Case Report ISSN 2768-6647

Medical and Clinical Case Reports

Relapsing Polychondritis: A 'Revival' in the American Indian/Alaska Native population

Prashant Kaushik, MD[1], Kaylee I. Mach, BS[2], and Caleb S. Alexander, MPH[2]

[1]*Chief of Rheumatology, Northeastern Health System, Tahlequah, OK; Associate Program Director, Internal Medicine Residency Program, TMG/OMECO at NHS, Tahlequah, OK; Clinical Professor of Medicine, OSU CHS Cherokee Nation, Tahlequah, Oklahoma, USA.*

[2]*Oklahoma State University College of Osteopathic Medicine at the Cherokee Nation, Tahlequah, Oklahoma, USA.*

***Correspondence:**

Prashant Kaushik, M.D., F.A.C.P., F.A.C.R., Rh MSUS, Dip ABLM, 1373 E. Boone St., Suite 2300, Tahlequah, Oklahoma, Phone Number: (918) 207-0025, Fax Number: (918) 207-0226.

Received: 18 Feb 2024; **Accepted:** 22 Mar 2024; **Published:** 31 Mar 2024

Citation: Prashant Kaushik, Kaylee I. Mach, Caleb S. Alexander. Relapsing Polychondritis: A 'Revival' in the American Indian/Alaska Native population. Med Clin Case Rep. 2024; 4(2): 1-4.

ABSTRACT

Relapsing polychondritis (RPC) is a systemic inflammatory immune-mediated rheumatic disease (SIIRD) primarily affecting the cartilaginous structures within organs such as the ear, nose, joints, tracheobronchial tree, and cardiovascular system but it can also impact organs that are not primarily cartilage-based, such as skin, blood vessels, eyes and inner ear. Here we present 3 cases of RPC as an SIIRD from the American Indian/Alaska Native (AI/AN) population of the Cherokee Nation (CN), Oklahoma. After a single-case of RPC in a Zuni Indian patient published in 1971, to the best of our knowledge, this is the first publication of a series of RPC in the AI/AN population.

Keywords

Relapsing polychondritis, American Indian, Alaska Native, SIIRD.

Introduction

Providing state-of-the-art healthcare to certain ethnic populations like the AI/AN communities has been at the very least 'challenging' [1]. It is more so a tall order when it comes to a subspecialty like Rheumatology with a worsening nationwide shortage of Rheumatologists especially in rural communities [2].

In January 2021, the first Division of Rheumatology was started at the Northeastern Health System in Tahlequah, Oklahoma (the capital of the CN). It has since been providing full-time Rheumatology services to a large population, including Cherokee Natives, via a mixed-model offering both face-to-face and virtual Rheumatology visits. This mixed-model combination helps overcome the barriers to accessing care posed by distantly living rural AI/AN patients, while also mitigating the limitations of solely virtual appointments [3,4].

Case Reports

During the past 3 years, 3 new cases of RPC have been revealed to the aforementioned Rheumatology service. The demographic, clinicolaboratory, treatment and response details are summarized in Table 1. All 3 patients were Cherokee AI/AN. Auricular chondritis was recurrent and bilateral in Patients 1 and 2. Inner-ear/vestibuloauditory affliction led to a significant degree of unilateral sensorineural hearing loss and vertigo in Patient 3. Involvement of the nasal cartilaginous bridge caused a mild saddle nose deformity in Patient 2, which is stable.

Interestingly and intriguingly, tracheal and/or bronchial cartilaginous involvement has not been seen clinically in any of the 3 patients so far. The inflammatory arthritis in patients 1 and 2 was acute, polyarticular, additive, involving the small and large joints of all four extremities, seronegative and non-erosive radiologically. In patients 1 and 2, a biopsy of the clinically acutely inflicted pinna showed intense acute neutrophilic auricular necrotizing chondritis. In patient 3, the biopsy of palpable purpuric cutaneous lesions on

the shin showed classic findings of leukocytoclastic vasculitis (LCV).

Table 1: Features of the 3 RPC AI/AN patients.

