

Viewing the Unseen: Scrub Encephalopathy as an Important Differential Diagnosis of AES

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Abstract

Japanese encephalitis (JE) is the important cause of Acute Encephalitis Syndrome (AES). However, in large proportion of AES cases, the specific cause cannot not be established. For this, scrub typhus is one such emerging cause. In line with this, first such case report on AES in Odisha due to scrub encephalopathy in paediatric age group is presented.

Key words: Scrub typhus, Japanese encephalitis, Acute encephalitic syndrome, Scrub encephalopathy

Introduction

Acute Encephalitis Syndrome (AES) poses a great public health problem in India, as 50,000 cases and 10,000 deaths annually have been reported¹. Traditionally Japanese encephalitis (JE) is important cause of AES, supported by the fact that AES surveillance is paralleled to JE surveillance. In 2014, the total numbers of AES cases and deaths reported from India were 10,853 and 1,717 respectively and the corresponding values for JE were 1,657 (~15%) and 293 (~17%) respectively. This implies that other undiscovered aetiology of AES, which accounts for about 85%, also exists. In various studies of patients with AES, in one-third cases the specific cause could not be established².

AES in India as per definition of WHO³ encompasses several other illnesses; like malaria, enteric encephalopathy, tubercular meningitis, dengue with neurological manifestations, scrub typhus, bacterial meningitis, etc.

For the cases of AES not explained by JE, aetiology could be scrub typhus, a hidden entity. The name typhus was derived from a Greek word meaning stupor; this name is justified by its CNS involvement. Aseptic meningitis is very commonly seen but other complication like cerebritis, myelitis and cerebral haemorrhage has been reported⁴. Study done by KarAetal found that among 20 consecutive patients with acute encephalitic syndrome (AES), six (30%) were due to scrub infection⁵.

Scrub typhus is emerging as a significant health problem in parts of India^{6,7,8,9}. Due to the varied presentation and lack of diagnostic facilities, and lack of exposure of doctor, it largely remains underdiagnosed. We here discuss a case report on AES in Odisha

due to scrub encephalopathy presenting to a tertiary care hospital in paediatric age group.

The Case

We are reporting six cases of scrub encephalopathy presented to a tertiary care hospital from June to Nov 2015. The patients were from adjoining districts of the hospital in the age group of 2-7 years referred from other hospitals. All of the patients followed the same sequence of events having the history of fever for six to seven days followed by head ache, altered sensorium on day five and six.

There was hepatosplenomegaly in all the six cases, lymphadenopathy in three cases and in one patient neck stiffness was present. Except for two patients we could not find any inoculation eschar. All the six patients presented to the hospital with an average GCS of 6- 8. Three of them required more than two anticonvulsants to control the seizure. Focal neurological deficit was not seen in any of the cases.

All the six patients had leucocytosis with polymorph predominant differential count, thrombocytopenia haemoglobin was within normal limit. Blood urea and serum creatinine was mild deranged SGOT and SGPT were remarkably elevated with hypoalbuminaemia.

CSF analysis showed 180-200 cell/mm³ with predominantly lymphocytic picture with mild increase in protein and normal glucose level. MRI done in two cases showed diffuse cerebral oedema, hyper intense lesions in the putamen and thalamus and CT head showed diffused cerebral oedema, in other two cases brain scan was not done due to financial constraints.

The patients were started with quinine, acyclovir, ceftriaxone, doxycycline empirically later continued with doxycycline and ceftriaxone once the diagnosis was confirmed for scrub typhus by ELISA IgM.

Discussion

Rickettsial diseases are caused by an intracellular parasite. Among the Rickettsial infections scrub typhus is one of the important cause of pyrexia of unknown origin.

Scrub typhus is caused by Oriental *tsutsugumushi*. Mite is the reservoir and natural vector. The larva known

as chigger is responsible for the human transmission. The patients of scrub typhus presents as prolonged fever (4-5 days), hepatosplenomegaly, and inoculation eschar. The serious complication usually seen after the second week, are pneumonia, myocarditis, azotemia, shock, ARDS, gastrointestinal bleed, and meningoencephalitis^{6,7,8,9}.

Epidemiological scenario:Scrub typhus is endemic in the 'tsutsugamushi triangle' which extends from northern Japan and eastern Russia in the north, northern Australia in the south and Pakistan in the west¹⁰.

Its presence has been documented in at least 11 Indian states including Tamil Nadu, Himachal Pradesh, Jammu, Pondicherry, Andhra Pradesh, Kerala and Meghalaya, among others^{11,12,13,14}. A main diagnostic criterion includes presence of eschar at site of tick bite along with patients travel history in the endemic region¹⁵.

Clinical Presentation:Illness varies from mild and self-limiting, to fatal¹⁶. After an incubation period of 6-21 days, onset is characterized by fever, headache, myalgia, cough, and gastrointestinal symptoms¹⁷. The symptoms gradually increase in severity and a macular rash may appear on the trunk¹⁸. If untreated, the patient may become stuporous as meningoencephalitis develops¹⁹.

Laboratory studies: In children, leukocyte and platelet counts are usually within normal ranges, although thrombocytopenia and leukocytosis may also occur¹⁷. Cerebrospinal fluid (CSF) examinations show a mild mononuclear pleocytosis with normal glucose levels¹⁹.The Weil-Felix agglutination test, oldest test in current use, detects cross-reacting antibodies to proteus mirabilis OXK. It shows \geq four times rise in titre to proteus OX-K and no reaction to proteus OX-2 or OX-19 (in 50-70% of patients); a single titre \geq 1:160 is also diagnostic (normal is \leq 1:40.). Other tests available are ELISA, western blot, indirect fluorescent etc^{20,21,22,23}.

