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*Case Report*

# Acute Disseminated Encephalomyelitis (ADEM): An Unusual Presentation of Scrub Typhus in Paediatric Patient

HY ***Ng***, KW ***Tsui***, KH ***Ma***, KY ***Liu***

**Abstract** ***Background:*** Scrub typhus is a notifiable disease in Hong Kong. The common presentation of scrub typhus can be non-specific such as pyrexia of unknown origin. Neurological manifestation is relatively uncommon, especially for acute disseminated encephalomyelitis in the globe. ***Findings:*** A 33-month-old girl presented with prolonged fever, confused consciousness, bilateral lower limb weakness, and urinary incontinence. Cranial and Spinal magnetic resonance imaging showed T2 hyper-intense signals over bilateral thalamus and long segments of spinal cord. Both clinically and radiologically suggested acute disseminated encephalomyelitis. Subsequent workup revealed significant four-fold increment in *Orientia tsutsugamushi* antibody level. She was given a course of methylprednisolone and intravenous immunoglobulins for disseminated encephalomyelitis and a course of doxycycline for scrub typhus infection. She achieved full recovery afterwards. ***Conclusion:*** As acute disseminated encephalomyelitis remains a diagnosis of exclusion and is commonly post-infection related. It is important to stay vigilant in screening for underlying atypical infection in refractory clinical presentation.

**Key words** Acute disseminated encephalomyelitis; Pyrexia of unknown origin; Scrub typhus

## Introduction

A 33-month-old girl with good past health presented with disorientation, bilateral lower limb weakness, and urinary incontinence on the 13th day of prolonged fever. Cranial and Spinal magnetic resonance imaging showed T2 hyper-intense signals over bilateral thalamus and long segments of spinal cord. Both clinical and radiological presentations were compatible with the diagnosis of acute disseminated encephalomyelitis. Subsequent workup revealed a four-fold increment in the antibody level for *Orientia tsutsugamushi*. The patient was given a course of ethylprednisolone and intravenous immunoglobulins due to progression of the neurological symptoms. She had also completed a course of doxycycline as treatment for scrub typhus infection. Subsequently, she achieved full recovery clinically and radiologically after half a month of duration. As acute disseminated encephalomyelitis remains a diagnosis of exclusion and is commonly post-infection related. It is important to stay vigilant in screening for underlying treatable atypical infection.

## Case

In September 2022, a 33-month-old girl with good past health with 2 weeks fever associated with coryzal symptoms and cervical lymphadenopathy not responding to oral Augmentin from private medical centre. There was no preceding vaccination nor exposure to risk factors of prolonged unexplained fever, such as travel history and

**Department of Paediatric and Adolescent Medicine, Alice Ho Miu Ling Nethersole Hospital, 11 Chuen On Road, Tai Po, N.T., Hong Kong SAR, China**

HY **Ng** (吳愷甄) *MBBS, FHKAM*
KW **Tsui** (徐炯環) *MBBS, FHKAM, Cert HKCPaed(PN)*
KH **Ma** (馬錦雄) *MBBS, FHKAM, Cert HKCPaed(PN)*
KY **Liu** (劉嘉儀) *MB ChB(CUHK), FHKAM*

Correspondence to: Dr. HY **Ng**
*Email: chernng7916@gmail.com*

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suspicious contact prior to fever onset. She had then developed neurological symptoms on day 13 of fever, including bilateral lower limb weakness and urinary overflow incontinence. She was admitted 2 days later due to worsening symptoms in which she could no longer bear weight. After admission, she developed a confused conscious state with bilateral decreased lower limb power to grade 3 over 5, left lower limb areflexia and right lower limb hyporeflexia together with distended bladder. Otherwise, other systemic examination was unremarkable. There was no abnormal skin rash observed on physical examination. She was suspected to have acute disseminated encephalomyelitis in view of the clinical picture of encephalopathy with paraparesis and bladder involvement.

