Rickettsial Encephalitis : A case report

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ABSTRACT

Rickettsia infections, being an important cause of pyrexia of unknown origin, is often misdiagnosed and treated without correct diagnosis because of it's symptoms mimic other causes and lack of confirmatory tests during initial phase of the illness. They are distributed worldwide with foci of endemicity. They are common in southern Europe. In India the cases of rickettsial infections have been documented mainly from South India. The disease presents with a classic triad of fever, rash and eschar. The clinical spectrum varies from a mild febrile illness to potentially life-threatening complication like meningoencephalitis. Definitive diagnosis of rickettsia infection requires the examination of serum for antibodies during the acute and convalescent phase of illness. Weil-Felix test is a non-specific agglutination test which detects antirickettsial antibodies in patient's serum. It is easily available, non-expensive and can be performed rapidly. It can be used to confirm a tentative diagnosis of rickettsial fever during acute phase of the disease. Inspite of its low sensitivity, WF test may be the only serological test available in developing countries like India. The rickettsial organisms are constantly susceptible to tetracyclines, thus making Doxycycline the drug of choice. We are reporting a case of encephalitis in a 20-year-old female who presented to hospital ER with 10 days history of fever, headache and seizures. Before coming to our institute. The patient was brought to the ER with status epilepticus. Status epilepticus treatment protocol was given in the ER, patient intubated and admitted to medical intensive care unit. In ICU, the patient was put on mechanical ventilation. Various blood Investigation including Weil Felix test was done. Treatment started with IV antibiotic, IV acyclovir, IV Levetiracetam and tab Doxycycline 100mg BID through RT. Weil-Felix test came positive for spotted fever group with titres being OX2 1:320, OX19 1:640 and OXK 1:20 . Course of Tab Doxycycline was given for 10 days. Patient improved gradually and was extubated on 5th day, and shifted to ward on 10th day. Patient was discharged to home after 2 weeks of hospital stay.

On follow up in neurology OPD, patient had no complaints and with no neurological sequelae. This case report underlines the importance of a high index of clinical suspicion and the benefits of empirical treatment in setting of compatible epidemiological data.

Key words: Rickettsial infection, Rickettsial encephalitis, Weil-Felix Test , doxycycline.

1. INTRODUCTION

Rickettsial infections are an important but often under recognised because of undifferentiated Febrile illness. It is often misdiagnosed and treated as other febrile illness because of its similarity of symptoms and lack of confirmatory laboratory tests during initial phase of illness. When untreated, Rickettsial disease can lead to fatal complications. In its severe form, rickettsial infections may be present as culture negative endocarditis, splenic rupture and infections of central nervous system (CNS). Rickettsial CNS infections ranges from simple headache to lethal Meningoencephalitis.

Rickettsial meningoencephalitis presents like any viral meningoencephalitis. High index of clinical suspicion is required to diagnose CNS rickettsial infection. It is very important to diagnose CNS rickettsial infection at the earliest as effective and specific treatment is available. we report a case of rare rickettsial encephalitis in the absence of typical general symptoms and signs.

2. CASE REPORT

A previously healthy 20-year-old Indian female presented to our hospital emergency department in December 2022, with 10 days history of fever, headache and seizures. The seizures were generalised, tonic-clonic about 8-10 episodes. No history of skin rash. No history of contact with pets. Before coming to our hospital, the patient was admitted in a local hospital for 4 days. Took discharge against medical advice. Patient reached our hospital in a state of status epilepticus. On examination, the patient was seizing. Pulse rate 160 bpm, respiratory rate 14 cpm, temperature 37^0C , BP 130/90 mm of Hg. There was mild pallor. There was no skin rash, no eschar, no jaundice and no significant lymphadenopathy.

