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# COVID-19, a phantomatic trigger for relapsing polychondritis

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## ABSTRACT

Relapsing polychondritis (RP) is an auto-immune disease which affects the cartilaginous parts of sites like the ear, nose or upper respiratory tract. The condition can also involve other cartilage-containing structures such as the eyes, joints, the heart, kidneys and central nervous system. Early diagnosis of RPis essential for preventing significant damage to vital organs that can lead to increased morbi-mortality rates. First-line therapy in RP is systemic glucocorticoids, while in refractory cases monoclonal antibodies can be used despite scarcity of efficacy data available in published literature. The link between RP and neoplasia, especially hematological malignancy, should not be omitted when screening patients with suspicion of RP diagnosis.

The onset of COVID-19 pandemic has generated a new source of immune mediated pathologies, such as small vessel vasculitis, immune thrombocytopenic purpura or Guillain-Barre syndrome and other auto-inflammatory syndromes triggered by COVID-19 seem to unveil.

The present case depicts a female patient who presented with erythematous and painful areas of her right ear after priorly experiencing similar episodes in both ears and nose bridge shortly after having the COVID-19 vaccine booster dose.

**Keywords:** relapsing polychondritis, COVID-19, cartilage, inflammation, autoimmunity, immunosupression

## INTRODUCTION

Relapsing polychondritis (RP) is a rare auto-immune condition that affects the cartilaginous structures of the nose and ears, due to their increased proteoglycan content. Pathological findings can also be identified in other organs such as the upper respiratory airways, namely the larynx, tracheae, upper bronchi that are dense in cartilages, but also the heart, kidneys, eyes, central nervous system or joints [1].

The end of 2019 points to the beginning of the COVID-19 pandemic, the infection exhibiting tropism for the upper respiratory tract and, in some cases, by pulmonary involvement with irreversible pulmonary fibrosis. So far, the pathophysiology of the virus is not fully understood, but it has been shown that SARS-CoV-2 is capable of triggering changes of the immune system [1] and severe inflammatory events like the "cytokine storm" [2]. The consequence of this immune dysregulation ranges from the production of autoantibodies to the onset of rheumatic autoimmune disease, such as in inflammatory idiopathic myopathies, systemic lupus erythematosus, sarcoidosis, as well as isolated cases of systemic sclerosis and adult-onset Still's disease being reported [3]. The vaccine also sparked controversy due to some reported adverse events like Guillain-Barre syndrome, auto-immune hepatitis or even systemic erythematous lupus [4].

## CLINICAL CASE

A 51-year-old female patient is admitted with intense rash and swelling involving the upper part of the right ear; she confirms repeated inflammatory attacks in the last three months, alternating between ears, sometimes with the nose being involved. Despite undergoing multiple schemes of antibiotic

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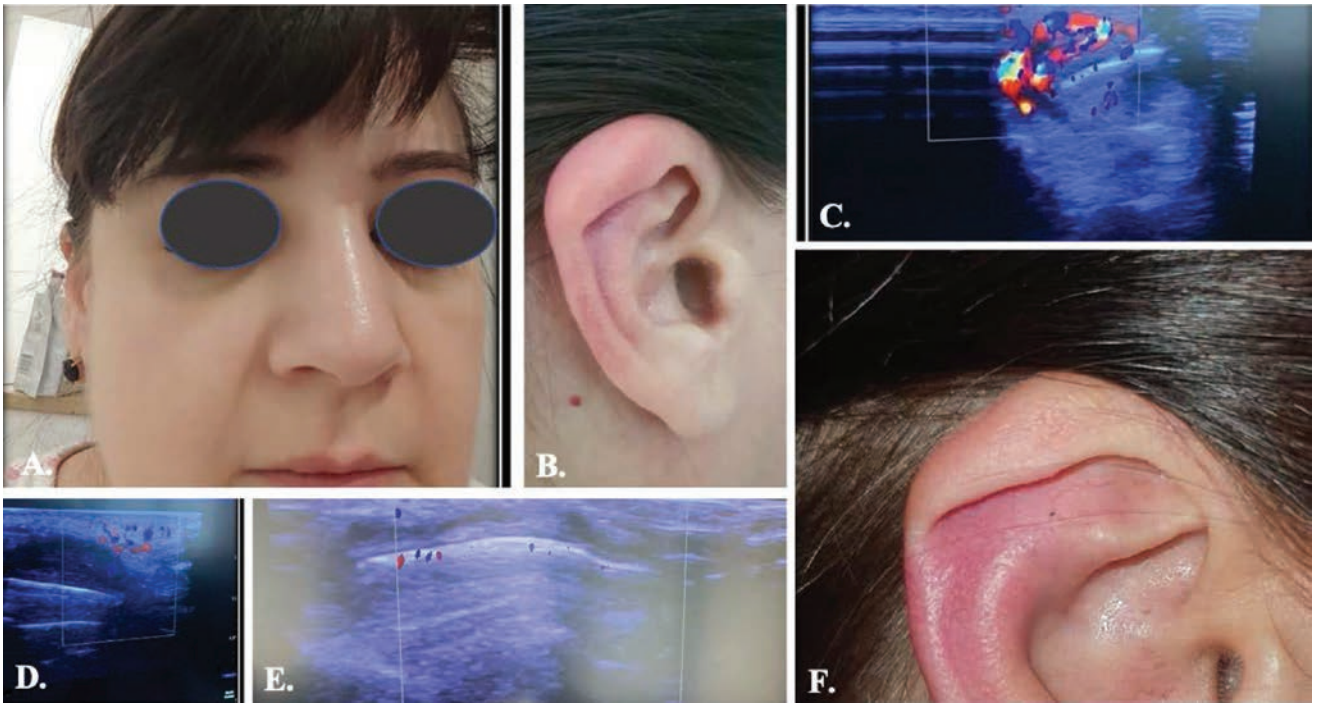


**FIGURE 1.** Figure A shows significant inflammation of the nasal bridge, figures B and F show inflammation of the upper part of both ears; figures C and D reflect the ultrasound examination with intense Doppler signal in both ear cartilages and figure E is a Doppler ultrasound of the nasal bridge

and non-steroidal anti-inflammatory drugs with incomplete clinical resolution, the patient continues having recurrent inflammatory signs of the cartilaginous areas. Eventually she receives a short course of medium-dose corticosteroids with significant clinical improvement, but early relapse after dose tapering. Patient's medical history is non-revealing except for a hysterectomy due to fibromatosis and a sinus tachycardia under beta-blocker treatment.

Patient admitted having a moderate COVID-19 infection in November 2021 that was treated with corticosteroids, but no hospitalization was imposed at the time. She confirms being fully vaccinated against SARS-CoV-2 with the booster dose being administered as well. The first inflammatory events first occurred two months after the SARS-CoV-2 infection.

Upon admission in the Rheumatology Department, an ultrasound was performed to assess the inflammatory state of the affected cartilages, confirming intense Doppler signal of the right ear and residual inflammation of the nose and the left ear (Figure 1).

The clinical setting with recurrent inflammatory episodes targeting the cartilaginous areas together with the ultrasound appearance led to establishing the diagnosis of relapsing polychondritis (RP) according to the McAdam criteria [1] and fulfilling the two major criteria, namely inflammation of both the auricular and nasal cartilage; however, no histopathological examination was available at the time. The temporal relation to COVID-19 vaccination is an indication of the disease trigger since the patient denied having previous infections.

Patient's paraclinical investigations revealed no significant changes, no positive autoantibodies or CT-scan suggesting a neoplastic association, ruling out a secondary cause for RP.

The case represents a mild phenotype of RP since the patient showed no organ involvement, including the upper respiratory tract and had no signs of associated malignancies or other autoimmune conditions. Corticosteroids in a tapering regimen together with methotrexate 10 mg weekly showed considerable benefit with no further signs of relapsing inflammatory events affecting the cartilages.

Since COVID-19 infection or vaccination and auto-immune pathologies are firmly linked in latest literature, authors can assume that this is a case of COVID19-induced RP [4,5,6]. Moreover, a similar case was previously published, leading to growing evidence that this viral infection can be responsible for RP.