Urgent magnetic resonance imaging of brain and spine (Figure 1) were performed showing compatible radiological features with T2 hyperintensity at dorsal medial aspect of thalami, T2 hyperintensity in cervical spine at C5 to C7 and T2 to T10 over long segments and also expanded cord at cervical segments suggestive of demyelinating disease. Electroencephalogram showed abnormal awake pattern with mild excessive posterior prominent delta waves, suggesting mild encephalopathy. Blood results showed elevated white cell count with neutrophils predominant, elevated erythrocyte sedimentation rate and deranged liver function with elevated alanine transaminase. Cerebrospinal fluid showed normal protein range and absent of white cell count, bacterial culture and virus study of cerebral spinal fluids were negative. Autoimmune encephalitis panel was negative for both cerebrospinal fluid and blood test. Antibody including anti-MOG and anti-aquaporin 4 were negative for demyelinating disease screening. In view of pyrexia of unknown origin, screening for atypical infection was also performed, with rickettsia serology by immunofluorescence assay revealed both elevated titer in the first set of samples up to 1:256 and subsequent fourfold increase to 1:1024 in the second sample (Figure 2), which was taken 14 days apart with the results available after 1 week from sampling. She was given intravenous methylprednisolone 30 mg/kg/day for 5 days then taper to oral prednisolone gradually over 4 weeks. However, in view of persistent slurred speech with weak hand grip and fecal incontinence 3 days after completing pulse steroid, another course of intravenous immunoglobulins 2 g/kg/day was given over 2 days. She was then noted to have improvement in overall motor performance with resolution of slurred speech. With the positive serological results of *Orientia tsutsugamushi* infection, she was treated with a

