

The association of relapsing polychondritis and spondylarthritis – three case reports

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ABSTRACT

Background. Relapsing polychondritis (RP) is characterized by recurrent episodes of progressive inflammation that lead to the destruction of cartilaginous structures. The etiopathogenesis is not fully elucidated, but it seems to be an immune-mediated mechanism directed against type 2 collagen.

Case reports. We present a series of 3 clinical cases, which associate RP and spondylarthritis – a woman with psoriatic arthritis (PsA) and two men with ankylosing spondylitis (AS). All cases presented with auricular chondritis, which is the emblem of RP. In the PsA case, RP presented typically, with recurrent auricular chondritis, manifested clinically with a cauliflower-like appearance of the ears. In one of the AS cases, a paradoxical immune reaction related to biological therapy was considered in the differential diagnosis of RP. In the other AS case, the patient had a single episode of chondritis, the recurrence of the disease remains to be proved.

Conclusions. The diagnosis of RP is usually based on clinical evidence and the elimination of differential diagnoses, since there is no specific laboratory or imaging test. In 20-30% of cases, RP is associated with other conditions, most frequently with vasculitis, but the association of RP with spondylarthritis is rare.

Keywords: relapsing polychondritis, ankylosing spondylitis, psoriatic arthritis

List of abbreviations (in alphabetical order):

ACPA – anti-citrullinated protein autoantibodies
 ANA – antinuclear antibodies
 ANCA – antineutrophilic cytoplasmic antibody
 ASDAS – Ankylosing Spondylitis Disease Activity Score
 BASDAI – Bath Ankylosing Spondylitis Disease Activity Index
 CRP – C-reactive protein
 CT – computed tomography
 DAPSA – Disease Activity index for Psoriatic Arthritis

ELISA – enzyme-linked immunosorbent assay
 ESR – erythrocyte sedimentation rate
 FLAIR – fluid attenuated inversion recovery
 HLA – human leukocyte antigen
 MRI – magnetic resonance imaging
 NSAIDs – non-steroidal anti-inflammatory drugs
 PsA – psoriatic arthritis
 RF – rheumatoid factor
 RP – relapsing polychondritis
 TNF – tumor necrosis factor

INTRODUCTION

Relapsing polychondritis (RP) is a rare systemic disease, primarily affecting the cartilage of the ears, nose and respiratory tract. It may also affect other

organs or tissues, particularly the joints, eyes, cochle-ovestibular system, skin and cardiovascular system. It can sometimes be associated with a myelodysplastic syndrome. RP usually begins in middle-aged indi-

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viduals (typically 40–55 years of age), but it can occur at any age. There is a discrete female predominance, less marked than in other autoimmune diseases. RP is a long-lasting and often unpredictable disease, evolving with flares and remission periods of variable length [1]. The etiology of RP is unknown, and the pathogenesis appears to be mediated by an autoimmune reaction to type 2 collagen, which is abundant in cartilage and sclera. Auricular chondritis is the most common clinical manifestation and is often the main presenting feature. It leads to erythematous inflammation and swelling of the external ear, sparing the lobule. Repeated episodes of chondritis may lead to permanent damage, such as cauliflower ear, extensive calcification or limp pinna (the forward listening ear). The conductive hearing loss may be experienced because of inflammation of the external auditory meatus. Ocular manifestations of RP are also common, such as scleritis, usually anterior, or episcleritis, conjunctivitis, keratitis and uveitis. Nasal chondritis is less common than auricular chondritis, but it follows a similar course. It is characterized by painful inflammation of the nasal cartilage and can lead to permanent damage in the form of a saddle-nose deformity. Costochondritis and arthralgia are commonly reported in RP patients. Peripheral joint disease in RP is asymmetrical and intermittent and affects both small and large joints, with axial sparing. It is usually a non-destructive, non-erosive, seronegative inflammatory oligo/polyarthritis. Tenosynovitis has been reported, although rarely. Up to half of patients with RP will develop respiratory problems during the course of the disease. Laryngeal chondritis occurs in more than half of patients and may present with hoarseness, tenderness of the tracheal rings, cough, breathlessness and stridor [2].

