Unusual Presentation of Relapsing Polychondritis in a Patient with Human Immunodeficiency Virus and Reactive Arthritis

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Patient: Female, 58-year-old
Final Diagnosis: Relapsing polychondritis
Symptoms: Ear pain • eye pain
Medication: —
Clinical Procedure: —
Specialty: Rheumatology

Objective: Rare disease
Background: Relapsing polychondritis (RP) is an uncommon autoimmune condition that impacts cartilaginous structures involving the ears, nose, respiratory tract, and joints. Its etiology is unknown; however, it may be associated with other systemic autoimmune diseases, malignancy, and rarely with human immunodeficiency virus (HIV) infection. RP has a variable pattern at presentation and may be associated with constitutional symptoms such as fever and arthralgia, in addition to various auricular, ocular, respiratory, and cardiovascular manifestations. Auricular and ocular signs are the most common presenting features; however, idiopathic orbital inflammatory syndrome is considered a rare manifestation of the disease. Systemic corticosteroids are the mainstay of treatment, but immunomodulatory therapy may be required for refractory cases.

Case Report: We present a challenging case of RP in a 58-year-old woman with HIV controlled by highly active anti-retroviral therapy (HAART) and stable chronic reactive arthritis on sulfasalazine who developed unilateral auricular chondritis associated with contralateral idiopathic orbital inflammation and scleritis as well as worsening arthralgia. She was initially treated empirically with antibiotics, without clinical improvement. The infectious diseases work-up was unrevealing, and other diagnostic possibilities were meticulously excluded. Clinical suspicion for RP ultimately led to appropriate therapy with corticosteroids and subsequent immunosuppression with methotrexate, resulting in clinical improvement and allowing for gradual tapering of steroids.

Conclusions: RP is an uncommon multisystem disorder that can occur in the setting of other underlying chronic illnesses, as seen in our patient. It has a variable presentation and course, with no diagnostic laboratory tests; therefore, clinical suspicion is imperative for appropriate diagnosis and management.

Keywords: Arthritis, Reactive • HIV • Polychondritis, Relapsing

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Background

Relapsing polychondritis (RP) is an uncommon systemic immune-mediated inflammatory disease that affects organs rich with cartilage, such as the ears, nose, laryngotracheobronchial tree, and joints. Less commonly, RP can affect the kidneys, eyes, central nervous system, blood vessels, and heart [1,2]. RP affects up to 3.5 in 1 million people per year [3,4]. Higher prevalence is reported in the fourth and fifth decades of life, with a slight preponderance in white people [3,5].

An underlying autoimmune process has been attributed to the pathogenesis of RP; however, the exact etiology is still unknown [3]. RP has a variable pattern at presentation, which varies from non-specific symptoms such as fever and arthralgia to auricular, ocular, respiratory, and cardiovascular manifestations [2,3]. Auricular and ocular manifestations are considered the most common presentations of RP; however, periorbital signs have been reported infrequently [3,6-10].

The coexistence of RP with other autoimmune diseases has been found in 30% of cases, most commonly with rheumatoid arthritis, while an association with reactive arthritis has not been previously reported [3]. Furthermore, the co-occurrence of HIV and RP has been only mentioned in a few cases in the literature [11-14]. Systemic corticosteroids are the mainstay of therapy; nevertheless, immunomodulatory agents may be required for refractory cases [15].

RP diagnosis requires a high index of suspicion, particularly in early stages of the disease. Herein, we report a case of RP in 58-year-old woman with controlled HIV and stable reactive arthritis who developed unilateral auricular chondritis and idiopathic orbital inflammatory syndrome with scleritis. The infectious diseases work-up was unrevealing, and she ultimately responded well to corticosteroids along with methotrexate.

Case Report

A 58-year-old white woman with human immunodeficiency virus (HIV) infection and chronic reactive arthritis presented to our Emergency Department (ED) with a 2-week history of severe acute left eye pain, redness, and swelling associated with blurred vision, photophobia, and watery discharge, but no itching or loss of vision. Ophthalmology diagnosed left eye scleritis with corneal ulceration. She also reported right ear burning pain, redness, and swelling, but no discharge, tinnitus, or hearing loss, as well as loss of appetite and arthralgia. She denied shortness of breath, cough, change in voice, fever, oral ulcers, rash, joint swelling, weight change, change in bowel habits, or urinary symptoms. Her medical history is significant for HIV controlled on HAART (Darunavir/Cobicistat/Emtricitabine/Tenofovir alafenamide 800-150-200-10 mg), chronic reactive arthritis (HLA-B27 negative) diagnosed 12 years prior on sulfasalazine 2 g divided twice daily, and hypertension on lisinopril 5 mg daily. She endorsed a family history significant for an unknown malignancy in her father. She was a former smoker and denied alcohol or drug use.

