When You “Can’t See” a Case of Relapsing Polychondritis

David Contreras, MD1, Navpreet Dhillon, BS1,2, Rupam Sharma, MD1,2, Varun Bali, MD1, Sabetian Katayon, MD1, Bao Quynh Huynh, MD1, and Arash Heidari, MD1,2

Abstract
Relapsing polychondritis (RP) is a rare and, if not treated, potentially lethal autoimmune disorder. Involvement of central nervous system (CNS) in RP is rare and, when present, makes it extremely difficult to diagnose. In this report, we present a case of a 22-year-old Hispanic woman who presented with sudden onset of headache and blurred vision. Magnetic resonance imaging (MRI) of her brain and orbit showed leptomeningeal enhancements in addition to asymmetrical thickening and enhancement of globes. Her lumbar puncture was consistent with aseptic meningitis picture, and she was placed on empirical treatment for presumptive CNS tuberculosis. Her vision deteriorated, and she was diagnosed with RP with CNS and ocular involvement and placed on high-dose steroids with dramatic rapid response. She has been on immunosuppressive treatment, including Sulfasalazine and Methotrexate, since then and her disease has been under control with decreased need for ophthalmic steroid drops. There have been only 19 previous cases found in literature reporting an association of RP with CNS involvement.

Keywords
relapsing polychondritis, aseptic meningitis, glucocorticosteroids, McAdam criteria, pleocytosis

Introduction
Relapsing polychondritis (RP) is a rare autoimmune disease that is characterized by inflammation of cartilaginous tissue, affecting particularly the ears, nose, respiratory tract, eyes, and joints.1 Most common presentation includes unilateral or bilateral inflammation of the external ear. This autoimmune disease affects 3.5 per 1 million people each year. Neurological involvement in RP is present approximately in 3% of cases with most common involvement of cranial neuropathies of the second, sixth, seventh, and eight nerves. Other clinical manifestations previously reported are stroke, meningoencephalitis, polyneuritis, and dementia.2 The presence of meningoencephalitis is a very rare neurological manifestation of RP, making the diagnosis extremely difficult for it is often missed or unrecognized for months to years. In this case report, a 22-year-old Hispanic woman with RP-related chorioretinitis and central nervous system (CNS) involvement manifested by decreased visual acuity and headache is presented.

Case Presentation
A 22-year-old Hispanic woman was in her usual state of health until she developed severe headache (8 of 10 scale) and blurred vision for last 5 days. She was seen at the ophthalmology clinic with marked reduction in vision of her right eye more than left that slowly progressed over 5 days. The patient reported this progressive loss of vision was interfering with her daily activities. She denied flashes of light and floaters in either eye. Her visual acuity examination showed right eye 20/70 and left eye 20/200. Her intraocular pressures and examination of conjunctivae, corneas, anterior chamber, and irises were within normal limits. The examination of posterior chamber after dilation revealed congestion of optic nerves and papilledema. There was subretinal fluid beneath the maculae and surrounding the optic nerves. Due to initial diagnosis of serous chiorioretinopathy and its underlying differential diagnosis of autoimmune, infectious, carcinomatous, or...
with contrast revealed generalized leptomeningeal enhancement with “sugar-coating” or “zuckerguss pattern” in her vermis region of cerebellum (Figures 1 and 2). Her orbital MRI showed increased signal thickening at the posterior aspect of globes and focal enhancements (Figure 3). Lumbar puncture showed an opening pressure of 150 mm H₂O, glucose 58 (normal range: 40-75) mg/dL, protein 46 (normal range: 15-45) mg/dL, WBC (white blood cell) 180 cells/μL, RBC (red blood cell) count 25, lymphocytes 96%, neutrophils 3%, and macrophages 1%.

She was started on empirical antifungal and antituberculosis medications due to the chronic aseptic meningitis picture. In the next following 15 days, she did not improve clinically and instead developed new symptoms. Her new symptoms included tinnitus in left ear, vertigo, hyperacusis, photophobia, retroorbital pain, and loss of color perception. She underwent 3 additional lumbar punctures to rule out increased intracranial pressure with similar cerebrospinal fluid (CSF) findings (Table 1). Comprehensive workup (Table 2) was unrevealing; therefore, her antifungal treatment was stopped.

