

Spotted fever rickettsiosis presenting with bilateral anterior uveitis and retinitis: A case report

Sohini Das¹, George A. Ninan¹, Smitha Jasper², Minu George², Ramya Iyadurai¹

Departments of ¹Medicine and ²Ophthalmology, Christian Medical College, Vellore, Tamil Nadu, India

ABSTRACT

Spotted fever is a common rickettsial disease in India. It is caused by *Rickettsia conorii*, which demonstrates vascular tropism and causes endothelial injury. Ocular manifestations include multifocal retinitis and disc edema. Anterior uveitis as a presenting feature of spotted fever is uncommon. We present a 32-year-old man with spotted fever and bilateral anterior uveitis.

Keywords: Eye manifestations of spotted fever, spotted fever with retinitis, spotted fever with uveitis

Introduction

Rickettsial infections in India include spotted fever and scrub typhus.^[1-3] Spotted fever accounts for 16% of acute undifferentiated febrile illness in South India.^[4] It is caused by *Rickettsia conorii*, an obligate intracellular bacterium, which demonstrates vascular tropism and causes endothelial injury.^[5,6] Multifocal retinitis and disc edema are frequent ocular manifestations of spotted fever.^[2,7] Bilateral anterior uveitis as a presenting feature of spotted fever is uncommon.^[8]

We describe a patient with spotted fever with bilateral anterior uveitis and retinitis during the febrile episode.

Case History

A 32-year-old man presented with high-grade fever, headache, myalgia and arthralgia involving both knees and ankles for 1 week. On day 4 of illness, he developed redness and pain in both eyes. There was no history of blurring of vision, diplopia, vomiting and seizures. He denied a history of recent travel,

consumption of unpasteurized milk and similar illness in family/neighbourhood. He had a pet dog at home.

On examination, he was febrile (temperature 102°F) and tachycardiac (pulse rate 112/minute). Discrete, non-tender axillary lymph nodes were palpable bilaterally. Purpuric rash was present over trunk, bilateral upper and lower distal extremities including palms and soles [Figure 1]. Slit-lamp examination showed bilateral non-granulomatous anterior uveitis. Fundus examination showed multiple hemorrhages, cotton wool spots, Roth's spots and disc edema bilaterally [Figures 2 and 3]. There was no cardiac murmur, eschar or neck stiffness. Differential diagnoses that we considered in this patient included rickettsial diseases (scrub typhus and spotted fever), dengue fever and chikungunya.

Blood investigations revealed thrombocytopenia and elevated transaminases [Table 1]. Workup for infective endocarditis (multiple blood cultures, transthoracic and transesophageal echocardiogram) was negative. Malarial parasite smears, dengue, scrub typhus and leptospira serology and HIV Elisa were negative. Weil-Felix test was positive for OX-19 and OX-2, consistent with spotted fever. Spotted fever IgM ELISA was also positive. This patient was started on intravenous doxycycline 100 mg twice daily and intensive topical steroids for his anterior

Address for correspondence: Dr. Sohini Das,
Department of Medicine, Christian Medical College,
Vellore - 632 004, Tamil Nadu, India.
E-mail: sohinidas@hotmail.com

Received: 14-11-2019

Revised: 09-01-2020

Accepted: 23-01-2020

Published: 28-02-2020

Access this article online

Quick Response Code:



Website:
www.jfmipc.com

DOI:
10.4103/jfmipc.jfmipc_1009_19

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Das S, Ninan GA, Jasper S, George M, Iyadurai R. Spotted fever rickettsiosis presenting with bilateral anterior uveitis and retinitis: A case report. J Family Med Prim Care 2020;9:1236-9.



Figure 1: Rash on the sole

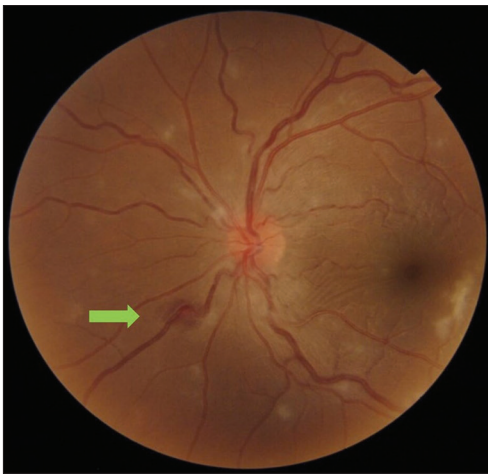


Figure 2: Left eye – Superficial hemorrhage (arrow) and multiple cotton wool spots