Conclusion

This is the first report of scrub meningoencephalitis from Odisha state in paediatric age group. Scrub typhus should be considered as differential diagnosis in AES patients.

References

1. Jain A, Jain P, Jain B. Unveiling the Undiscovered: Etiology of Acute Encephalitis Syndrome in North India. *J Neuroinfect Dis* 2015;6:e101. doi: 10.4172/2314-7326.1000e101.
2. Misra UK, Kalita J, Goel D, et al. Clinical, radiological and neurophysiological spectrum of JEV encephalitis and other non-specific encephalitis during post-monsoon period in India. *Neurol India* 2003;51:55–9.
3. Chrispal A, Boorugu H, Gopinath KG, Prakash JA, Chandy S, Abraham OC, et al. Scrub typhus: An unrecognized threat in South India-Clinical profile and predictors of mortality. *Trop Doct* 2010;40:129–33.
4. Jamil MD, Hussain M, Lyngdoh M, Sharma S, Barman B, Bhattacharya PK. Scrub typhus meningoencephalitis, a diagnostic challenge for clinicians: A hospital based study from North-East India. *J Neurosci Rural Prac* 2015;6(4):488–493. doi:10.4103/0976-3147.169769.
5. Kar A, Dhanaraj M, Dedeepiya D, Harikrishna K. Acute encephalitis syndrome following scrub typhus infection. *Indian J Crit Care Med* 2014;18:453-5
6. Frequently asked questions, Scrub Typhus. World Health Organization, Regional Office for South East Asi 2010. Available at http://www.searo.who.int/entity/emerging_diseases/CDS_faq_Scrub_Typhus.pdf?ua=1
7. Mahajan SK. Scrub typhus. *J Assoc Physicians India* 2005;53:954–8.
8. Pattnaik SK, Ray B, Sinha S, Mohanty A, Sahu S. Outbreak of scrub typhus in odisha-an emerging threat. *Intensive Care Medicine Experimental*. 2015 Oct 1;3(1):1.
9. Sinha P, Gupta S, Dawra R, Rijhawan P. Recent outbreak of scrub typhus in North Western part of India. *Indian J Med Microbiol* 2014;32:247-50
10. Mccrumb FR Jr, Stockard JL, Robinson CR, et al. Leptospirosis in Malaya. I. Sporadic cases among military and civilian personnel. *Am J Trop Med Hyg* 1957;6:238–56.
11. Mahajan SK, Rolain JM, Kashyap R, Bakshi D, Sharma V, Prasher BS, Pal LS, Raoult D. Scrub typhus in Himalayas. *Emerg Infect Dis* 2006;12(10):1590-2.
12. Mahajan SK, Kashyap R, Kanga A, Sharma V, Prasher BS, Pal LS. Relevance of Weil-Felix test in diagnosis of scrub typhus in India. *J Assoc Physicians India* 2006;54:619-21.
13. Chaudhry D, Garg A, Singh I, Tandon C, Saini R. Rickettsial diseases in Haryana: not an uncommon entity. *J Assoc Physicians India* 2009;57:334-7.
14. Mathai E, Rolain JM, Verghese GM, Abraham OC, Mathai D, Mathai M. Outbreak of scrub typhus in southern India during the cooler months. *Ann N Y AcadSci* 2003;990:359-64.
15. Drevets DA, Leenen PJM, Greenfield RA. Invasion of central nervous system by intracellular bacteria. *ClinMicrobiol Rev* 2004;17(2):323-47.
16. Walker DH, Dumler JS, Marrie T. Rickettsial Diseases. (Part 8, Section 10, Chapter 174) In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, editors. *Harrison's Principle of Internal Medicine*. 18th ed. USA: The McGraw-Hill Companies 2012;1413.
17. Goldman L. Approach to the patient with possible cardiovascular disease In: Goldman: Cecil textbook of medicine.
18. Corrales-Medina VF, Shandera W. Viral-Rickettsial Infections In: Mc Phee SJ, Papadakis MA, editors. *Current Medical Diagnosis and Treatment*. 50th ed. USA: Mc Graw Hill companies; 2011. p. 1283.
19. Dumler JS, Siberry GK. Scrub Typhus (OrientalTsumugamushi) In: Kliegman RM, Behrman Re, Jenson HB, Stanton BF, editors. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders, Elsevier; 2007. p. 1295–6.
20. Koh GC, Maude RJ, Paris DH, Newton PN, Blacksell SD. Diagnosis of scrub typhus. *Am J Trop Med Hyg* 2010;82:368–70.
21. Raoult D. Orientiatsugamushi. In: Mandell GL, Bennett JE, Dolin R, editors. *Principles and Practice of Infectious Diseases*. 7th ed. Philadelphia: Churchill Livingstone; 2009. p. 2529–30.
22. Wallach J. Hematologic Diseases. In *Interpretation of Diagnostic Tests*. Philadelphia, 1996, 293-316.
23. Saah AJ. Orientiatsugamushi (scrub typhus). *Principles and practice of infectious disease*. 5th ed. Philadelphia, Pa: Churchill Livingstone. 2000. p. 2056-7.