Upon further detail intake of her medical history, it was found that she had an episode of epistaxis accompanied with nasal cartilage inflammation and nasal septal deviation in the past. She has complained of rib cage pain on multiple occasions and also endorsed joint stiffness and pain involving her hands and back in the past. Her chest x-ray (CXR) and hand x-rays were unremarkable. The thoracic spine x-ray revealed moderate degenerative arthritis. Her mother disclosed to have a known diagnosis of seronegative rheumatoid arthritis and it was always a fear that she had passed it to her daughter. She also mentioned that she sought medical evaluation for her daughter at the age of 12 but never followed up thereafter. On further examination, she was found to have thinning of bilateral pinna without erythema. She met the criteria and diagnosis of RP with chorioretinitis and CNS involvement. She was initiated on pulse therapy with high dose of methylprednisolone 1000 mg for 3 days. During her pulse therapy and following days after, her visual acuity improved, color vision returned, and vertigo and hyperacusis resolved.
Her multidisciplinary team decided to complete 12 months of empirical tuberculosis treatment and she was discharged on prednisone 60 mg daily with plan to slowly taper and move to steroid-sparing immunosuppression. Follow-up lumbar punctures showed significant improvement (Table 1). Her follow-up brain MRI also showed resolution of leptomeningeal enhancement and sugar-coating enhancements in her vermis. Since then, over the last 3 years she has been followed up in ophthalmology and rheumatology clinics. She also underwent several minor relapses of her chorioretinitis without CNS involvement. She is currently responding to sulfasalazine, methotrexate, and ophthalmic steroid drops.

### Discussion

Currently in literature, there are only 19 previously reported cases of RP with CNS involvement. Neurological involvement is an extremely rare complication in RP which occurs in only 3% of patients. Among the previous 19 cases, the average age of the patients was 56 years. What makes our case even more unique is that till date there have been no cases reported in literature in which the patient was below the age of 30 years. There is a report published of 13 men cases reported in literature in which the patient was below average age of the patients was 56 years. What makes our case even more unique is that till date there have been no cases reported in literature in which the patient was below the age of 30 years.3 There is a report published of 13 men cases reported in literature in which the patient was below average age of the patients was 56 years. What makes our case even more unique is that till date there have been no cases reported in literature in which the patient was below the age of 30 years.3 There is a report published of 13 men cases reported in literature in which the patient was below average age of the patients was 56 years. What makes our case even more unique is that till date there have been no cases reported in literature in which the patient was below the age of 30 years.3 There is a report published of 13 men cases reported in literature in which the patient was below average age of the patients was 56 years. What makes our case even more unique is that till date there have been no cases reported in literature in which the patient was below the age of 30 years.3 There is a report published of 13 men cases reported in literature in which the patient was below average age of the patients was 56 years. What makes our case even more unique is that till date there have been no cases reported in literature in which the patient was below the age of 30 years.3 There is a report published of 13 men cases reported in literature in which the patient was below average age of the patients was 56 years. What makes our case even more unique is that till date there have been no cases reported in literature in which the patient was below the age of 30 years.3 There is a report published of 13 men cases reported in literature in which the patient was below average age of the patients was 56 years. What makes our case even more unique is that till date there have been no cases reported in literature in which the patient was below the age of 30 years.3 There is a report published of 13 men cases reported in literature in which the patient was below average age of the patients was 56 years. What makes our case even more unique is that till date there have been no cases reported in literature in which the patient was below the age of 30 years.3 There is a report published of 13 men cases reported in literature in which the patient was below average age of the patients was 56 years. What makes our case even more unique is that till date there have been no cases reported in literature in which the patient was below the age of 30 years.3 There is a report published of 13 men cases reported in literature in which the patient was below average age of the patients was 56 years. What makes our case even more unique is that till date there have been no cases reported in literature in which the patient was below the age of 30 years.3 There is a report published of 13 men cases reported in literature in which the patient was below average age of the patients was 56 years. What makes our case even more unique is that till date there have been no cases reported in literature in which the patient was below the age of 30 years.3 There is a report published of 13 men cases reported in literature in which the patient was below average age of the patients was 56 years. What makes our case even more unique is that till date there have been no cases reported in literature in which the patient was below the age of 30 years.3