Figure 3: Right eye – Central white clearing with a surrounding hemorrhage (Roth's spot) (arrow)

uveitis. He was afebrile after 2 days of initiating treatment, following which he was given oral doxycycline to complete 1 week of antibiotic therapy. His cutaneous manifestations

Table 1: Relevant laboratory investigations

Test	Result	Normal Range
Complete Blood Count		
White Blood Cells	4200/ μ L	4400-11,000/ μ L
Neutrophils	63%	40%-70%
Lymphocytes	33%	20%-40%
Monocytes	4%	2%-6%
Haemoglobin	13.6 g/dL	12-15 g/dL
Platelets	$66 \times 10^3/\mu$ L	150×10^3 - $450 \times 10^3/\mu$ L
Biochemistry		
Urea (mg/dL)	18	10-40
Creatinine (mg/dL)	0.9	0.7-1.4
Total Bilirubin (mg/dL)	1.5	0.1-1.2
Direct Bilirubin (mg/dL)	0.9	< 0.4
Total Protein (g/dL)	6.2	6-8.1
Albumin (g/dL)	3.2	3.5-0.5
Alkaline Phosphatase (IU/L)	161	55-120
AST (IU/L)	267	10-40
ALT (IU/L)	316	12-55
ESR (mm/h)	44	0-20
CRP (mg/L)	84	<3

improved with regress in a rash. Anterior uveitis symptoms had improved at discharge.

Discussion

Common clinical features of spotted fever include fever, headache, myalgia, rash, eschar and lymphadenopathy. Vasculitis leads to development of skin rash, and it can lead to lifethreatening complications such as interstitial pneumonitis, noncardiogenic pulmonary edema and multiorgan dysfunction syndrome.^[9-11]

Adnexal and anterior chamber involvement in spotted fever includes eyelid edema, conjunctival hyperaemia, chemosis and non-granulomatous anterior uveitis.^[12,13]

Agahan *et al.* looked at seven patients with rickettsial uveitis recruited from an Ophthalmology Clinic in Spain. Loss/blurring of vision and floaters were present in six (86%) and three (43%) patients, respectively.^[13]

Rickettsial infection is usually diagnosed, retrospectively, during an etiologic workup for anterior uveitis. Madsen *et al.* looked at 48 Swedish patients with anterior uveitis, of which seven (14.6%) had seroconversion consistent with active rickettsial infection. However, none of the patients in this study had clinical features/rash/eschar consistent with spotted fever.^[14]

Another case report from Portugal describes a 10-year-old boy with bilateral progressive loss of vision for 2 months. He had bilateral anterior uveitis and serous retinal detachment in the right eye. Though he did not have a history of fever, IgG and IgM antibodies to *R. conorii* were sent as a part of a workup for

infectious diseases, and they were positive. He was treated with erythromycin and corticosteroids, with the resolution of ocular lesions and recovery of vision.^[15]

Anterior uveitis during febrile episodes in spotted fever is rare. Pradeep *et al.* reported a 52-year-old man with spotted fever with bilateral anterior uveitis and vitreous inflammation. This patient had developed eye symptoms 1 day after the onset of fever. Despite treatment with systemic corticosteroids and doxycycline, this patient had poor visual recovery.^[8]

Retinal lesions in spotted fever rickettsiosis include haemorrhages, white lesions, retinal detachment, cystoid macular edema and optic disc edema.^[7,16] In a study by Kalal *et al.*, retinitis was seen in 10% of children with rickettsial infections.^[2] However, up to 70% of the patients with spotted fever retinitis may be asymptomatic. In the absence of ocular complaints, retinitis in spotted fever maybe overlooked.^[7,17] Pathogenetic mechanisms in rickettsial retinitis include tissue hypoperfusion and immune-complex deposition.^[18]

In a study by Balasundaram *et al.* from India, 75% (9/12) patients with rickettsial eye manifestations had bilateral involvement. Multifocal retinitis and macular hard exudates were seen in all patients in this study. The vision was impaired in all patients (100%, 12/12) at presentation. After treatment with doxycycline and systemic corticosteroids, only 25% (4/12) had impaired visual acuity.^[16]

Doxycycline is the drug of choice and given at a dose of 100 mg twice daily for 7 days.^[19] Topical steroids are required for the patients with anterior uveitis. Oral prednisolone has been used for cases with severe retinitis.^[16]

