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**UNDIFFERENTIATED
FEVER**

- 30/ male
- **Admitted at local hospital**
 - High grade fever
 - Headache
 - Redness of skin

 - Ceftriaxone
 - Antimalarial

- **After 2 days**
 - Seizures
 - Altered sensorium
- **Transfer to tertiary care center**
 - Ventilator support
 - Inj Meropenem and vancomycin

Blood investigations

- viral markers: Negative
- CXR : N
- **SGPT: 240 u/l**
- **Creat: 1.8 mg/dl**
- Dengue NS1, Malaria Parasites by card : negative
- Urine routine :
 - **5-6 pus cells**
 - **8-10 RBCS**
 - **Granular cast+**

CBC

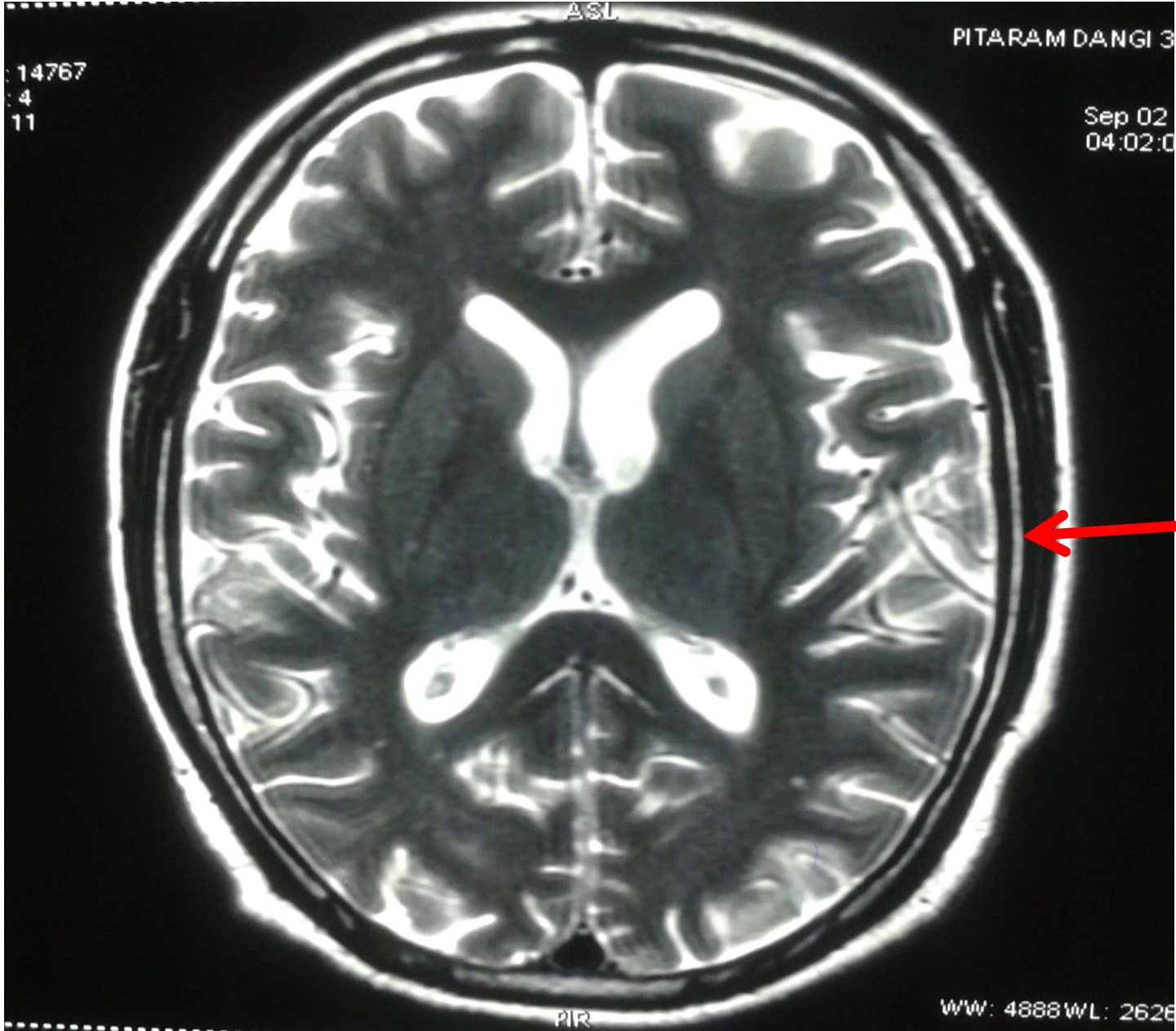
DATE	31/8/22	3/9/22	4/9/22	7/9/22
HB	12	9.3 ↓	8.9 ↓	7.5 ↓
TC	4800	6400	3400 ↓	2000 ↓
PLATELETS lacks	5	2 ↓	1.5 ↓	1.25 ↓
SGOT	116		240 ↑	116
SGPT	90			180 ↑

MRI Brain P+ C

IMPRESSION:-

MRI findings shows mild abnormal pachy-meningeal enhancement along both cerebral convexities, possibility of changes of meningitis. No evident intraparenchymal focal abnormality or acute lesion.