The diagnosis of RP requires a broad differential diagnosis, starting with infections (especially erysipelas) and ranging from sunburn to lymphoma. It should be noted that in infections and other diseases, auricular chondritis is not limited to the cartilaginous part of the external ear [3].

CASE REPORT 1

A 42-year-old smoking urban-dwelling woman developed in September 2021 inflammation of the left ear, followed shortly by the right one, which spontaneously remitted after 3 days. In November 2021, she reported swelling of hand joints which responded to NSAIDs. In January 2022, bilateral auricular chondritis reappeared, multiple cultures were negative for infection, but prophylactic antibiotic therapy and NSAIDs were administered. MRI of the head showed an infiltrated appearance of the external ears, with FLAIR hypersignal in the skin, subcutaneously, on the anterior side of the earlobe and cartilage, respecting the subcutaneous fatty layer on the posterior side of the earlobe, which had a fatty signal (Figure 1). In March 2022, the patient presents with hand arthritis, elevated acute phase reactants (ESR = 44 mm/h, CRP = 5.8 mg/L, normal < 5), positive RF (25 IU/mL, normal < 20), but negative IgG ANA, ACPA, p-ANCA and c-ANCA. At this stage, the diagnosis of RP was made and treatment with methotrexate (gradually to 20 mg/week) and prednisone (5 mg/day) was initiated. The patient independently stopped methotrexate in August 2022, and continued with prednisone with over-the-counter NSAIDs. In December 2022 she relapsed, presenting bilateral ear swelling, pain, erythema, without involving the auricular lobe, but leading to conduction hearing loss and bilateral tinnitus (Figure 2). Small,

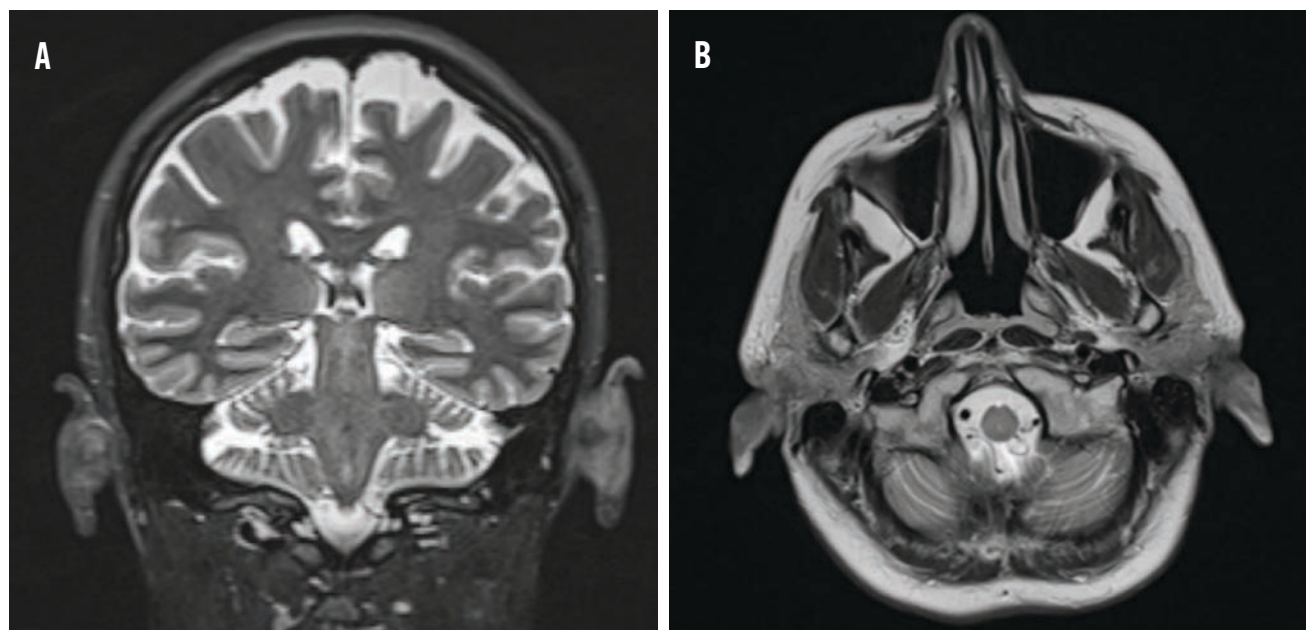


FIGURE 1. Case 1 – Head MRI showing bilateral chondritis (left, STIR; right, T2)