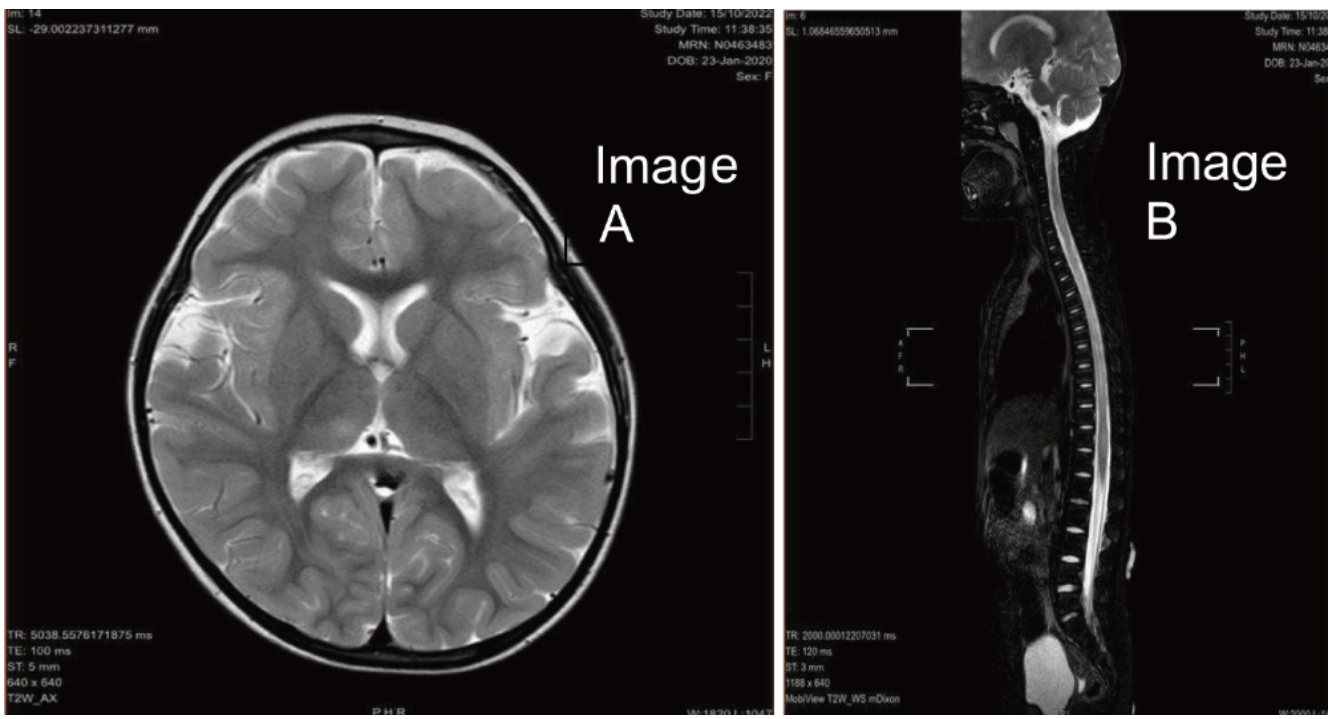


**Figure 1** Investigation results including Weil Felix test and MRI imaging. (A) T2 hyperintensity at dorsal medial aspect of thalami with right more involved than left. (B) Long segment involvement over C5 to C7 and T2 to T10.

course of doxycycline 2 mg/kg/day for 7 days (Figure 3).

Follow-up magnetic resonance imaging of brain and spine showing interval solution of bilateral thalamic changes with regressed spinal cord T2 changes after 2 to 3 weeks of time. She was able to achieve full recovery with normal gross motor performance, speech performance, bowel and bladder control after 2 to 3 weeks of time with concomitant physiotherapy and occupational therapy training.

## Discussion

Scrub typhus was once known as an endemic disease considered to be more prevalent among northern Japan, far eastern Russia, to northern Australia and to Pakistan, forming the Tsutusgamushi triangle.[1] There are 1 million cases per year in the locality of Tsutsugamushi triangle.[2] Recently, scrub typhus was not only limited within the aforementioned region,

| | Upon admission | | Sampling 14 days after |
|---|---|---|---|
| Weil Felix test | Proteus OX 19 Antibody | 40 | N/A |
| | Proteus OX 2 Antibody | <20 | |
| | Proteus OX K Antibody | 49 | |
| *Orientia Tsutugamushi* antibody titre | 256 | | 1024 |

**Figure 2** Result of *Orientia tsutugamushi* antibody titre.

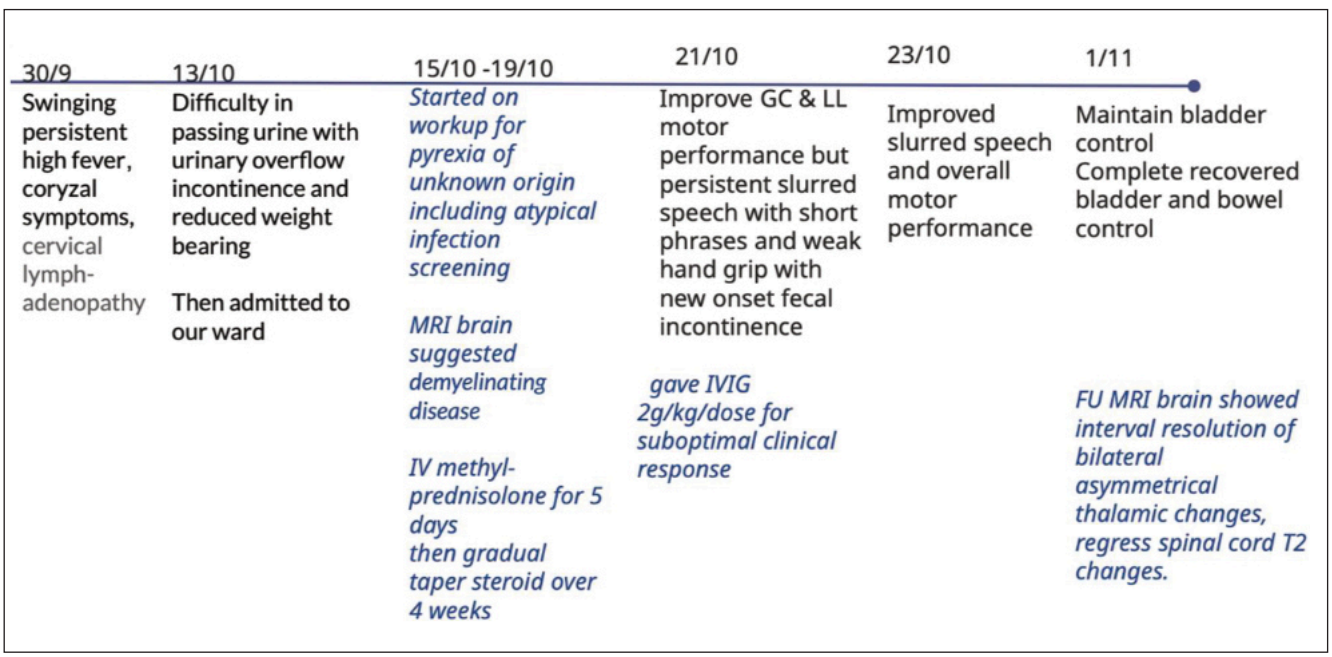


**Figure 3** Timeline of symptoms, investigations and management.

there were also reported cases in Africa and Europe.[3] It is also a notifiable disease in Hong Kong, with 21 cases reported per year in the past 10 years.[4] The common presentations include pyrexia of unknown origin,[5] presence of eschar and generalised lymphadenopathy. Neurological manifestation is uncommon, especially for acute disseminated encephalomyelitis in the global population. According to a narrative review in India.[5] Twenty percent of infected cases presented with neurological symptoms, with meningoencephalitis as the most common presentation.

Our patient presented with clinical picture compatible to classical acute disseminated encephalomyelitis. With an episode of febrile illness 13 days before onset of neurological symptoms and peak over 3 days then lasted for 2 weeks. The major neurological manifestation consisted of confused conscious state, paraparesis with impaired bladder and bowel control showing both encephalopathic and multifocal involvement. Acute disseminated encephalomyelitis is an autoimmune disorder commonly triggered by preceding infection. Apart from common viruses of the gastrointestinal and respiratory tract,[6] atypical bacterial infection and parasitic infection can also be the immune triggering factor. There were total 7 cases on National Library of Medicine reporting acute disseminated encephalomyelitis secondary to scrub typhus in the past 10 years, distributing among India[7] and China.[8,9] Age could range from 5 years old to 77 years old. All of the cases were presented with similar clinical presentation including prolonged fever, confused conscious state, speech difficulty, bladder incontinence and generalised weakness. Variable results for cerebral spinal fluid analysis, ranging from normal protein and white count same as our case to elevated protein and white cell count with either mononuclear or lymphocyte predominant picture. Majority of the cases were able to achieve satisfactory improvement after a course of methylprednisolone and doxycycline as the standard treatment for both scrub typhus and acute disseminated encephalitis. All of the above cases were serologically positive for scrub typhus infection confirmed by either Weil Felix screening test or enzyme-linked immunosorbent assay. Immunofluorescence assay is one of the gold standards with high sensitivity and specificity in detecting scrub typhus infection that was adopted by the Hong Kong public health laboratory service. The region-specific standard antibody cut-off would be 1:128 or fourfold increment in the paired samples with 14 days difference in sampling. As it may take time for the sampling and test processing, this highlighted the current limitation of turn-around-time for diagnostic investigation, and hence, it is important for clinicians to actively look for any possible underlying infection, prompting early diagnosis and treatment of atypical infection for better clinical outcome. Prophylactic treatment is also advocated if any clinical suspicion arises.

## Conclusion

Acute disseminated encephalomyelitis remains a diagnosis by exclusion. Clinicians should always be aware of alternative diagnoses if frequent relapses occur or if the patients are not responding to usual treatment. With the evolving epidemic pattern, it is also important to be aware of any possible atypical infection, which prompts earlier investigation and prophylactic management to treat underlying bacteria or parasitic infection.

## Conflicts of Interest

The authors have disclosed no conflicts of interest.

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