Clinical correlation and further work-up is recommended.



- **Lumbar puncture**

- WBC 54 L 98%
- Protein 89 mg
- Sugar 60 mg/dl
- CSF/blood glucose 0.6
- ADA 3.4 (NEGATIVE)
- **CSF culture: no growth**
- **BLOOD culture : no growth**

- **On the 6th day of meropenem and vancomycin**
 - **Persistent fever spikes and altered sensorium**

- **ID consultation**

- **On General Examination**

- Febrile
- **Generalized erythematous blanching maculopaular rash**
- No Eschar, petechial
- No Purpura, ecchymosis
- No Lnodes, Organomegaly
- **CNS Examination**
 - **Confused**
 - **Neck stiffness: present**
 - **Planter: extensor B/L**
 - **POWER : 5/5 ALL 4 limbs**



- Travel history

had leisure trip of kumbhalgadh 5 days before illness

Differential Diagnosis ??????

- Fever with rash**
- Liver/Kidney/ Bone Marrow/CNS involvement**

Differential Diagnosis

- Meningitis
 - Viral
 - TB
 - Meningococcal
- Scrub typhus (Rickettsial fever)
- Dengue

Differential diagnosis

Associated symptoms	Rickettsia	Malaria	Enteric fever	Dengue fever	Leptospirosis	Drug fever
Chills	+	++	+	+	+	+
Rash	+			+	+	+
Myalgia	++				Calf tenderness	+++
Backache, retro orbital pain				+++		
Eschar	+++					
Abdo pain, diarrhea			++	++		
Arthralgia, arthritis	++		Late	++	+	+
Dark coloured urine	+	Cola colored				
Jaundice	++	+		+	+	++
Lymphadenopathy	+		Abdomen			++
Splenomegaly	+/-	+	+		+/-	+
Pericholecystic fluid, ascites, pl.effusion				+		

- Started iv doxycycline 100 bd

TEST	RESULTS	UNIT	EXPECTED VALUE
	Ab to Scrub Typhus (IGM) By Elisa		
Ab to Scrub Typhus(IGM)	<u>POSITIVE</u>		Negative

- **Afebrile after 16 hours**
- **Improved sensorium**
- **doxycycline for 2 weeks**

Scrub typhus meningitis

Scrub Typhus

- A mite-borne, zoonotic bacterial infection
- *Orientia tsutsugamushi* (*Rickettsia tsutsugamushi*)
,intracellular, GNGB
- Vector: chiggers (larva of trombiculid mite - *Leptotrombidium*)
- Reservoir: chiggers & rats
- Humans incidentally infected