FIGURE 2. Case 1 – Clinical aspect of RP

painful retro-auricular ganglia were palpable. The patients also had asymmetrical hand arthritis of the proximal and distal interphalangeal joints, with low prehension force (Figure 3). Hand X-rays revealed periarticular erosions and periostitis, without carpal involvement (Figure 4), while foot and sacroiliac X-rays were normal. Hand ultrasound noticed the same erosions, but also power Doppler-positive synovitis (observable also on the palmar side). Laboratory

tests revealed and ESR of 70 mm/h, CRP of 19 mg/L, positive RF (33.6 IU/mL, normal < 30), negative ANA (by ELISA) and ACPA. Lung X-rays and CT were normal. Consequently, a diagnosis of psoriatic arthritis (PsA) was made, presenting with high disease activity (DAPSA = 28.1). Leflunomide (20 mg/day) and prednisone (15 mg/day, in progressively lower doses) were started. After 3 months, the patient had the same swollen and tender joints, RP remitted and acute

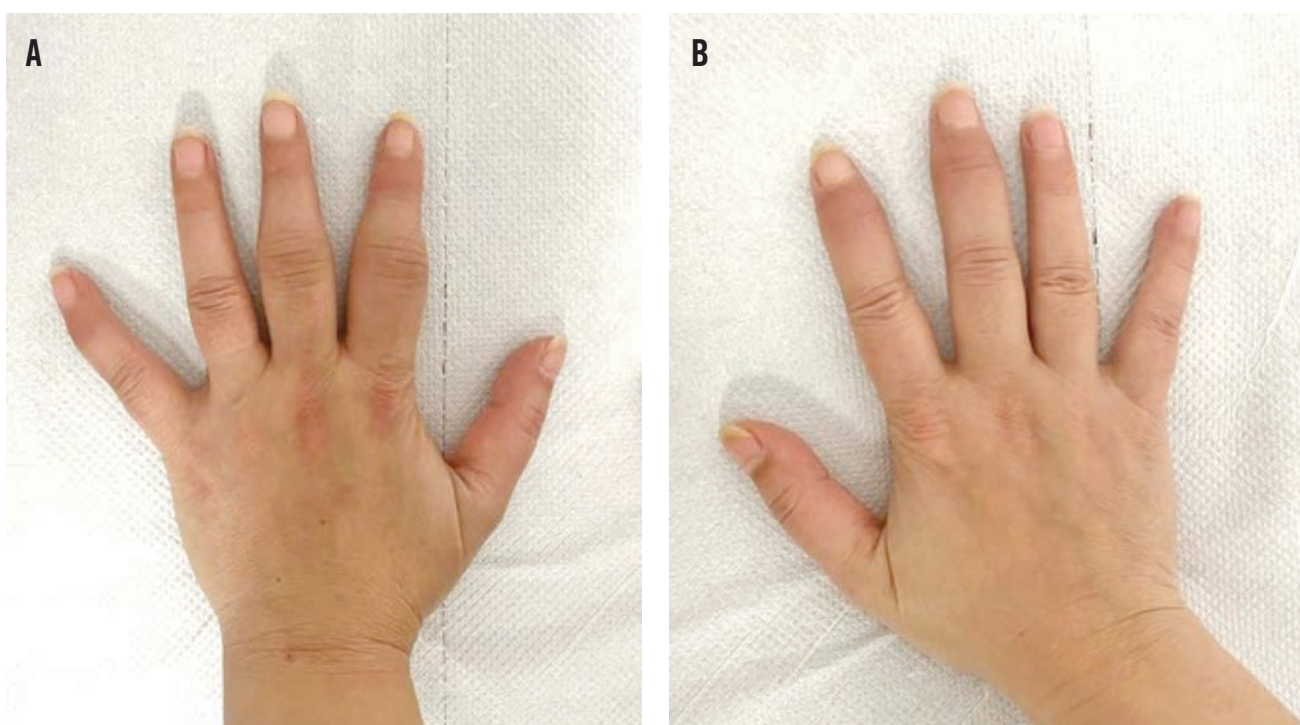


FIGURE 3. Case 1 – Clinical aspect of hand arthritis



phase reactants were normal. In June 2023, the patient stopped leflunomide because of a diarrheal syndrome and ear damage secondary to RP persisted, taking a more severe form (Figure 5), accompanied by inflammatory biological syndrome (ESR = 40 mm/h, CRP = 9.6 mg/L). Methotrexate was again recommended (20 mg/week), in association with prednisone (7.5 mg/day). In October 2023, the patient presented with painless swelling of hand joints and improved hand functionality. Hand ultrasound revealed fewer and inactive synovitis. She continued methotrexate and decreased prednisone to 5 mg/day.

FIGURE 4. Case 1 – Hand X-rays showing erosions and periostitis



FIGURE 5. Case 1 – Clinical aspect of relapsed chondritis

CASE REPORT 2

A 46-year-old urban-dwelling smoking man, with history of alcohol abuse, NSAIDs consumption for chronic back pain and psoriasis vulgaris, presented with physical asthenia and fatigue, abdominal pain and melanic stool, weight loss of 5 kg in the last 3 months and febrile episodes (undocumented during hospitalization). Laboratory tests indicated severe iron-deficiency anemia (hemoglobin = 6.1 g/dL), thrombocytosis and leukocytosis, accompanied by an important inflammatory biological syndrome (ESR = 140 mm/h; CRP = 89 mg/L, normal < 5). Upper digestive endoscopy observed only a small transhiatal gastric herniation. The patient's severe iron deficiency anemia was partially corrected by transfusion with 2 units of erythrocyte mass. During hospitalization in the internal medicine department, the patient developed swelling, pain and erythema of the nasal root (suggestive for chondritis) which was relieved under paracetamol, followed by chondritis of the left ear. He also complained of inflammatory back and knee pain. Thus, he was referred to the rheumatology department with: pain, swelling and erythema of the left ear, sparing the ear lobe (Figure 6); inflammatory back pain with significant functional impairment (evolving for 5 years, initially

classified as sciatica, with progressive worsening in the past year and requiring daily NSAIDs, inducing reduced spine mobility indices: Schober test 2 cm, lateral flexion 14 cm, finger-to-floor distance 23 cm, chin-sternum distance 5.5 cm, occiput-to-wall distance 1 cm); left knee and left ankle arthritis; and psoriatic lesions on the left elbow. Laboratory tests indicated severe iron deficiency anemia (hemoglobin = 7.7 g/dL), decreasing thrombocytosis and leukocytosis, important biological inflammatory syndrome (ESR = 110 mm/h; CRP = 126 mg/L), positive HLA-B27, negative RF and ACPA. X-rays of the pelvis revealed third stage bilateral sacroiliitis (Figure 7), while X-rays of the dorsal spine, hands, forelegs and lungs were normal. The diagnoses of highly active ankylosing spondylitis (AS) with peripheral involvement (BASDAI = 6.2, ASDAS = 5.37) and RP were made and the patient received in-hospital treatment with intramuscular dexamethasone (8 mg/day) and oral colchicine (1 mg/day). The episode of ear chondritis subsided shortly after this regimen. During follow up, RP did not relapse, but persistent AS activity prompted the initiation of infliximab in September 2023, with a significant clinical and biological response.