In the ED, she was afebrile with stable vital signs, breathing comfortably with an oxygen saturation of 95% on room air. The physical exam was remarkable for right auricular erythema, swelling, and tenderness, with no ear discharge. There was left scleral redness with mild left eyelid erythema and swelling, along with clear watery discharge, but no change in vision (Figure 1A, 1B). The remainder of her physical exam, including chest and musculoskeletal exam, was unremarkable.

Laboratory investigations revealed white blood cell count 11 K/uL (normal 4.5-11.0 K/uL), hemoglobin at 11.9 g/dL (normal 12-16 g/dL), erythrocyte sedimentation rate (ESR) 67 mm/h (normal 0-15 mm/h), and C-reactive protein (CRP) 6.99 mg/dL (normal 0.00-0.74 mg/dL). Kidney and liver function test results were within normal ranges. Urinalysis was unremarkable for protein or active sediments. Her COVID-19 RT-PCR (reverse

Figure 1. (A, B) Views of left eye and right ear pre-treatment revealing right auricular erythema and swelling in association with left scleral erythema and left eyelids swelling. (C, D) Views of left eye and right ear after treatment, revealing significant improvement of auricular and ocular erythema and swelling.
tapers due to recurrence of left eye scleritis. Her course was prolonged prednisone taper.

Over the next 2 months, she failed multiple attempted steroid treatment (prednisone 40 mg twice daily and non-steroidal anti-inflammatory drugs) for idiopathic orbital inflammation/idiopathic orbital inflammatory syndrome (IOIS).

Computed tomography (CT) of the head without contrast was unremarkable. CT of facial bones, orbits, and sinuses showed left periorbital soft tissue swelling with mild induration in the intra-orbital fat without mass, asymmetry of the extraocular muscles or exophthalmos, consistent with idiopathic orbital inflammation (Figure 2). She was treated with 1 dose of intravenous methylprednisolone 125 mg and started empirically on cefazolin 1 g every 8 h.

An infectious diseases work-up for syphilis, tuberculosis, and Lyme disease was unrevealing. Blood and urine cultures remained negative. The CD4 count was 610 cells/μL (normal 430-1800 cells/μL) with an undetectable HIV viral load.

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An infectious diseases work-up for syphilis, tuberculosis, and Lyme disease was unrevealing. Blood and urine cultures remained negative. The rest of her autoimmune work-up was unrevealing, including anti-nuclear antibody, rheumatoid factor, complement C3 and C4 levels, anti-nuclear cytoplasmic antibody (ANCA), anti-dsDNA, and anti-SSA/SSB.

Relapsing polychondritis was diagnosed in the setting of left eye idiopathic orbital inflammation, scleritis, and right auricular chondritis. The patient was started empirically on prednisone 40 mg twice daily and non-steroidal anti-inflammatory drugs for pain control. She improved significantly with steroid treatment (Figure 1C, 1D) and was discharged home on a prolonged prednisone taper.

Over the next 2 months, she failed multiple attempted steroid tapers due to recurrence of left eye scleritis. Her course was complicated by steroid dysglycemia and she was started on insulin. Her HAART was switched to Bictegravir-Emtricitabine-Tenofovir Alafenamide 50-200-25 mg, as Cobicistat raises blood glucose levels. She additionally sustained 2 acute compression fractures of T6 and T7, attributed to long-term steroid use, despite a recent normal bone density scan. Steroid-sparing treatment with azathioprine 50 mg daily was initiated (after normal thiopurine methyltransferase activity was confirmed), which led to severe transaminitis with AST at 195 U/L (normal 10-42 U/L) and ALT 348 U/L (normal 10-60 U/L), resulting in discontinuation. Although an invasive scleral biopsy at a specialized center was considered, after her liver function tests normalized, she was cautiously treated with methotrexate 10 mg weekly and folic acid, and the methotrexate dose was titrated up to 15 mg weekly. Liver function tests remained within normal limits, and she demonstrated remarkable clinical improvement within approximately 2 months. Methotrexate 15 mg weekly was continued, and her prednisone dose was progressively tapered down to 5 mg daily, with a significant decline in her inflammatory markers, with CRP of 0.14 mg/dL (normal 0.00-0.74 mg/dL) and ESR of 12 mm/h (normal 0-15 mm/h).

