited high disease activity of ankylosing spondylitis, with ASDAS-CRP 3.5 and BASDAI 6.0. After treatment failure using a combination of an anti-TNFα inhibitor and methotrexate, we achieved remission of both co-existing autoimmune diseases using an IL-17 inhibitor (secukinumab).

Conclusions: Further investigations are needed to better understand the pathogenesis of this rare condition. The existence of various reports on the controversial effects of treatment with different biologic agents, including IL-17 antagonists, raises several questions, including whether the onset of relapsing polychondritis is a side effect of the use of biologics or if it is an autoimmune disease that occurs independently of the treatment. This is the first time that the use of an anti-IL-17 agent is reported to have successfully suppressed an aggressive, progressive form of this disease, without any symptom-free period before the initiation of secukinumab.

Keywords: Polychondritis, Relapsing • Spondylitis, Ankylosing • Treatment Adherence and Compliance

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/946916

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Introduction

Relapsing polychondritis is a rare autoimmune disease of unknown etiology. It can affect all types of cartilage, including the hyaline cartilage of peripheral joints, the fibrocartilage of extra-articular sites, and proteoglycan-rich tissues including the media of the arteries, the heart, and the conjunctiva and sclera of the eye [1]. Impairment of the cartilage in the ears, nose, and tracheobronchial tree may lead to floppy ears, saddle nose, and in severe cases, laryngotracheal collapse [2].

The prevalence of the condition is low, estimated to range between 4.5 to 25 cases per million [3]. However, the precise incidence of the disease remains unknown [4]. The peak age of onset is typically between the fourth and fifth decades, although it can affect individuals of any age. While most studies report a predominance among women [5], some suggest that the gender distribution is similar for men and women [4].

The pathogenesis is not well understood. The cartilage is infiltrated by neutrophils, T-lymphocytes, and natural killer T-cells. CD4+ T-cells secrete cytokines, including interleukin-8, monocyte chemoattractant protein-1, and macrophage inflammatory protein 1-alpha, which recruit monocytes and macrophages [4]. Macrophages release metalloproteinase-3, proteolytic enzymes, and cathepsins K and L, which leads to cartilage destruction [6]. Another hypothesis suggests that the uncontrolled production of autoantibodies against types II, IX, and XI collagens, matrilin-1, and cartilage oligomeric matrix proteins (COMPs) plays a crucial role in the pathogenesis of the disease [7]. Molecular mimicry between different microorganisms and components of the cartilage matrix has also been observed, and this phenomenon is possibly involved in the pathogenesis [8].

There are no defined protocols for treatment, and the management of relapsing polychondritis depends on the physician's knowledge and empirical experience. The available data on the management of relapsing polychondritis with biologic disease-modifying antirheumatic drugs (bDMARDs) are derived from single case reports or small case series, usually involving no more than 100 patients [4]. TNF blockers (adalimumab, etanercept, and infliximab), an anti-IL-6 antagonist (tocilizumab), an anti-CD20 agent (rituximab), and a CTLA4 fusion protein (abatacept) are among the treatment recommendations for this condition. An overview reported that complete resolution of the symptoms was observed in 26 (45.6%) patients treated with infliximab, 7 (36.8%) with etanercept, 12 (37.5%) with adalimumab, 2 (100%) with golimumab, 1 (100%) with certolizumab, 2 (11.1%) with rituximab, 9 (50%) with anakinra, 14 (46.6%) with tocilizumab, and 3 (37.5%) with abatacept [4]. Other authors have linked the appearance of relapsing polychondritis or the ineffectiveness of its treatment to the use of TNF blockers [9,10], IL-17 inhibitors [11], and rituximab [12].

Evaluation of the success rates of each specific biologic agent is challenging due to the conflicting results from the limited number of studies on the treatment of relapsing polychondritis with different bDMARDs, as well as controversial conclusions regarding the link between biologic agents used and reported adverse events or complications. In addition, there is a lack of randomized controlled trials. The heterogeneity in phenotypic presentation and the lack of long follow-up analyses further complicate the interpretation of treatment effects on clinical outcomes [12].