FIGURE 6. Case 2 – Unilateral left ear chondritis



FIGURE 7. Case 2 – Sacroiliac X-rays showing bilateral sacroiliitis

CASE REPORT 3

A 61-year-old smoking man, from an urban environment, diagnosed with AS since 1993, failed multiple NSAIDs and, because of persistent very high disease activity, started parenteral original infliximab in January 2020. In October 2020 he presented to a cardiology service for persistent anterior chest pain, subsequently associating fever. Chest CT noted consolidations with bilateral basal atelectatic appearance and pleuro-pericarditis (confirmed by ultrasound). Because of the difficult positioning of the pericardial fluid collection, puncture was not performed. The suspicion of tuberculosis could not be ruled out despite repeated negative QuantiFERON tests. Even though the etiology of the pleuro-pericarditis could not be established, the patient had significant improvement with NSAIDs (ibuprofen, later lornoxicam), colchicine and doxycycline. When stable, infliximab was switched to secukinumab (150 mg/month) for prudence. In June 2021, he presented fever, erythema, pain and swelling of the right ear and nasal pyramid. The diagnosis of chondritis of the right ear was made, for which he received systemic antibiotic treatment (cefuroxime, later amoxicillin with clavulanic acid) and local treatment (ethacridine lactate, ciprofloxacin ear drops and glucocorticoid ointment), without clinical benefit. Soon after, he also developed left knee and ankle arthritis, worsened inflammatory back pain, asthenia, loss of appetite and weight loss of 6 kilograms in the last month.

Clinical examination also found dactylitis of the second toe from the right foot. Sulfasalazine (up to 3 g/day) to address the AS peripheral manifestations and oral methylprednisolone (16 mg/day) for RP were added. AS disease activity and clinical RP persisted, therefore treatment was switched from secukinumab to etanercept (50 mg/week) in combination with sulfasalazine, and respectively from methylprednisolone to colchicine (1 mg/day). Under this regimen, chondritis remitted and AS activity dropped to low.

DISCUSSION

Approximately 20-30% of RP cases are associated with other diseases, most frequently with vasculitis [1], but the association with spondylarthritis is rare [4-12]. The treatment is guided according to the clinical manifestations and their severity, but there are no randomized clinical trials, only the opinion of experts. In mild cases, glucocorticoids are used in small and medium doses, but also colchicine and dapsone. In resilient clinical forms, methotrexate and biological therapies are used [1]. A 2022 review that included 11 clinical trials with a total of 177 patients revealed variable results, but the best response clinical responses were attained with methotrexate, infliximab, adalimumab and tocilizumab [3]. In cases presented above, axial and peripheral manifestations of spondylarthritis dictated the therapeutic decision. This overlap with spondylarthritis probably comes

as a therapeutic advantage, especially considering that anti-TNF agents are reimbursed by the public health system only for active spondylarthritis. On the other hand, a paradoxical immune reaction related to biological therapy or a rare manifestation of the disease should be considered for RP differential diagnosis. There have been few reports of patients with AS and PsA associated with RP and, among them, only 2 PsA patients who developed a single episode of chondritis during biological therapy, especially under anti-TNF agents, which resolved with glucocorticoids [5]. A paradoxical RP reaction has been reported to secukinumab [7]. In general, with the exception of one case, all associations presented a unique episode of RP.

CONCLUSION

RA and spondylarthritis are rarely associated. Anti-TNF agents and colchicine are efficient treatment options. The question arises whether RP is a paradoxical effect of spondylarthritis treatment, a

rare overlap syndrome or a rare disease manifestation of spondylarthritis.

Patient consent:

Patient consent was offered for scientific use and publication of medical data. Anonymity was assured.

Conflict of interest:

The authors declare that they have no conflicts of interest.

Author's contributions:

Conceptualization, DEM, CCP, CC; methodology, EADL, DEM, LE, CCP, CC; software, EADL, CCP; validation, EADL, DEM, LE, CCP, CC; writing—original draft preparation, EADL; writing—review and editing, EADL, CCP; supervision, DEM, LE, CC. All authors have read and agreed to the published version of the manuscript.