| Day   | CSF protein (mg/dL) (15.0-45.0) | CSF glucose (mg/dL) (40.0-75.0) | Opening pressure (mm H₂O) | WBC count | RBC count | Lymphocyte % | Monocyte % | Neutrophil % |
|-------|-------------------------------|-------------------------------|--------------------------|-----------|-----------|--------------|------------|-------------|
| Day 1 | 46                            | 58                            | 150                      | 180       | 25        | 96           | n/a        | 3           |
| Day 2 | 52                            | 49                            | 160                      | 190       | 11        | 95           | 4          | 1           |
| Day 8 | 78                            | 44                            | 150                      | 340       | 58        | 87           | 8          | 4           |
| Day 15| 44                            | 39                            | 60                       | 330       | 36        | 98           | 2          | 4           |
| Day 73| 28                            | 58                            | Not done                 | 12        | 32        | 98           | 2          | 0           |
| Day 293| 21                          | 55                            | Not done                 | 1         | 3         | NA           | NA         | NA          |

Abbreviations: CSF, cerebrospinal fluid; WBC, white blood cell; RBC, red blood cell; NA, not applicable.
| Cerebrospinal fluid Results | Serum Results |
|-----------------------------|--------------|
| **AFB culture** | No mycobacteria isolated |
| **AFB smear** | No AFB seen |
| **ACE level** | <5 Not detected |
| **Brucella IgM/IgG** | Nonreactive |
| **Borrelia burgdorferi PCR** | Not detected |
| **Cocci Immunodiff IgG** | Nonreactive |
| **Cocci Immunodiff IgM** | Nonreactive |
| **Cryptococcus Ag** | Not detected |
| **Cysticercosis IgG** | Nonreactive |
| **Cytopathology** | No evidence of malignant cell |
| **Enterovirus RNA PCR** | Not detected |
| **Fungal culture** | No growth |
| **HSV 1 and 2 DNA PCR** | Not detected |
| **LCM Virus IgM/IgG** | Nonreactive |
| **Lyme Ab serology** | Not detected |
| **MTB Comp PCR** | Not detected |
| **Toxoplasmosis DNA PCR** | Not detected |
| **Tropheryma whipplei DNA PCR** | Not detected |
| **VDRL** | Nonreactive |
| **West Nile IgM/IgG** | Nonreactive |
| **ACE level** | 30 U/L |
| **ANA screen, IFA** | Negative |
| **Anti-ribosomal P Protein Ab** | <1 Negative |
| **Beta-2-Microglobulin** | 1.07 (Reference range: ≤2.51 mg) |
| **Brucella IgM/IgG** | Nonreactive |
| **Cardiolipin IgA** | <11 APL Negative |
| **Cardiolipin IgG** | <14 GPL Negative |
| **Cardiolipin IgM** | <12 MPL Negative |
| **CCP Ab IgG** | <16 Negative |
| **Chlamydia/Chlamydophila Ab Panel** | Negative (trachomatis, pneumoniae, and psittaci) |
| **Chromatin Ab** | <0.1 Negative |
| **Cocci Immunodiff IgG** | Nonreactive |
| **Cocci Immunodiff IgM** | Nonreactive |
| **Collagen Type II Ab** | 4.5 EU/mL Negative |
| **Complement C3** | 145 mg/dL |
| **Complement C4** | 26 mg/dL |
| **CRP** | 2.2 mg/dL |
| **Cryptococcus Ag** | Not detected |
| **Cysticercosis IgG** | Negative |
| **DNA (ds) Ab, Crithidia, IFA** | Negative |
| **FTA-ABS** | Nonreactive |
| **Hep A IgM Ab** | Nonreactive |
| **Hep B Surf Ag** | Nonreactive |
| **Hep C IgG Ab** | Nonreactive |
| **Histoplasma Ag** | Not detected |
| **HIV Ab/Ag screen** | Nonreactive |
| **Immunoglobulin IgG** | 998 mg/dL |
| **Immunoglobulin IgM** | 88 mg/dL |
| **LCM Virus IgM/IgG** | Nonreactive |
| **Lupus Anticoagulant PTT-LA** | 34 (Reference range <40 seconds) |
| **DRVVT screen** | 65 (Reference range <45 seconds) |
Contreras et al

In our case, administration of prednisone initially resulted in improvement of our patient's headache and vision. However, the patient experienced multiple episodes of relapse with ocular inflammation and arthralgia during the periods of steroid taper. With the addition of sulfasalazine, followed by methotrexate, her symptoms were under better control with fewer relapses. Of note, sulfasalazine was used first because the patient was concerned about the teratogenic side effect of methotrexate. However, when her symptoms were not as well controlled with steroid eye drops and sulfasalazine 500 mg twice daily, she agreed to add methotrexate. She also was educated and complied with contraceptive use. Our case illustrates that sulfasalazine may not be as effective as methotrexate in treating RP.