Discussion

RP is an uncommon autoimmune disorder characterized by inflammation of multiple cartilaginous and connective tissues in the body, including the ears, nose, eyes, joints, skin, respiratory, central nervous, renal, and cardiovascular systems [16]. Although the etiology is unclear, it is believed that an autoimmune mechanism is involved in the pathogenesis of RP, which may be caused by autoantibodies to type II collagen in the cartilage [3,17]. RP has very diverse and non-specific presentations, which makes it challenging to diagnose, often leading to delays in management [3]. Patients with RP can present with fever, malaise, arthralgias, auricular and nasal chondritis, ocular symptoms, respiratory tract involvement manifested as cough, wheezing, and dysphonia, neurological, and cardiac valvular involvement [16]. Auricular chondritis is the most common manifestation in up to 80-90% of patients [3]. Ocular features are reported in up to 50-60% of cases, and the most frequent presentations are episcleritis, scleritis, and conjunctivitis [3]. However, orbital inflammatory syndrome is an uncommon presentation of RP and has only been reported in a few cases in the literature [6-10]. Idiopathic inflammatory orbital disease, also known as orbital pseudotumor, is a benign inflammatory condition of the orbit manifesting with pain, periorbital swelling, conjunctivitis, chemosis, and ophthalmoplegia. It is usually idiopathic but has been also associated with autoimmune diseases such as Crohn disease, RP, lupus erythematosus, and giant cell arteritis [8,18].
RP is associated with various other autoimmune disorders in approximately 30% of cases, such as systemic lupus erythematosus, vasculitis, Sjogren’s syndrome, and, most commonly, with rheumatoid arthritis [3]. However, its association with reactive arthritis has not been previously reported in the literature. The coexistence of RP and HIV has been reported in 5 cases in the literature; 2 of them had co-existing autoimmune disease (sarcoidosis and Bechet’s disease) and 1 case had acquired immunodeficiency syndrome (AIDS) [11-14]. In addition, RP is associated with malignancies, such as myelodysplastic syndrome (MDS), in 27% of cases [3]. A recent study by Beck et al suggested an association between myeloid-restricted X-linked somatic mutation in the UBA1 gene, a major enzyme in ubiquitylation, and some inflammatory rheumatologic syndromes such as RP, known as VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome, which has been reported to be more common in men [19]. Our patient did not have any hematologic findings suggestive of MDS. Interestingly, specific genetic testing of our patient was pursued, and was negative for the VEXAS/UBA1 mutation.

The diagnosis of RP is mainly clinical. McAdam et al established diagnostic criteria, which suggest the presence of 3 of the 6 following features for RP diagnosis: bilateral auricular chondritis, non-erosive seronegative inflammatory polyarthritis, nasal chondritis, ocular inflammation, respiratory tract chondritis, and audio-vestibular damage [20]. Damiani and Levine modified the prior criteria to the presence of 1 of the criteria described by McAdam with histopathological confirmation or 2 criteria with favorable response to corticosteroid or dapsone therapy [21]. In 1986, Michel et al published new criteria which require the presence of proven inflammation in 2 of 3 areas (auricular, nasal or laryngotracheal cartilage), or proven inflammation in the cartilage in 1 of these areas plus 2 other signs, including ocular inflammation, vestibular dysfunction, seronegative inflammatory arthritis, or hearing loss [16,22]. Our patient fulfilled the criteria proposed by Damiani and Levine for RP (auricular chondritis, ocular inflammation, and seronegative arthritis) with good response to corticosteroids and methotrexate [21]. Although our patient did not present with bilateral chondritis, patients often do not present initially with multiple areas of involvement. However, other diagnostic possibilities were meticulously excluded. Since our patient improved with corticosteroids and methotrexate, an invasive biopsy, with associated morbidity, was ultimately not required.

Mild RP can be treated with NSAIDs, dapsone, or colchicine. Corticosteroids are the treatment of choice in more severe forms of RP. However, immunosuppressive agents such as methotrexate, azathioprine, or cyclosporine can be used for refractory cases [3,5,15]. Our patient developed severe transaminis with a low dose of azathioprine, but interestingly was able to tolerate methotrexate well.

Most published cases of RP have presented with auricular inflammation and/or respiratory symptoms, but only a few cases manifested idiopathic orbital inflammation [1,2,16,17,23]. Those cases were commonly associated with ANCA vasculitis, ankylosing spondylitis, systemic lupus erythematosus, or Sjogren’s syndrome; however, none have been reported with reactive arthritis [1,24]. Only few reported an association with HIV infection [11-14]. The mainstay of treatment in most cases was systemic corticosteroids with or without immunosuppressive agents [1,2,16,17,23].

Conclusions

We present a unique patient with HIV and stable reactive arthritis who developed unilateral auricular chondritis associated with contralateral ocular scleritis, and idiopathic orbital inflammatory syndrome in the setting of a negative infectious diseases work-up, leading to a diagnosis of RP. Systemic corticosteroids along with methotrexate resulted in a favorable outcome.

Declaration of Figures Authenticity

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References: