CASE REPORT

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A Rare Case of Triple Pathogen Co-Infection with Rickettsia, Varicella Zoster Virus, and Plasmodium vivax Confirmed by PCR in an Immunocompetent Adult

ABSTRACT

A 33-year-old immunocompetent male presented with high-grade fever, generalized maculopapular rash, myalgia, and headache after returning from rural Southeast Asia. Investigation by PCR based Tropical Fever Panel confirmed co-infection with Varicella-Zoster Virus, Rickettsia spp., and Plasmodium malariae. Patient was treated for all three infection concurrently and showed improvement in his symptoms after which he was discharged. This case highlights the importance of considering multiple concurrent tropical infections in endemic regions even in patients with no comorbidities.

Key words: Endemic infections, Monsoon-related diseases, Tropical fever, Pustular rash.

INTRODUCTION

Southeast Asia is recognized as a critical region globally due to its heightened vulnerability to emerging infectious diseases. This region is home to over 30% of the world's population, making it a significant area of concern. Various human-related factors contribute to the rise of infectious diseases, including population growth, poverty, malnutrition, increased international travel, large-scale migration triggered by war, natural disasters, or economic challenges, as well as cultural practices and sexual behavior. The global rise in metabolic and immunosuppressive conditions like diabetes and HIV, bioterrorism, urban expansion, deforestation, and human intrusion into wildlife habitats further exacerbate the risk. Additional contributors include shifts in agricultural practices, industrial food production, mixed farming systems, occupational hazards, recreational exposure, antimicrobial resistance, and the misuse of antibiotics. Genetic mutations in pathogens also play a significant role in disease emergence. Often, weak public health systems are unable to effectively respond to such outbreaks.

Varicella zoster virus (VZV) is a DNA virus classified under the alpha subfamily of Herpesviridae, known to cause both initial and recurrent infections. The primary infection, commonly referred to as chickenpox (varicella), is a systemic illness characterized by a distinctive itchy vesicular rash. This rash typically evolves in stages—starting as macules, progressing to papules, vesicles, pustules, and finally forming crusts—and often appears in multiple waves over several days. The rash usually begins on the face, trunk, and back, with subsequent spread to the scalp, mucous membranes of the mouth, and genital areas. In addition to the rash, affected individuals may develop mild systemic symptoms, including low-grade fever, general malaise, reduced appetite, and irritability. These symptoms often emerge during the prodromal phase, which typically precedes the rash by 1 to 2 days.[2]

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Among the rickettsial diseases in India, scrub typhus is the most frequently reported. In many areas, this disease remains underdiagnosed and often goes unnoticed, potentially accounting for up to half of all cases of undifferentiated fever presenting at hospitals and lack of investigation facilities. Rickettsia represent a diverse group of obligate intracellular, gram-negative bacteria, typically appearing as coccobacilli or short rods. Transmission to humans generally occurs through arthropod vectors such as ticks, mites, fleas, or lice. The clinical presentation commonly includes fever, eschar formation at the site of the bite, skin rashes, and swollen lymph nodes. In some cases, more severe complications can develop, including gastrointestinal disturbances, pneumonia, myocarditis, acute kidney injury, and acute respiratory distress syndrome (ARDS).[3]

Rickettsial infections in India are largely endemic and remain significantly underdiagnosed, primarily due to their nonspecific clinical presentation. The increasing incidence of rickettsial diseases in India is also influenced by the movement of travelers from endemic regions of other countries, contributing to the wider spread and re-emergence of these infections.[4]

Malaria is highly endemic in India. Although concurrent infections are reported, but not very common.[5]

This case report highlights an unusual co-infection involving varicella zoster virus, Plasmodium species, and Rickettsia, underscoring the importance of considering multiple etiologies in patients presenting with undifferentiated febrile illnesses with skin rash especially in endemic areas.