Conclusion

This case report highlighted the rarity and uniqueness of CNS involvement secondary to RP, along with explanation
of this very easily misdiagnosed condition. Thorough clinical assessment, exclusion of other infectious diseases, and radiological imaging comprehensively lead to the appropriate diagnosis. Corticosteroids and immunosuppressive agents are found to serve as the best form of treatment, yet it is recommended that each case be individualized.

Acknowledgments

This case was orally presented at the American Federation for Medical Research (January 2019), Carmel, CA, USA. This case was also presented at Kern Medical Research Forum (2020) Bakersfield, CA, USA.

Disclaimer

Views expressed in this article are our own and do not the official position of the institutions listed.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval

Ethical approval to report this case was obtained from the Kern Medical Institutional Review Board ( Approval ID: 20031 ).

Informed Consent

Informed consent for patient information to be published in this article was obtained.

ORCID iDs

Rupam Sharma https://orcid.org/0000-0003-3457-4371
Arash Heidari https://orcid.org/0000-0003-1091-348X

References

1. Emmungil H, Aydin SZ. Relapsing polychondritis. Eur J Rheumatol. 2015;2(4):155-159. doi:10.5152/eurjrheum.2015.0036.
2. Puéchal X, Terrier B, Mouton L, et al. Relapsing polychondritis. Jt Bone Spine. 2014;81(2):118-124. doi:10.1016/j.jbspin.2014.01.001.
3. Kao KT, Potrebic S, Evans JR. Relapsing polychondritis presenting as meningoencephalitis with valvular abnormality: a case report. Clin Rheumatol. 2007;26(11):1985-1988. doi:10.1007/s10067-007-0600-7.
4. McAdam LP, O’Hanlan MA, Bluestone R, Pearson CM. Relapsing polychondritis: prospective study of 23 patients and a review of the literature. Medicine (Baltimore). 1976;55(3):193-215. http://www.ncbi.nlm.nih.gov/pubmed/775252. Accessed October 4, 2021.
5. Borgia F, Giuffrida R, Guarneri F, Cannavò SP. Relapsing polychondritis: an updated review. Biomedicines. 2018;6(3):84. doi:10.3390/biomedicines6030084.
6. Ophir D. Relapsing polychondritis. Harefuah. 1988;115(7-8):182-183.
7. Wang ZJ, Pu CQ, Wang ZJ, et al. Meningoencephalitis or meningitis in relapsing polychondritis: four case reports and a literature review. J Clin Neurosci. 2011;18(12):1608-1615. doi:10.1016/j.jocn.2011.04.012.
8. Damiani JM, Levine HL. Relapsing polychondritis—report of ten cases. Laryngoscope. 1979;89(6, pt 1):929-946. http://www.ncbi.nlm.nih.gov/pubmed/449538. Accessed October 4, 2021.
9. Michet CJ, McKenna CH, Luthra HS, O’Fallon WM. Relapsing polychondritis: survival and predictive role of early disease manifestations. Ann Intern Med. 1986;104(1):74. doi:10.7326/0003-4819-104-1-74.
10. Hanslik T, Wechsler B, Piette JC, Vidaillhet M, Robin PM, Godeau P. Central nervous system involvement in relapsing polychondritis. Clin Exp Rheumatol. 1994;12(5):539-541. http://www.ncbi.nlm.nih.gov/pubmed/7842537. Accessed October 4, 2021.
11. Shen K, Yin G, Yang C, Xie Q. Aseptic meningitis in relapsing polychondritis: a case report and literature review. Clin Rheumatol. 2018;37(1):251-255. doi:10.1007/s10067-017-3616-7.
12. Ota M, Mizukami K, Hayashi T, Sumida T, Asada T. Brain magnetic resonance imaging and single photon emission computerized tomography findings in a case of relapsing polychondritis showing cognitive impairment and personality changes. Prog Neuropsychopharmacol Biol Psychiatry. 2005;29(2):347-349. doi:10.1016/j.pnpbp.2004.11.024.
13. Kemta Lekpa F, Kraus VB, Chevalier X. Biologies in relapsing polychondritis: a literature review. Semin Arthritis Rheum. 2012;41(5):712-719. doi:10.1016/j.semarthrit.2011.08.006.