This is the first reported case of refractory relapsing polychondritis in which the disease activity was fully suppressed using an IL-17 inhibitor (secukinumab). This report highlights the need for a more detailed evaluation of disease pathogenesis, as well as more extensive studies on alternative treatment options.

Case Report

A 32-year-old woman, diagnosed with ankylosing spondylitis (bilateral sacroiliitis, grade 3, negative for the human leukocyte antigen-B27, with a history of iridocyclitis) in April 2016, presented to our rheumatology department in February 2023 with severe pain and redness in both ears, along with a cough. The symptoms had started suddenly 3 weeks earlier, with a fever of up to 38.8°C and throat pain radiating to the right ear. Several days later, the patient developed severe pain and redness in the same ear. There was no history of trauma or other provoking factors. The otolaryngologist diagnosed cellulitis and prescribed treatment with amoxicillin 1000 mg, 1 tablet twice daily for 10 days. Due to a lack of efficacy, the antibacterial agent was replaced with clindamycin 600 mg thrice daily, metronidazole 500 mg twice daily, and doxycillin 100 mg twice daily for 7 days. Despite these treatments, the symptoms progressed, affecting also the left ear. During treatment with methylprednisolone 12 mg daily, which had been prescribed 2 months earlier (in December 2022) due to ankylosing spondylitis activity, the following symptoms were reported: inflammatory pain in sternocostal junctions (causing difficulty with deep breathing), pain in the lumbosacral spine, arthritis in the knee joints, and persistent stiffness throughout the day.

One year prior (in July 2022) and 9 months after her second delivery (in September 2021), the patient had reported an episode of redness and pain in the nose. The condition was determined as an acute bacterial infection (cellulitis) and treated with beta lactamase antibiotics. The symptoms were self-limited and resolved spontaneously within a month. Over time, the nasal septum collapsed, resulting in a saddle-nose deformity (**Figure 1**). The patient experienced a symptom-free period of 1 year. During this time, she reported a mild pain in the lumbosacral region and morning stiffness lasting 15 minutes, which

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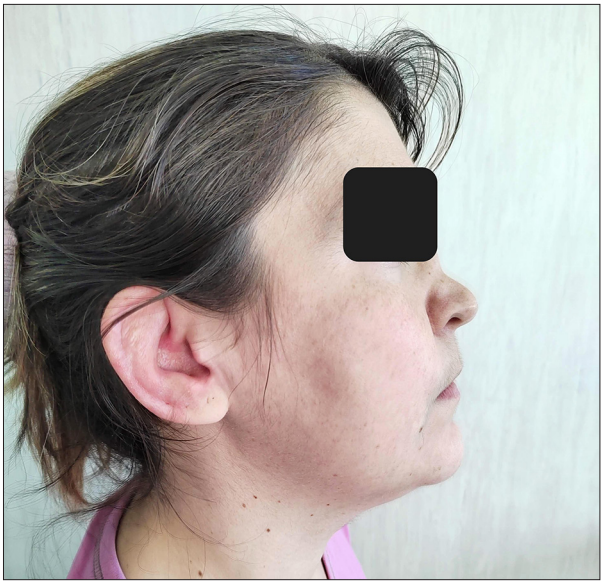

Figure 1. Cartilage involvement in relapsing polychondritis leading to the formation of a saddle-nose deformity.