	Patient 1	Patient 2	Patient 3
Age	35	47	61
Gender	Male	Male	Female
Ethnicity	AI/AN	AI/AN	AI/AN
Diagnostic-Hiatus	3 months	2 months	1 month
Auricular chondritis	Yes	Yes	No
Inner-ear involvement	No	No	Yes
Nasal chondritis	No	Yes	Yes
Ocular inflammation	Conjunctivitis	Episcleritis	Uveitis
LTR involvement	No	No	No
Inflammatory arthritis	Yes	Yes	No
Biopsy proven	Yes	Yes	Yes
Concomitant SIIRD	None	None	LCV
ANA, RF, CCP, MCV	Negative	Negative	Negative
ANCA/MPO/PR3	Negative	Negative	Negative
SPEP	Normal	Normal	Normal
Treatment	CS → Dapsone	CS + AZA → ADA	CS → AZA
Current status	Remission	Remission	Remission

RPC: relapsing polychondritis, AI/AN: American Indian/Alaska Native, Diagnostic hiatus = time-lag from the onset of symptoms to diagnosis and treatment of RPC, LTR: laryngotracheal/respiratory, SIIRD: Systemic inflammatory immune-mediated rheumatic disease, LCV: Leukocytoclastic vasculitis, ANA: Antinuclear antibody, RF: Rheumatoid factor, CCP: Cyclic citrullinated peptide antibodies, MCV: Mutated citrullinated vimentin antibodies, ANCA: Anti-neutrophil cytoplasmic, MPO/PR3: myeloperoxidase/proteinase 3 antibodies, SPEP: serum protein electrophoresis, CS: corticosteroids, AZA: azathioprine, ADA: adalimumab.

An underlying infectious or malignant condition was eliminated diligently in all 3 patients by a detailed clinically appropriate work-up. Family history was noncontributory in all 3 patients for any known SIIRD. Nonspecific constitutional symptoms such as fever, fatigue and malaise were not observed in any of the 3 patients. Clinically significant aortic or mitral valvular disease or the less frequent cardiac manifestations of RPC including pericarditis, heart block or myocardial infarction due to coronary arteritis were not seen in our 3 patients. Renal, central nervous system, gastrointestinal or hematological/bone marrow involvement has also not become conspicuous in the 3 patients so far.

Remission was successfully induced/achieved in all 3 patients with high dose corticosteroids (prednisone 1 mg/kg body weight, not to exceed 60 mg/d in a consolidated morning-dose followed by a gentle tapering schedule over several weeks). With an intention to serve as a disease-modifying anti-rheumatic drug (DMARD) therapy as well as a steroid-sparing agent, (anticipating long-term steroid-use), we initiated dapsone therapy in patient 1, and azathioprine therapy in patients 2 and 3; synchronously with corticosteroid therapy. Azathioprine was chosen in patient 3 due to associated inflammatory eye disease. Patient 1 is still requiring a low dose (2.5 mg daily) of prednisone in conjunction with dapsone, but is nearing a successful complete tapering off prednisone having been in remission for 2 years now. Patient 2 did not tolerate azathioprine well (significant nausea with persistent transaminitis and leukopenia), which led to its discontinuation. He has been successfully weaned off the prednisone since, and the RPC remains in remission for 18 months with the use of adalimumab monotherapy 40 mg subcutaneously every 2 weeks.

Discussion

The first case of RPC was described by Jaksch-Wartenhorst in 1923, while the term “relapsing polychondritis” was first used by Pearson, Kline and Newcomer in 1960 [5,6].

Case series describing RPC from all over the world have provided some insight into demographics of age, ethnicity, and gender. The average age of adult-onset RPC is typically between 40 and 60 years of age; however, the age range at disease onset can be 4–93 years (a roughly similar prevalence in different populations; however, due to the rarity of the disease, there is a scarcity of comprehensive epidemiological studies across different ethnic groups) [7]. Contrary to a commonly held notion, RPC might not be so very rare. Literature mentions 23 patients seen from 1960-1975, with a total of 159 reported cases by 1976 [8]. Data from the Mayo clinic in the 1980's found an incidence of RPC in the United States of 3.5 cases per million [9]. Although widely believed that RPC is most prevalent in White individuals, there is no clearly defined predilection for any specific ethnic group. In the AI/AN population, there has been a sheer paucity of publications on RPC. One case of RPC was published in 1971 in a Zuni AI/AN patient [10]. Ever since then, over the past 50+ years, there has not been any description of RPC in the AI/AN population, to the best of our knowledge based on a diligent literature-search.

The initial diagnostic criteria of RPC - the McAdam's criteria - required meeting three out of six of the following: bilateral auricular chondritis, nasal chondritis, nonerosive seronegative inflammatory arthritis, ocular inflammation, respiratory tract chondritis, and audiovestibular damage [8]. Modifications to these criteria were proposed due to the variability of clinical manifestations occurring at any given point in time. According to the modified criteria, one of the following is required: At least three of McAdam’s diagnostic criteria OR one or more of the clinical findings included in the McAdam’s criteria, with positive histologic confirmation OR chondritis at two or more separate anatomic locations with a response to corticosteroids and/or dapsone [11]. Yet another set of modified criteria requires proven inflammation in at least two of three areas including the nasal, auricular, or laryngotracheal cartilages OR proven inflammation in at least one of the previously mentioned cartilaginous areas plus two other symptoms including ocular inflammation, seronegative inflammatory arthritis, vestibular dysfunction, or hearing loss [12]. All 3 of our AI/AN patients fulfilled McAdam’s criteria as well as both the modified versions.

Cardiovascular and respiratory complications of RPC are associated with high morbidity and mortality [12]. None of our 3 patients have had these complications so far, fortunately. In the only available case-report of RPC published in a Zuni AI/AN patient published in 1971, costochondral, laryngotracheal, or cardiovascular involvement was also not seen [10]. Unilateral or bilateral external ear inflammation is the most common presenting feature of RPC (seen in approximately 40 percent of patients; however, it eventually appears in nearly 90 percent of patients); other areas that can be involved in RPC include the nose, costal cartilage, airways, skin, eyes, heart, vasculature, musculoskeletal system, kidneys, and nervous system; and up to one-third of patients with RPC can present with a recognizable form of systemic vasculitis, connective tissue disease, another autoimmune disorder, or a malignant condition [13] (only 1 of our 3 patients had identifiable vasculitis; none had a malignancy). Muco-cutaneous manifestations can affect up to a third of the patients with RPC, and include aphthous ulcers, papules, pustules, purpura, nodules, livedo reticularis, superficial thrombophlebitis, and neutrophilic dermatosis [14]. Due to paucity of a randomized clinical study in RPC, treatment remains empirical to date. In a recent systematic review of available evidence regarding the treatment of RPC, while conventional synthetic disease modifying anti-rheumatic drugs (DMARDs) like methotrexate and azathioprine are still used widely, tumor necrosis factor alpha inhibitors, abatacept (a selective T-cell costimulation blocker), and tocilizumab (an interleukin-6 antagonist) were the biologic DMARDs associated with the best outcomes [15]. One of our patients (Patient 2) has responded stupendously to adalimumab, a TNFi with a sustained remission for 18 months now. Given its multisystem complex clinical nature, and lack of specific laboratory biomarkers so far, patients with RPC, especially in remote rural areas with a shortage of Rheumatologists can often experience delays in proper diagnosis and treatment. This can adversely affect their quality of their lives and overall prognosis. Moreover, patient management is limited/complicated by the lack of approved metrics to gauge the disease's severity [7]. The average diagnostic-hiatus/time-lag to diagnosis/treatment in our 3 patients was only 1.5 months, which is relatively comforting.

RPC can occur in patients with other SIIRDs such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and the syndrome of remitting, seronegative, symmetrical synovitis with pitting edema (RS3PE) [16]. Only 1 of our patients [Patient 3] had LCV as a concomitant SIIRD to the RPC. None fulfilled the criteria for RA, SLE or RS3PE.