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REFERENCES

1. Arnaud L, Costedoat-Chalumeau N, Mathian A, Sailler L, Belot A, Dion J, et al. French practical guidelines for the diagnosis and management of relapsing polychondritis. *Rev Med Interne*. 2023;44(6):282-94. doi: 10.1016/j.revmed.2023.05.005. Epub 2023 May 24. PMID: 37236870.
2. Kingdon J, Roscamp J, Sangle S, D'Cruz D. Relapsing polychondritis: a clinical review for rheumatologists. *Rheumatology (Oxford)*. 2018;57(9):1525-32. doi: 10.1093/rheumatology/kex406. PMID: 29126262.
3. Petitdemange A, Szejkowski C, Damian L, Martin T, Mouthon L, Amoura Z, et al. Treatment of relapsing polychondritis: a systematic review. *Clin Exp Rheumatol*. 2022;40 Suppl 134(5):81-5. doi: 10.55563/clinexp/rheumatol/h9gq1o. Epub 2022 Jan 28. PMID: 35238756.
4. Park H, Gon Kim J, Kim WU. A Rare Case of Ankylosing Spondylitis Coexisting with Relapsing Polychondritis, Antiphospholipid Syndrome, and Myelodysplastic Syndrome. *Intern Med*. 2022;61(15):2367-71. doi: 10.2169/internalmedicine.8784-21. Epub 2022 Jan 13. PMID: 35022354; PMCID: PMC9424073.
5. Icacan OC, Yalcin Mutlu M, Yildirim F, Bes C. Relapsing Polychondritis in a Patient with Ankylosing Spondylitis under Two Different Tumor Necrosis Factor Alpha Inhibitors Treatment. *Clin Ter*. 2022;173(2):97-8. doi: 10.7417/CT.2022.2400. PMID: 35385029.
6. Duro T, Li S, Jose D, Khawar T. Polychondritis in a Patient With Ankylosing Spondylitis on an Anti-TNF-alpha Biosimilar Agent. *J Clin Rheumatol*. 2021;27(8S):S656. doi: 10.1097/RHU.0000000000001650. PMID: 35073638.
7. Zheutlin A, Schioppa E. Relapsing Polychondritis following Treatment with Secukinumab for Ankylosing Spondylitis: Case Report and Review of the Literature. *Case Rep Rheumatol*. 2018;2018:6760806. doi: 10.1155/2018/6760806. PMID: 30057845; PMCID: PMC6051248.
8. Azevedo VF, Galli NB, Kleinfelder AD, D'Ippolito JF, Gulin Tolentino A, Paiva E. Relapsing polychondritis in a patient with ankylosing spondylitis using etanercept. *Case Rep Rheumatol*. 2014;2014:353782. doi: 10.1155/2014/353782. Epub 2014 Sep 9. PMID: 25276463; PMCID: PMC4172987.
9. Bahiri R, Bzami F, Benbouazza K, Saoud B, Hajjaj-Hassouni N. Relapsing polychondritis and ankylosing spondylitis in the same patient. *Joint Bone Spine*. 2006;73(4):482-4. doi: 10.1016/j.jbspin.2005.12.011. Epub 2006 Apr 19. PMID: 16725363.
10. Lee HC, Tsai TF. Relapsing polychondritis-like ear disease responding to etanercept in two patients with psoriasis and psoriatic arthritis. *J Am Acad Dermatol*. 2011;64(5):1006-7. doi: 10.1016/j.jaad.2009.12.020. PMID: 21496717.
11. Raffayova H, Rovensky J. Concurrence of relapsing polychondritis and psoriatic arthritis. *J Clin Rheumatol*. 2002;8(2):120-2. doi: 10.1097/00124743-200204000-00014. PMID: 17041338.
12. Moraillon I, Pouget F, Cosnes A, Revuz J. Polychondrite chronique atrophiante et rhumatisme psoriasique [Relapsing polychondritis and psoriatic arthritis]. *Ann Dermatol Venerol*. 1991;118(11):815-6. French. PMID: 1789641.