CASE REPORT

A 33-year-old immunocompetent male presented to the hospital with high-grade fever with chills, and generalized myalgia which progressed over the first three days. On day four, he developed a maculopapular rash initially appearing on the trunk and subsequently spreading to the back, face, and all four limbs. The maculopapular rash eventually progressed to fluid filled vesicles with intense pruritic as seen in Fig 1 and 2. He also experienced a mild frontal headache. By the sixth day, the patient reported increasing fatigue and joint pain predominantly affecting his upper and lower limbs. There was no vomiting, pain in abdomen, loose stools, neck pain, giddiness, blurring of vision, bleeding tendencies. There was no history of any prior medication use. Patient had a recent history of travel to Kolkata after 2 days the above symptoms started. He was in Kolkata for three weeks and did not take any pre-travel vaccination or prophylaxis.

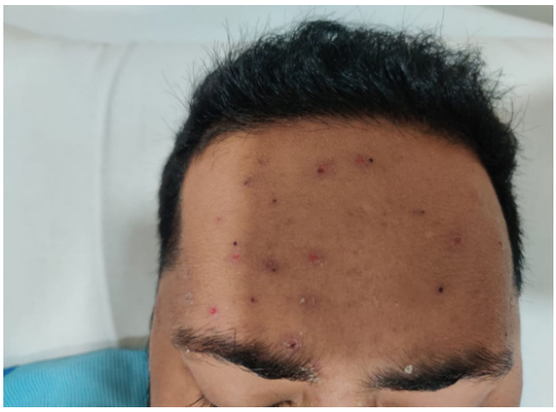

Fig1: varicella zoster infection on the patients forehead

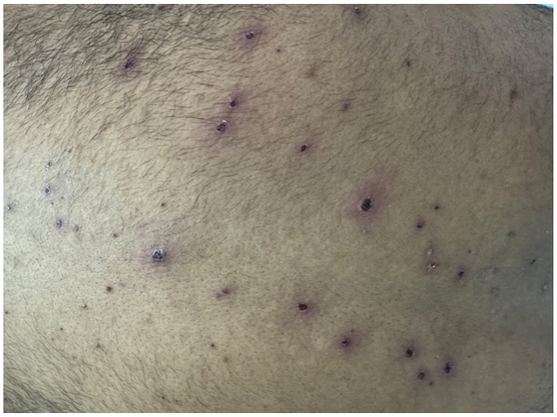

Fig 2: Varicella Zoster infection on the patients abdomen

On physical examination, he was conscious, oriented and following all verbal commands. He was febrile with a temperature of 101 F with a pulse of 108/min, blood pressure of 110/70 mmHg, respiratory rate of 28 per min, oxygen saturation of 99 % on room air. The rash was present on trunk, back, face and all four limbs. On further systemic examination of all systems were found to be normal. Laboratory findings were as follows-Hemoglobin of 13.5 g/dL (normal value 13-17 g/dl), ,White Blood Cell Count of 5890 /µL (4000 -10000/µL), platelet Count of 81 x10^3/µL (150-400 /µL), SGOT - 69 (normal value 0 - 40), SGPT - 119 (normal value 0 - 40) , Bilirubin - 0.49 (<1.2), GGT- 43.4 (normal value 0 - 60) , Alkaline phosphate - 104 (normal value 40 - 129), Tropical Fever Panel PCR (blood) - positive for Plasmodium and Rickettsia , peripheral blood smear s/o Plasmodium Vivax, Rapid Malarian Antigen test was positive, Weil Felix test done on 9th day of fever - showed a titre of 1:80 (which was borderline), Varicella IgM- Positive (titre > 2.3), HIV/autoimmune panel was found to be negative. Ultrasound Abdomen showed mild hepatosplenomegaly, Chest Xray was normal. ECG was of normal sinus tachycardia. Patient was started initially on Tab Valcivir 1gm thrice a day with antihistaminic and other supportive treatment. As patient continued to have low grade fever further investigations were suggestive of being positive for Varicella Zoster, Rickettsia as well as Plasmodium on Tropical fever panel by PCR technique. He was then initiated on Inj. Doxycycline 100mg twice a day for 4 days and followed by oral medicine, Inj Falcigo (Artesunate) intravenous 120mg stat and followed by 60 mg twice a day for 5 days. Patient started showing improvement and his fever resolved completely. His other symptoms of headache, myalgia started gradually improving. There was scab formation over his trunk, limbs, face, chest as seen in Fig 3. Patient was symptomatically better and was hemodynamically stable and hence was discharged after 12 days of completing his course in the hospital.