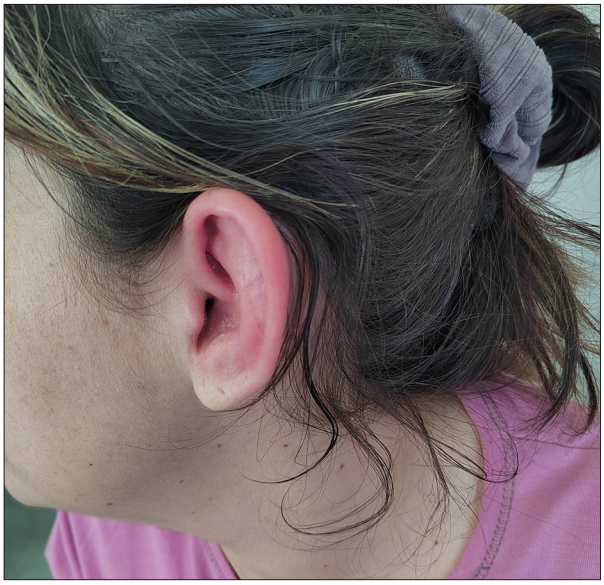

Figure 2. Edematous ear with severe hyperemia, sparing the earlobes, due to relapsing polychondritis.

did not require treatment. Family history was unremarkable. There was no information about co-existing diseases in the patient except for the ankylosing spondylitis. She had no history of tobacco smoking or alcohol or other substance abuse.

On physical examination, the patient appeared to be alert and aware of space and time. She had a fever of up to 38.8°C. Her outer ears were painful and edematous, with severe hyperemia, but sparing of the earlobes (**Figures 1, 2**). Saddle nose deformity was observed. A lung examination revealed pure vesicular breathing, with a respiratory rate of 17 breaths per minute. No wheezing or stridor were detected. Regarding cardiovascular function, tachycardia was seen, with a frequency of 112 beats per minute, regular rhythm; no murmurs, rubs, or clicks. Blood pressure was 90/60 millimeters of mercury. The abdomen was flat, soft, and non-tender, with physiological bowel sounds. The central nervous system and the peripheral nervous system were functioning normally. She had normal mental status, muscle strength, and power, and normal reflexes. A musculoskeletal examination revealed palpable pain in the area of the sternocostal junctions. Assessment of spine mobility yielded the following results: Schober test – 4 cm; Tragus to wall distance – left 13 cm, right 12 cm; occiput to wall distance – 1 cm; lateral flexion right – 23 cm, left – 24.7 cm. Blood tests showed evidence of high disease activity with thrombocytosis, activity with thrombocytosis together with elevated CRP and erythrocyte sedimentation rate (**Table 1**). Focal infections were excluded. Other infectious conditions were also ruled out.

The diagnosis was revised by rheumatologists to relapsing polychondritis. To rule out possible involvement of the tracheobronchial tree, we performed a functional respiratory examination and assessed carbon monoxide perfusion, both of which were normal. The echocardiography and CT scan of the lungs were also normal.

The dose of methylprednisolone was increased to 250 mg daily for 5 days (4 mg/kg daily). Several authors have reported achieving remission of relapsing polychondritis using TNFα inhibitors. In an effort to address both relapsing polychondritis and ankylosing spondylitis activity, we decided to continue the treatment with methotrexate 15 mg weekly, adalimumab at a dose of 40 mg subcutaneously (s.c.) every other week, and corticosteroids at a dose of 60 mg of prednisolone equivalent daily for 1 month. After 4 months of receiving adalimumab, methotrexate, and methylprednisolone (in July 2023), the gradual reduction in the corticosteroids below 15 milligrams of prednisolone equivalent daily led to an exacerbation of both conditions – relapsing polychondritis and ankylosing spondylitis (worsening of the pain in the sternocostal junctions and the sacroiliac joint, accompanied by morning stiffness lasting over 3-4 hours) (**Table 1**).

Due to failure of the treatment with adalimumab and the aggressive prolonged course of relapsing polychondritis, we decided against switching to another anti-TNFα agent. The high cost of IL-6 inhibitors and rituximab, which are not reimbursed for ankylosing spondylitis or relapsing polychondritis, supported the decision to initiate treatment with the IL-17 inhibitor secukinumab at a dose of 150 mg subcutaneously (in July 2023). After 3 months of treatment, the dose was increased to 300 mg s.c. per month, resulting in an excellent clinical response and complete resolution of the symptoms (**Figure 3**).