On systematic examination, patient was deeply sedated (due to IV anticonvulsants given in previous hospital) with no sign of meningeal irritation. Her breath sounds were vesicular and equal on both sides with no added sounds. Abdomen was soft, non-tender with no hepatosplenomegaly. First and second heart sounds were normal with no murmur. Patient was given status epilepticus treatment Protocol in ER, intubated and admitted to medical intensive care unit.

Following were the results of blood investigations. Hb 10.8g/dl, TLC 21000/mm^3, with 60% of neutrophils and 30 % of lymphocytes, platelet count 1.8 lakhs, ESR 13mm/1^{st} hour, and RBS 98mg/dl. Liver function tests, Renal function tests, Serum electrolytes, Coagulation profile and urine analysis were within normal limits. HCV, HBsAg, HIV, Dengue fever, Leptospira and malaria titres were negative. Weil-Felix test came positive for spotted fever group with OX2 1:320, OX19 1:640, and OXK 1:20 titres. CSF analysis, Non contrast CT of brain and EEG were normal. In ICU the patient was put on Mechanical Ventilation and started on IV antibiotic(ceftriaxone), IV acyclovir, IV levetiracetam, Tab Doxycycline 100mg BID through Ryles tube and other supportive treatment. The Patient improved gradually. Doxycycline was given for 10 days. Acyclovir was stopped after 2 days. Antibiotic was given for 7 days to treat secondary aspiration pneumonia. Patient extubated on the 5^{th} day, shifted to ward on the 11^{th} day and discharged home in stable condition after 2 weeks of hospital stay. On follow up in neurology OPD after one month, the patient had no complaints and no neurological sequelae.

3. DISCUSSION

Rickettsiae are a heterogeneous groups of small, obligate intracellular, gram-negative coccobacilli and short bacilli. They derive their name from the American researcher, Howard Ricketts, who discovered them in 1909 in Montana, USA as the cause of a serious disease (Rocky Mountain Spotted Fever). Rickettsia species are mainly distributed into 3 groups.

1. Spotted fever group which includes R.rickettsii (Rocky mountain spotted fever), R. conorii(Mediterranean spotted fever), R. japonica(Japanese/oriental spotted fever), R. Africae(African tick bite fever), R.stoveca (Tick borne lymphadenopathy).

2. Transitional group which includes R.akari (Rickettsial pox), R.australis (Queensland tick typhus), R.felis (Flea-bone rickettsiosis).

3. Typhus group which includes R.prowazeki (Epidemic typhus), R.typhi(Murine/endemic typhus).

O.tsutsugamushi which causes scrub typhus is phylogenetically closely related to rickettsia species. In our case the organism was from spotted fever group.

Most rickettsial organisms are transmitted to humans by the bites or infectious fluids (feces) of ectoparasites such as ticks, fleas, mites and lice.

Rickettsial infection are distributed worldwide in foci of endemicity with sporadic and often seasonal outbreaks. They are common in Southern Europe. In India the case of rickettsial infections have been documented mainly from South India[1]. The eastern Uttar Pradesh region of India is known for its endemicity of acute encephalitis syndrome(AES). It was found that 5.34% of AES cases were due to rickettsial infections. Orientia tsutsugamushi, the rickettsial pathogen responsible for Scrub typhus has been found to be the substantial contributor(>60%)
For the AES cases[2,3].

The disease is usually characterized by the classic triad of fever, eschar and rash. The clinical manifestation of all the acute presentations during the first 5 days are fever, headache, and myalgias. As the course progresses, different clinical manifestations such as rash, eschar, pneumonitis, and Meningoencephalitis occurs. Our case presented with CNS involvement in the form of encephalitis. There was no rash and/or eschar. The most common neurological manifestations reported in rickettsial infection include meningitis, encephalitis and acute disseminated encephalo-myelitis[4].