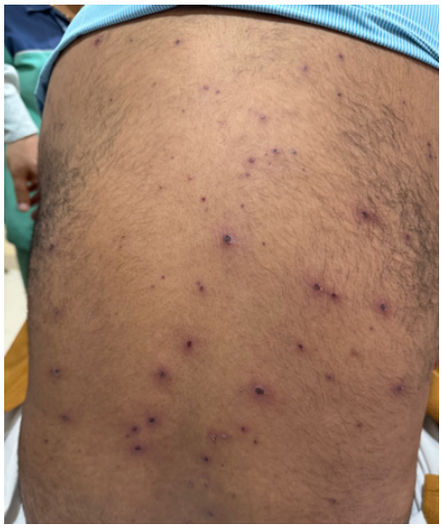

Fig 3: Varicella zoster on the patients back. Scab formation is seen

DISCUSSION

South East Asia, which includes the subcontinent of India, is highly prone to tropical infections like malaria, Leptospira, dengue scrub typhus, and other vector-borne diseases especially in tropical climate, causing high amount of disability and death. These being vector-borne diseases, the occurrence at the same time can be due to the same breeding period of the vectors during the monsoons.[5]

Varicella zoster virus (VZV) is highly contagious and in temperate regions, the virus demonstrates an exceptionally high transmission rate. For laboratory confirmation of VZV infection, Polymerase chain reaction (PCR) testing is the most sensitive technique and can be performed on samples obtained from skin vesicles, including swabs, vesicular fluid, or scab material. Acyclovir, famciclovir and valacyclovir a guanosine analogue, inhibits viral DNA synthesis and is the primary antiviral agent used in the treatment of VZV infections. It reduces the risk of visceral dissemination. Other newer antiviral options include valaciclovir and famciclovir.[6]

Serological testing remains the cornerstone of rickettsial disease diagnosis, with the indirect immunofluorescence assay (IFA) regarded as the gold standard. However, due to the delayed antibody response, serological results are often negative during the early phase of illness. Molecular techniques, particularly real-time polymerase chain reaction (PCR), have enhanced diagnostic sensitivity compared to conventional or nested PCR methods, capable of detecting fewer than 10 copies of bacterial genomic DNA per reaction. Doxycycline remains the first-line treatment for rickettsial infections.[7]

Traditionally, the gold standard for diagnosing P. vivax infection has been microscopic examination of thick and thin blood smears to identify asexual parasite stages. Advancements in molecular diagnostics have led to the development of high-volume polymerase chain reaction techniques. These methods enable the amplification of larger quantities of DNA, significantly improving the sensitivity and allowing for more accurate detection of low-level parasitemia. Treatment of Plasmodium vivax malaria typically involves chloroquine or artemisinin-based combination therapy (ACT) to target the blood-stage parasites.[8]

The patient's history of travel to Kolkata—a known endemic zone for malaria and rickettsial diseases.[9]—combined with monsoon-related exposure, likely facilitated multiple infections.[10]

The presence of pustular lesions and positive Varicella IgM pointed toward a concurrent varicella infection, while PCR positivity for Rickettsia and Plasmodium confirmed co-infections. Interestingly, the patient was immunocompetent and responded well to standard treatments for all three pathogens.

This case exemplifies the diagnostic complexity posed by concurrent endemic infections, particularly during India's monsoon season—a period marked by heightened vector activity and viral transmission. Rickettsia, Plasmodium, and Varicella can each cause febrile illness with rash, complicating clinical differentiation.

CONCLUSION

In endemic regions and seasons conducive to disease outbreaks, even healthy individuals may present with overlapping symptomatology from multiple pathogens.[11]

Concurrent infections with Varicella, Rickettsia, and Plasmodium in an immunocompetent adult during the monsoon season in India highlights the need for vigilant clinical suspicion, comprehensive diagnostic testing and prompt targeted therapy involving all the organisms involved. This case reinforces the importance of region-specific epidemiological context in clinical decision-making.

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