## DISCUSSION

The disease was initially described by Jacks-Wartenhorst, however its recurrent pattern was mentioned in 1960, that allowed the development of diagnostic criteria to prompt early diagnosis and treatment initiation [7].

The estimated reported incidence of relapsing polychondritis is under 3.5 per million per year making it a rather rare condition. It mainly affects women in

their 4-5th age decade but pediatric cases have also been reported [8].

The autoimmune origin of the disease is supported by its frequent association with other auto-immune conditions, the presence of CD4 positive T lymphocytes in biopsies as well as the presence of autoantibodies targeting type II, IX and XI collagen. Moreover, the genetic background is considered to play a part, with human leukocyte antigen (HLA)-DR4 being more frequently reported [7,9].

Potential triggers of RP consist of mechanical stimuli such as local trauma like piercings that can expose antigens of the cartilaginous matrix, further inducing an autoimmune process. Certain drugs or supplement administration are thought to induce the onset of RP, as well as infectious agents that share structural similarities with cartilaginous autoantigens and can cross react. The development of the disease during pregnancy suggests possible hormonal involvement, but current data on this relationship is uncertain [9].

The most common clinical form of presentation is through mono or, more frequently, biauricular chondritis and the recurrent inflammatory attacks may come and go in days or weeks. In time, the tissue reparatory processes lead to the deformity of the outer ear that turns into a ”cauliflower”-like structure. Other signs and symptoms involving the ear may include vertigo, tinnitus and deafness which may be either a conductive hearing loss due to changes in the ear’s anatomy or neuro sensorial hearing loss because of recurrent inflammation [5,9].

Nasal chondritis is observed in a smaller number of patients and should be a warning sign for clinicians to thoroughly investigate because the vast majority are strongly associated with upper respiratory airway involvement. Similar to the ear changes in structure, the frequent inflammatory attacks followed by the reparatory cascade will lead to nasal bridge deformity, also known as ”saddle nose” deformity [7].

Due to the disease’s frequent association with other major pathologies, RP has been classified into three phenotypes, as follows: mild, respiratory and hematological. The hematological subtype indicates that the disease can be seen as a paraneoplastic syndrome since it signals the potential presence of bone marrow malignancies, namely myelodysplastic syndromes. The respiratory phenotype that encompasses nasal involvement, consists of tracheal narrowing due to erosion of the cartilaginous pieces, tracheal stenosis and decrease in the respiratory volumes. These patients are more prone to severe pulmonary infections, because of insufficient organ clearance [6].

Regarding RP treatment, using non-steroidal anti-inflammatory (NSAIDs) can be an initial step in non-severe, non-organ threatening cases. In patients who fail to respond to NSAIDs, systemic corticosteroids can be an option. In case of relapsesor intolerance to steroids, the treatment may include immunosuppression with cyclophosphamide, azathioprine, methotrexate, or cyclosporine. Dapsone can be used for chondritis or in case of disease flares. Despite not having enough evidence, TNF inhibitors, anti-interleukin (IL)-1 or anti-IL-6 can be used in severe cases as published case series confirm [7].

## CONCLUSION

When confronted with a case of RP, clinicians should consider investigating potential pulmonary involvement that can range from tracheal stenosis or laryngeal deformities to severe ventilatory obstruction, especially if the patient has a history of nasal inflammatory episodes [10].

The present case can be classified as a mild phenotype of relapsing polychondritis since the patient showed no involvement of the upper respiratory airways and had no signs of associated malignancies or other autoimmune conditions. A significant challenge in the presented case was electing the optimal treatment since the patient had difficulties tolerating corticosteroids and relapsed after discontinuation. As such methotrexate 10 mg weekly was initiated with progressive steroid tapering with considerable benefit and no further signs of relapsing inflammatory events affecting the cartilages.

With COVID-19 induced auto-immune pathologies being on the rise, we can assume that this case of RP was a response to the infectious disease, thus further research on the link is needed.

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