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Table 1. Laboratory tests. Blood parameters at the onset of the relapsing polychondritis and their changes during treatment with bDMARDs. Notably, there was an improvement in acute-phase reactants such as ESR and CRP, as well as normalization of leukocyte and thrombocyte counts, reflecting the suppression of disease activity.

	Jan 2023	Feb 2023	July 2023	April 2024	Oct 2024	Reference ranges
WBC	20.35	20.5	19.22	10.85	5.97	3.5-10.5×10^{12}/L
RBC	4.62	3.84	4.52	4.47	4.75	4.2-5.4×10^{12}/L
HGB	100	82	105	123	120	120-160 g/L
MCV	71.6	70.1	74.8	74.7	73.4	82-92 fL
HCT	0.33	0.27	0.34	0.33	0.31	0.36-0.46%
PLT	434	305	610	407	430	140-440×10^{9}/L
ESR	88	97	94	22	20	0-15 mm/h
CRP	190.3	159	106.34	7.1	5.35	0-5 mg/L
Total protein	74.6	62.7	78.1	–	–	63-85 g/L
Albumin	24.8	29.4	41.5	–	–	35.0-52.0 g/L
ASAT	22.3	9.9	16.5	13.6	40.7	5-40 U/L
ALAT	38.6	13.7	22.5	9.4	37.9	5-40 U/L
Creatinine	65	57	64	60	61	58.0-100.0 µmol/L
Urea	3.8	4.4	3.1	3.6	4	2.8-8.3 mmol/L

bDMARDs – biologic disease-modifying antirheumatic drugs; WBC – white blood cells; RBC – red blood cells; HGB – hemoglobin; MCV – mean cell volume; HCT – hematocrit; PLT – platelets; ESR – erythrocyte sedimentation rate, ASAT – aspartate aminotransferase; ALAT – alanine aminotransferase; CRP-C – reactive protein.

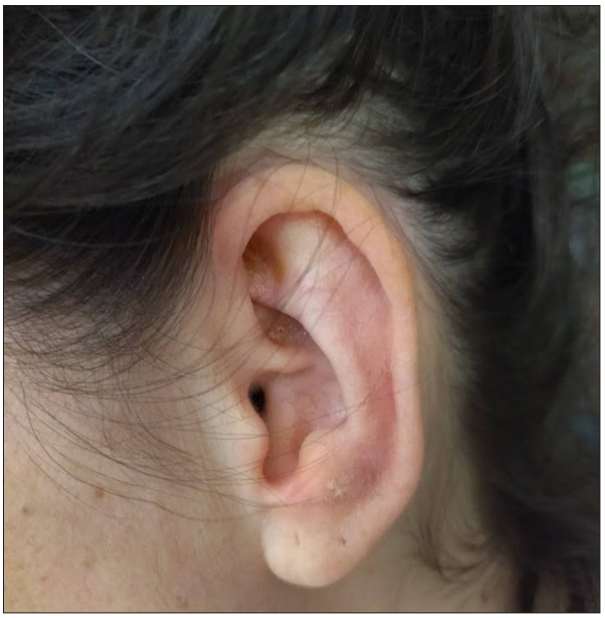

Figure 3. The ear after successful suppression of the disease activity, demonstrating near-complete recovery of normal anatomy.

Table 2. Diagnostic criteria for relapsing polychondritis.

Diagnostic criteria
McAdam's criteria (3 or more of the following clinical features required) [13]
(a) Bilateral auricular chondritis
(b) Nonerosive seronegative inflammatory polyarthritis
(c) Nasal chondritis
(d) Ocular inflammation
(e) Respiratory tract chondritis
(f) Audiovestibular damage
Modified Damiani criteria (1 of the following required) [14]
(a) At least 3 of McAdam's diagnostic criteria
(b) One or more of McAdam's findings with positive histologic confirmation
(c) Chondritis at 2 or more separate anatomic locations with a response to treatment

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That allowed for the slow tapering and discontinuation of the corticosteroids (Table 1). An 18-month follow-up of the patient revealed 3 mild exacerbations (characterized by slight sensitivity and redness in one or both ears), with symptom-free periods in between. These exacerbations were triggered by acute respiratory tract infections and managed with the addition of low doses of methylprednisolone (8 mg daily), followed by rapid tapering and discontinuation of the corticosteroids within 15 days. No adverse effects related to the treatment with secukinumab were detected.