Spotted fever should be considered as a differential diagnosis in the patients with anterior uveitis and concurrent/preceding febrile episode. Primary care physicians should be aware of ocular manifestations of spotted fever. Spotted fever associated anterior uveitis and retinitis have sight-threatening complications that necessitate prompt initiation of therapy. A dilated fundoscopic examination should be done by the treating doctor at the primary care level for all patients with spotted fever rickettsiosis. Referral to an ophthalmologist for detailed evaluation and follow-up is prudent. Recognition of uveitis and retinal involvement in spotted fever is crucial, as early detection and prompt initiation of therapy can lead to a complete resolution.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Abhilash K, Jeevan J, Mitra S, Paul N, Murugan T, Rangaraj A, *et al.* Acute undifferentiated febrile illness in patients presenting to a Tertiary care hospital in South India: Clinical spectrum and outcome. *J Glob Infect Dis* 2016;8:147-54.
2. Kalal BS, Puranik P, Nagaraj S, Rego S, Shet A. Scrub typhus and spotted fever among hospitalised children in South India: Clinical profile and serological epidemiology. *Indian J Med Microbiol* 2016;34:293-8.
3. Khan SA, Bora T, Chattopadhyay S, Jiang J, Richards AL, Dutta P. Seroepidemiology of rickettsial infections in Northeast India. *Trans R Soc Trop Med Hyg* 2016;110:487-94.
4. Stephen S, Ambroise S, Gunasekaran D, Hanifah M, Sangeetha B, Pradeep J, *et al.* Serological evidence of spotted fever group rickettsiosis in and around Puducherry, South India - a three years study. *J Vector Borne Dis* 2018;55:144-50.
5. Walker GV, Walker DH. Infection of the endothelium by members of the order Rickettsiales. *Thromb Hemost* 2009;102:1071-9.
6. George F, Brouqui P, Boffa MC, Mutin M, Drancourt M, Brisson C, *et al.* Demonstration of *Rickettsia conorii*-induced endothelial injury *in vivo* by measuring circulating endothelial cells, thrombomodulin, and von Willebrand factor in patients with Mediterranean spotted fever. *Blood* 1993;82:2109-16.
7. Khairallah M, Ladjimi A, Chakroun M, Messaoud R, Yahia SB, Zaouali S, *et al.* Posterior segment manifestations of *Rickettsia conorii* infection. *Ophthalmology* 2004;111:529-34.
8. Pradeep TG, Satyanarayanan S, Krishnaswamy M. Bilateral uveitis in Rickettsial disease. *J Infect Dis Bilater Ther* 2015;3:1-2.
9. Valbuena G, Walker DH. Changes in the adherens junctions of human endothelial cells infected with spotted fever group rickettsiae. *Virchows Arch* 2005;446:379-82.
10. Sekeyová Z, Danchenko M, Filipčík P, Fournier PE. Rickettsial infections of the central nervous system. *PLoS Negl Trop Dis* 2019;13:1-18.
11. Ehelepola ND, Kumara GD, Sapurugala SA, Buddhadasa WM, Dissanayake WP. An atypical case of Rickettsial spotted fever myocarditis mimicking weil's disease. *Case Rep Infect Dis* 2019;2019:1-6.
12. Pinna A. Ocular manifestations of Rickettsiosis: 1. Mediterranean spotted fever: Laboratory analysis and case reports. *Int J Med Sci* 2009;6:126-7.
13. Agahan AL, Torres J, Fuentes-Páez G, Martínez-Osorio H, Orduña A, Calonge M. Intraocular inflammation as the main manifestation of *Rickettsia conorii* infection. *Clin Ophthalmol* 2011;5:1401-7.
14. Madsen KB, Wallménus K, Fridman A, Pålsson C, Nilsson K. Seroprevalence against *Rickettsia* and *Borrelia* Species in Patients with Uveitis: A Prospective Survey. *J Ophthalmol* 2017;2017:1-10.

15. Marques SHM, Guerra MG, Almeida C, Ribeiro M. Ocular manifestations of rickettsia in children: Common but frequently overlooked. *BMJ Case Rep* 2018;2018:1-4.
16. Balasundaram MB, Manjunath M, Baliga G, Kapadi F. Original article ocular manifestations of *Rickettsia conorii* in South India. *Indian J Ophthalmol* 2018;66:1840-4.
17. Khairallah M, Yahia SB, Jelliti B, Ben Romdhane F, Loussaief C, Attia S, *et al.* Diagnostic value of ocular examination in Mediterranean spotted fever. *Clin Microbiol Infect* 2009;15:273-4.
18. Gong B, Lee YS, Lee I, Shelite TR, Kunkeaw N, Xu G, *et al.* Compartmentalized, functional role of angiogenin during spotted fever group rickettsia-induced endothelial barrier dysfunction: Evidence of possible mediation by host tRNA-derived small noncoding RNAs. *BMC Infect Dis* 2013;13:285.
19. Raoult D, Drancourt M. Antimicrobial therapy of rickettsial diseases. *Antimicrob Agents Chemother* 1991;35:2457-62.