Revelations continue to appear on the screen of consciousness in the realm of RPC. Serum cartilage oligomeric matrix protein (COMP) is being investigated as a potential biomarker of disease activity in RPC [17]. More recently VEXAS (Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic) syndrome, a disease due to mutations in UBA1 gene, has been identified as the cause of 8% of the patients with a clinical diagnosis of RPC [7,18]. This suggests that VEXAS is likely the cause of a previously described "hematologic subgroup" in RPC. However, none of our patients has gone on to develop features of this syndrome so far.

To sum up, RPC still remains a very infrequently identified/described/published disease in the AI/AN population. It is a challenging SIIRD, both diagnostically and therapeutically. Time is of the essence to lessen the burden of potentially severe morbidity and mortality from this condition. Although RA and SLE have been studied to some extent in the AI/AN population, RPC is still seeking attention. This article is a humble, earnest endeavor towards a continuing effort aimed at increasing the level of awareness about the un/under-recognized presence of RPC amongst the healthcare providers 'serving the deserving yet underserved' AI/AN population.

References

1. Sequist TD. Improving the Health of the American Indian and Alaska Native Population. JAMA. 2021; 325: 1035-1036.
2. Lennep DS, Crout T, Majithia V. Rural health issues in rheumatology: a review. Curr Opin Rheumatol. 2020; 32: 119-125.
3. Kaushik P, Bastible S, Marak C. On telemedicine in rheumatology. Arthritis Care Res. (Hoboken). 2022; 75: 1385-1386.
4. Kaushik P, Ashraf A, Marak CP, et al. Virtual Rheumatology during COVID-19: 'A gift in a seemingly ugly package'. Oklahoma State Medical Proceedings. 2021; 5: 2.
5. Jaksch-Wartenhorst R. Polychondropathia. Wiener Archiv für Innere Medizin. 1923; 6: 93-100.
6. Pearson CM, Kline HM, Newcomer VD. Relapsing polychondritis. New Engl J Med. 1960; 263: 51-58.
7. Mertz P, Sparks J, Kobrin D, et al. Relapsing polychondritis: Best Practice & Clinical Rheumatology. Best Pract Res Clin Rheumatol. 2023; 37: 101867.
8. McAdam LP, O'Hanlan MA, Bluestone R, et al. Relapsing polychondritis: prospective study of 23 patients and a review of the literature. Medicine (Baltimore). 1976; 55: 193-215.
9. Chopra R, Chaudhary N, Kay J. Relapsing polychondritis. Rheum Dis Clin North Am. 2013; 39: 263-276.
10. Barrow MV, Hummel EE Jr. Relapsing polychondritis in a Zuni Indian. Arch Intern Med. 1971; 127: 950-952.
11. Damiani JM, Levine HL. Relapsing polychondritis--report of ten cases. Laryngoscope. 1979; 89: 929-946.
12. Michet CJ Jr, McKenna CH, Luthra HS, et al. Relapsing polychondritis: survival and predictive role of early disease manifestations. Ann Intern Med. 1986; 104: 74-78.
13. Kent PD, Michet CJ Jr, Luthra HS. Relapsing polychondritis. Curr Opin Rheumatol. 2004; 16: 56.
14. Ferrada MA. Clinical manifestations of relapsing polychondritis. 2024. https://www.uptodate.com/contents/clinical-manifestations-of-relapsing-polychondritis
15. Petitdemange A, Sztejkowski C, Damian L, et al. Treatment of relapsing polychondritis: a systematic review. Clin Exp Rheumatol. 2022; 134: 81-85.

16. Manganelli P, Delsante G, Bianchi G, et al. Remitting seronegative symmetrical synovitis with pitting oedema in a patient with myelodysplastic syndrome and relapsing polychondritis. Clin Rheumatol. 2001; 20: 132.

17. Kempta Lekpa F, Piette JC, Bastuji-Garin S, et al. Serum cartilage oligomeric matrix protein (COMP) level is a marker of disease activity in relapsing polychondritis. Clin Exp Rheumatol. 2010; 28: 553.

18. Beck DB, Ferrada MA, Sikora KA, et al. Somatic Mutations in UBA1 and Severe Adult-Onset Autoinflammatory Disease. N Engl J Med. 2020; 383: 2628-2638.