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AES DUE TO SCRUB TYPHUS IN 2014 ASSAM, INDIA- A REPORT

Microbiology

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ABSTRACT

Background: Acute encephalitic syndrome (AES) is a complication of Scrub typhus(ST), an important re-emerging disease in India. In Japanese encephalitis(JE) endemic Assam, non JE AES cases remain under diagnosed and ST is likely to be an important but unsuspected etiology.

Objectives: Study burden of AES due to ST in 7 districts of Assam reporting sporadic cases of ST.

Methods: 246 samples from cases of AES found JE negative tested for ST IgM from February 2014 to December 2014 by enzyme-linked immunosorbent assay (ELISA).

Results: 61 samples showed positive ST IgM ELISA accounting for 24.8%. Highest number of cases (31) seen in Lakhimpur district. All positive cases responded well to Doxycycline therapy.

Conclusion: In Assam ST should be tested in all AES cases that are JE negative as ST involving central nervous system is not uncommon and it responds dramatically to Doxycycline therapy thus bringing down morbidity and mortality..

KEYWORDS:

Acute encephalitic syndrome (AES), Scrub typhus(ST), enzyme-linked immunosorbent assay (ELISA).

INTRODUCTION

Scrub typhus is a vector borne disease caused by *Orientsia tsutsugamushi*. Symptoms include fever, headache, muscle pain, cough, and gastrointestinal symptoms resembling other typhus fevers. Pneumonitis, encephalitis, and myocarditis occur in the late phase of Scrub typhus. More virulent strains of *O. tsutsugamushi* can cause hemorrhage and intravascular coagulation.

Scrub typhus is transmitted by the bite of Trombiculid mites called "chiggers", commonly *Leptotrombidium deliense* found abundantly in scrub vegetation. The bite leaves a characteristic black eschar which is helpful in diagnosis but found in only 40% of the cases. Morbilliform rash, splenomegaly and lymphadenopathies are other typical signs.

In Assam which is endemic for Japanese Encephalitis (JE), several Acute encephalitic syndrome (AES) cases are attributable to it. In fact Assam is one of the first states where both children and adult JE vaccination has been carried out since 2013 supplementing the JE vaccination of children below 15 years which has been in place from 2011. However the huge number of non JE AES cases presenting in similar seasonal trend as JE evident from the Intergrated Disease Surveillance Programme (IDSP) Assam data, demanded that we look beyond JE.

In Assam we regularly encounter sporadic cases of Scrub typhus(ST) from few districts of upper Assam. Sometimes clustering has also been seen in a couple of districts. Acute encephalitic syndromes (AES) is one of the late manifestations and complications of ST although the load of AES due to ST in Assam is still elusive with only few documented data to fall back on. In this study we have tried to find out the contribution of ST in the overall AES picture in 7 districts of upper Assam.

MATERIALS AND METHODS

We defined AES case according to the definition given by the National Vector Borne Disease Control Programme (NVBDCP), India.

Case definition of Acute Encephalitis Syndrome (AES): Clinically, a case of AES is defined as a person of any age, at any time of year with the acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) AND/OR new onset of seizures (excluding simple febrile seizures). Other early clinical findings may include an increase in irritability, somnolence or abnormal behavior greater than that seen with usual febrile illness

For all cases, information on personal details (age and sex), place of residence, time of onset of illness, presenting complaints, status of JE immunization and details of samples was recorded in AESF-3 form which is used to line-list AES/JE cases under NVBDCP.

The tests were done at Deptt. of Microbiology, Assam Medical College and Hospital (AMCH), Dibrugarh (173 nos samples) and at Regional Medical Research Centre (RMRC), Lahowal, Dibrugarh (73 nos samples).

Serum samples were tested for Scrub Typhus Immunoglobulin M (IgM) by enzyme-linked immunosorbent assay (ELISA) by Scrub Typhus Detect™ IgM InBios, Seattle WA kit, supplied by CDC, Atlanta, USA under the AEFI Project by NIMHANS Bangalore at AMCH and Scrub Typhus Detect™ IgM InBios International, Inc., USA kit at RMRC. Altogether 246 JE negative samples were tested for ST IgM from February 2014 to December 2014.

RESULTS

61 samples (38 at RMRC, Dibrugarh and 23 at AMCH, Dibrugarh) showed positive result in the ST IgM ELISA. All the positive cases have been treated with Doxycycline 100mg BD for 7 days. The positive cases belonged to 7 districts of upper Assam (Figure 1). The 7 districts

are Dhemaji-12 cases, Lakhimpur- 31 cases, Dibrugarh- 10 cases, Tinsukia- 3 cases, Sivasagar- 3 cases, Jorhat- 1 case, Golaghat- 1 case

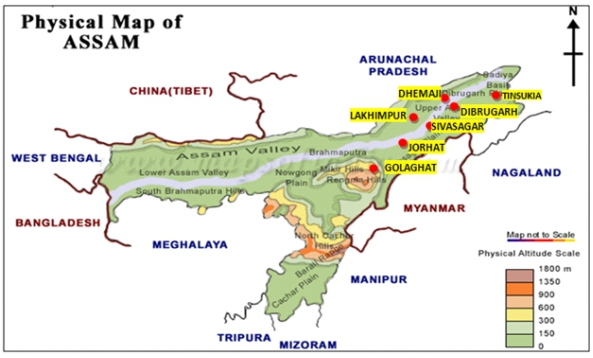

Figure 1: Districts of Upper Assam with ST positive AES cases

Male to female ratio : There were 41 males and 20 females who were ST IgM ELISA positive giving a male: female ratio of 2.05:1

Age distribution of the case (Figure 2): The youngest patient in the study was of 3 years and the oldest patient was 74 years old. Maximum cases belonged to the age group of 15-30 years

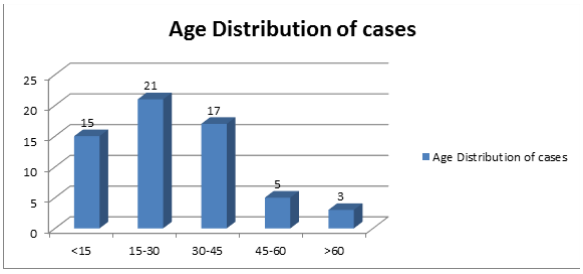

Figure 2: Age distribution of ST positive AES cases

Seasonal trend (Figure 3): The seasonal trend seen in the study - maximum cases were seen during July-September which is almost similar to the JE trend in Assam which occurs between June –August with cases peaking during the month of July.

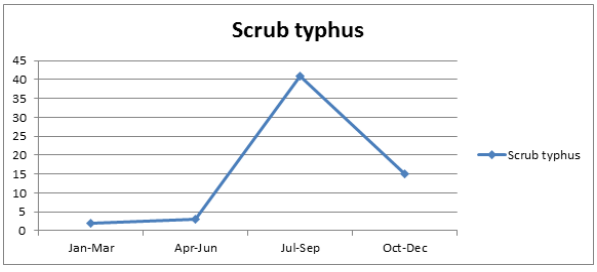

Figure 3: Seasonal Trend of ST

DISCUSSION

Scrub typhus(ST) is reported from atleast 16 states in India (Jammu & Kashmir, Himachal Pradesh, Rajasthan, Haryana, Maharashtra, Karnataka, Andhra Pradesh, Kerala, Tamil Nadu, Pondicherry, West Bengal, Sikkim, Uttaranchal, Assam, Arunachal Pradesh, and Nagaland)[1] but it is grossly under-diagnosed in India due to its non specific clinical presentation, limited awareness and low index of suspicion among clinicians, and lack of diagnostic facilities[7] . In Assam it has been reported from atleast 9 ditricts under IDSP (Dhemaji, Dibrugarh, Dima Hasao, Golaghat, Lakhimpur, Jorhat, Sivasagar, Sonitpur and Tinsukia). From these districts sporadic cases are reported throughout the year and in some pockets clustering of cases have also been seen on few occasions. ST is one of the re-emerging infections in the north east India[8] and Assam certainly is in complete conformity with this fact.

As Japanese Encephalitis is endemic to Assam every case of AES is tested for JE IgM ELISA and very scarce data is available on the etiology of the bulk of non JE cases. When it comes to ST, usual complications anticipated are hepatorenal failure, acute respiratory distress syndrome, myocarditis, septic shock and muliti organ dysfunction syndrome [5,6,7] but central nervous system (CNS) involvement in the form of meningitis or meningoencephalitis is also common in ST[6,9].

Despite all the above facts, the likelihood of ST in AES etiology has remained unexplored in Assam. In 2013 out of 1420 AES/JE cases, 491 were JE while in 2014, of the 2339 samples of AES/JE cases tested, 770 were JE. During this period RMRC, Dibrugarh, tested 433 samples from JE negative cases from across north east India and found only 1(one) case positive for ST[2]. In another study Malakar *et al*[3] found 7 positive cases of ST among 98 JE negative samples from the Dhemaji district of Assam. In this study we have found 61 cases positive for ST out of 246 JE negative samples accounting for 24.8% of the JE negative cases. Clearly there has been an increase in the number of ST cases. The finding is only slightly less than found by Kar *et al*[4] who found 30% ST positivity among the 20 AES cases tested.

The presenting symptoms of the above cases were those seen typically in a patient of AES viz.fever, headache, bodyache, altered mental status, seizure and loss of consciousness. Few of the cases also complained of skin rashes. The black eschar of scrub typhus could not be found in any of the cases similar to a study by S R Sharma *et al*[11]. In a study by Kedareshwar *et al*[5] eschar was seen in only two of the 44 patients studied. Absence of eschar does not rule out scrub typhus[11]. Also the eschar, though pathognomonic, is often not present, and as the larval bite is painless, a history of insect bite is unlikely to be solicited from the patient[6]. However among a fraction of the cases, similarities were observed across some factors that emerged to constitute risk factors for ST . These include:

1. Place of residence: pockets of districts from where sporadic cases of ST are regularly being reported
2. Surrounding environment: presence of scrub vegetation
3. Occupation: outdoor activities like farming,livestock rearing, etc
4. Lifestyle: low socioeconomic background, low level of Knowledge Attitude Practice (KAP) in health issues

All the ST positive cases of the above study were given treatment with Doxycycline once diagnosed and all the cases showed clinical improvement. Successful treatment of ST with Doxycycline has also been reported in studies from other parts of India[1,4,7,10]. Infact prompt resolution of fever and other symptoms 1-3 days after starting Doxycycline seen in some studies advocates that rapid resolution of fever following doxycycline is so characteristic that it can be used as a therapeutic test[7,10]. While dramatic therapeutic response to Doxycycline usually occurs in ST, it is also advised to start treatment early for prompt resolution[4,10]. Thus there is more reason to test a JE negative case of AES for ST in Assam as with Doxycycline therapy we can reduce mortality of patients we may otherwise lose from under diagnosis.

CONCLUSION

Cases of AES that are JE negative should be regularly tested for ST as firstly it is one of the causes of AES in Assam and secondly ST positive cases respond well to Doxycycline. The above study has included only 7 districts of upper Assam but for correct picture of AES attributable to ST in Assam a comprehensive cohort matched case control study covering all the districts of Assam is necessary. Also there is a need to address the vector status and entomological surveys for the same should be conducted, beginning in the endemic districts.

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