Discussion

Four years after the initial diagnosis of ankylosing spondylitis and following her second delivery, the coexistence of refractory and aggressive relapsing polychondritis presented a serious challenge for treatment and disease outcome. The diagnosis was based on McAdam's [13] and the modified Damiani [14] diagnostic criteria for relapsing polychondritis (Table 2).

The disorder is characterized by clinical polymorphism [4]. The second most common clinical manifestation, after nasal and auricular chondritis, is arthritis. It is present in 50% to 85% of patients with relapsing polychondritis [1]. Various patterns of involvement may occur, including erosive or nonerosive arthritis, lupus arthritis or spondyloarthropathy [15]. McAdam et al reported that 25 to 35% of patients with relapsing polychondritis have a concurrent autoimmune disease [13]. The combination of ankylosing spondylitis and relapsing polychondritis is relatively rare. Only a few cases have been reported [16,17], with the incidence of these co-morbidities being approximately 13%.

Due to the saddle nose deformity as part of the differential diagnosis, we considered granulomatosis with polyangiitis or Cogan's syndrome; however, the bilateral auricular involvement excludes these diseases. Another condition with a similar clinical presentation is bacterial infection of the pinna, which can be distinguished by unilateral involvement, including the earlobe. Trauma to the ear presenting with redness and pain can also be mistaken for relapsing polychondritis.

The co-existence of relapsing polychondritis and other autoimmune diseases, along with positive reports regarding their treatment with bDMARDs, raises several questions about common pathways. To date, more than 1000 cases have been reported [4], all emphasizing the need for a more detailed understanding of the pathogenesis and the search for additional reliable and effective treatment options. Biya et al reported that anti-TNFα inhibitors are effective in 67.8% of men and 60.1% of women with relapsing polychondritis [18]. Azevedo et al reported a case of relapsing polychondritis after treatment with etanercept for ankylosing spondylitis [19]. Fernando et al performed a literature review regarding treatment of relapsing polychondritis with biologics. There were reports discussing treatment with TNFα blockers (n=43), rituximab (n=11), anakinra (n=5), tocilizumab (n=2), and abatacept (n=1). Biologics were effective in 27 patients, partially effective in 5 patients, and not effective in 29 patients [20]. Zheutlin et al reported a patient with ankylosing spondylitis and secukinumab-induced relapsing polychondritis [11]. Other authors reported a worsening of relapsing polychondritis with the use of an IL-17 inhibitor [21].

The main limitation of the present report is that this is not a case series; however, it highlights the potential success of IL-17 inhibition.

Conclusions

Relapsing polychondritis is a severe disease with a high mortality rate. In recent years the prognosis has become much more favorable thanks to new medications such as bDMARDs. It is important for other specialists to be familiar with this diagnosis, as timely recognition and appropriate treatment are crucial for improving the disease outcome. More extensive research into the pathogenesis and treatment of relapsing polychondritis is needed. The existence of various reports on the controversial effects of the treatment with different bDMARDs raises several questions, including whether the onset of relapsing polychondritis is a side effect of the use of biologics or if it is an autoimmune disease that occurs or progresses independently of the treatment. This is the first time that the use of an anti-IL-17 agent is reported to have successfully suppressed an aggressive, progressive form of the disease without any symptom-free period before the initiation of secukinumab.

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Statement

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Consent for Publication

The patient was informed that the images will be used in a scientific publication and gave consent for publication of the images and data.

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Declaration of Figures' Authenticity

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