CNS involvement is frequent in Rocky mountain spotted fever (RMSF), Epidemic typhus, and Murine typhus. Our patient belonged to spotted fever group. The CNS notably appears to be one of the major systems involved during the latest stages of RMSF pathogenesis[5]. Encephalitis, which may be fatal, is a frequent manifestation in case of delayed diagnosis and treatment. In addition, severe sequelae such as hemiparesis, deafness, visual disturbances have been reported in patients who survived RMSF with CNS involvement[6,7]. There were no such sequelae in our patient. A few reports in the literature have described CNS involvement in the course of Mediterranean spotted fever presenting as meningitis[8], encephalitis[(8)] and meningoencephalitis[9]. Sequelae were severe among the patients who survived these severe forms despite an appropriate treatment with doxycycline. Epidemic typhus causes frequent neurological manifestations. In murine typhus, the occurrence of neurological manifestation varies from 2 to 20% of cases[10]. Headache is common but meningitis and encephalitis are occasionally reported[11].

CNS involvement is rare in Japanese spotted fever, African tick bite fever, Rickettsial pox, Queensland tick typhus, Flea-borne spotted fever, and scrub typhus. A case of Japanese spotted fever with post-infectious encephalitis has been reported in literature[12]. The patient required IV immunoglobulin in addition to doxycycline for complete improvement and recovery.

Diagnosis of rickettsia infection poses certain problems because (1) Rickettsial organisms cannot be isolated from blood by routine laboratory procedure (2) Latency in antibody response during the initial phase of illness. In addition, due to the presence of shared protein and lipopolysaccharide antigens, it is extremely difficult to distinguish closely related agents within the rickettsia spotted fever group by serological methods[13]. Definitive diagnosis requires the examination of serum sample for the antibodies during the acute and convalescent phase of illness. High index of clinical suspicion is based on epidemiological data, history of exposure to vectors or reservoir animals, travel to endemic locations, and clinical manifestation (including rash or eschar). In our case there were no typical general symptoms. There was no eschar or rash. Possibility of rickettisal infection was suspected since patient came from a place where cases of rickettsial infection is endemic. This tentative diagnosis was confirmed by positive Weil-Felix test.

Weil-Felix test is a nonspecific agglutination test which detects anti- rickettsial antibodies in patient serum. It is based on cross-reaction between antibodies produced in acute rickettsial infections and antigens of OX strains of proteus species (OX19,OX2,and OXK). A four-fold rise in the agglutinin titres 2-4 weeks apart, or a single titre dilution of >1:320 considered positive. Its sensitivity is 46% and specificity 100%. In the study conducted in south India, the sensitivity of patient's antibodies was 30% at a titre breakpoint of 1:80, but specificity and positive predictive value were 100%[14].

WF test, which is inexpensive, easily available and rapidly performed may be the only serological test available in developing countries like India in confirming a tentative diagnosis of rickettsial fever.

Doxycycline is the drug of choice. It is given orally the dose is 100mg twice daily. It can be given intravenously or through RT in comatose patients. It should be administered till 3-5 days after defervescence. Our patient received 100mg of doxycycline twice daily for 10 days. Initially through RT and then orally.

4. CONCLUSION

Rickettsial infections may present as CNS infections and should be included in the differential diagnosis of meningitis, encephalitis, and meningoencephalitis. Rickettsial CNS infection ranges from simple headache to lethal meningoencephalitis. Surviving patients may suffer from incapacitating sequelae. Definitive diagnosis of rickettsial infection relies mainly on serological methods that can be of limited value in the initial phase of illness due to latency in antibody response, emphasizing the need for a high clinical suspicion. Weil-Felix test may be the only serological test available in developing countries because of its easy availability, rapid result, and inexpensiveness. Early treatment should be instituted empirically, since it improves prognosis and diminishes mortality and sequelae associated with severe form of rickettsial infection. The good news is that rickettsial organisms are constantly susceptible to tetracyclines. Doxycycline is the drug of choice. There are an increasing number of reports regarding emerging rickettsial species responsible for incomplete and atypical presentations that should be considered while diagnosing rickettsial infections.

Ethical Approval:
As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent
As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

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