Chigger's Habitats

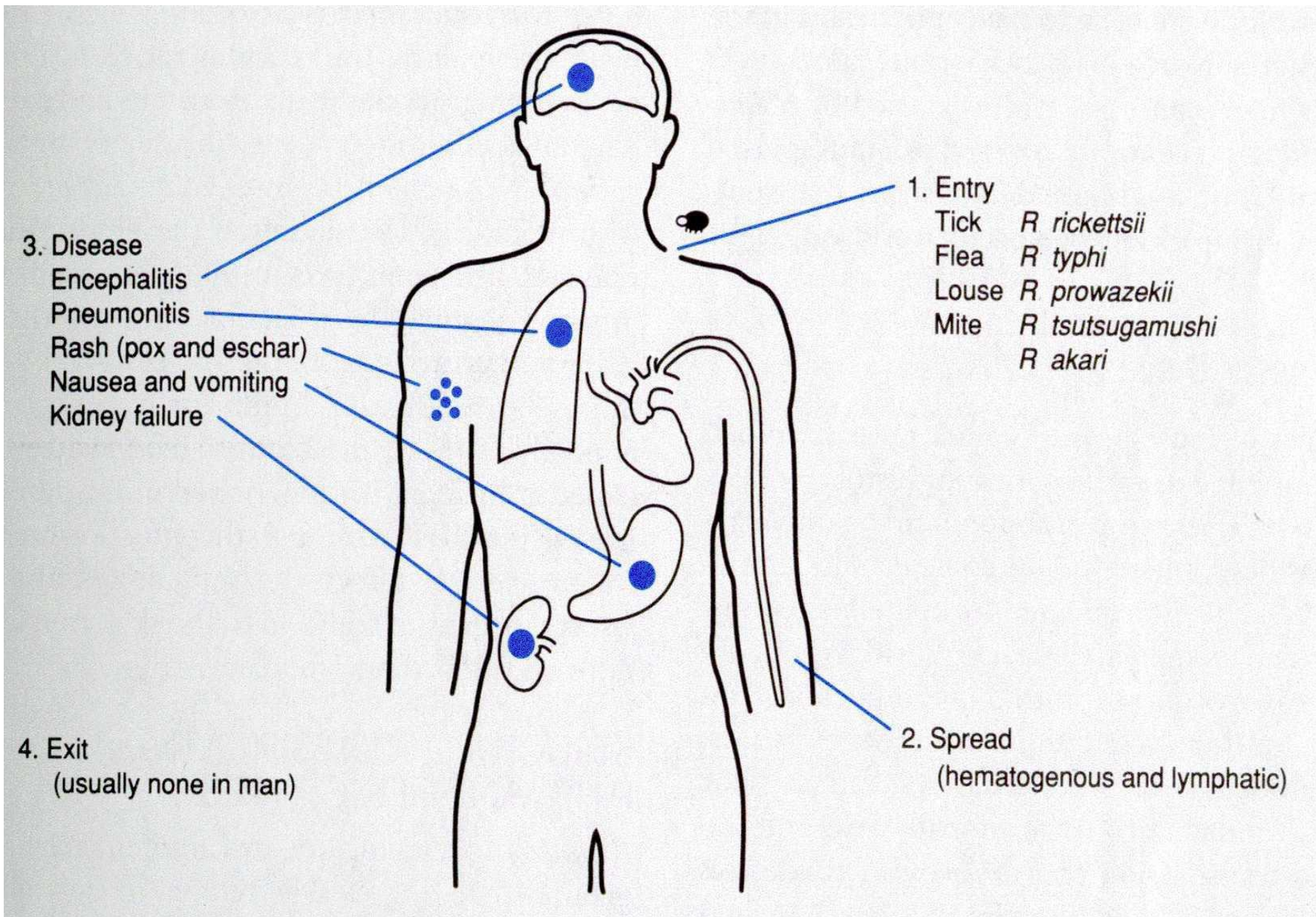


Pathogenesis and Immunity

- Predominantly infects endothelial cells causing vasculitis
- Destruction of cells
 - Multi-focal areas of endothelial injury and blood vessel damage
 - Leakage of blood into tissues (rash & edema)
 - Organ and tissue damage

Clinical Syndrome -Scrub Typhus

- Incubation period -1 to 3 weeks
- fever, headache, myalgia and multiple organ involvement
- Delirium, nausea, vomiting, cough, jaundice
- Eschar
- Maculopaular rash
 - Begins on trunk and spreads to extremities (centrifugal spread)
- Mortality rates variable



Organ Involvement & Complications

- ARDS 44% pneumonitis >60%
- Liver involvement >80%
- Refractory shock –25%
- meningitis or meningoencephalitis–19%
- Renal failure –13%

Scrub Typhus Meningitis in South India — A Retrospective Study

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Abstract

Background: Scrub typhus is prevalent in India although definite statistics are not available. There has been only one study on scrub typhus meningitis 20 years ago. Most reports of meningitis/meningoencephalitis in scrub typhus are case reports

Methods: A retrospective study done in Pondicherry to extract cases of scrub typhus admitted to hospital between February 2011 and January 2012. Diagnosis was by a combination of any one of the following in a patient with an acute febrile illness- a positive scrub IgM ELISA, Weil-Felix test, and an eschar. Lumbar puncture was performed in patients with headache, nuchal rigidity, altered sensorium or cranial nerve deficits.

Results: Sixty five cases of scrub typhus were found, and 17 (17/65) had meningitis. There were 33 males and 32 females. Thirteen had an eschar. Median cerebrospinal fluid (CSF) cell count, lymphocyte percentage, CSF protein, CSF glucose/blood glucose, CSF ADA were 54 cells/ μ L, 98%, 88 mg/dL, 0.622 and 3.5 U/mL respectively. Computed tomography was normal in patients with altered sensorium and cranial nerve deficits. Patients with meningitis had lesser respiratory symptoms and signs and higher urea levels. All patients had received doxycycline except one who additionally received chloramphenicol.

Conclusion: Meningitis in scrub typhus is mild with quick and complete recovery. Clinical features and CSF findings can mimic tuberculous meningitis, except for ADA levels. In the Indian context where both scrub typhus and tuberculosis are endemic, ADA and scrub IgM may be helpful in identifying patients with scrub meningitis and in avoiding prolonged empirical antituberculous therapy in cases of lymphocytic meningitis.

Large necrotic Eschar at bite site



Eschar

- Seen in ~ 50%
- Usually single
- **Location:** Axilla, inguinal, perianal, scrotum, buttocks and the thigh
- **Appearance:** an ulcer often covered by a dark scab
(cigarette burn)



Diagnostic test

	OX 19	OX 2	OX 3
Spotted fever	+++	+	-
Epidemic typhus	+++	+	-
Endemic typhus	+++	+	-
Murine typhus	+++	+	-
Scrub typhus	-	-	+++

- **Weil Felix is highly specific 1:80 but not sensitive for scrub typhus (Vivekanandam M JAPI 2010 , 58, 24-8)**
Due to cross reaction not recommenced
- **Anti scrub typhus IgM ELISA 86.5% SENSITIVE**
False positive with malaria ,typhoid, TB
(JAJ Prakash trop doc 2006: 36, 212-213)
- **Since Lab diagnostic is difficult , treatment should not be delayed if suspected on clinical ground**

Treatment

- **Doxycycline** **the drugs of choice**
 - clinical response within 24-72 h
- **Chloramphenicol** an alternative
- Rifampin & Azithromycin (pregnant and tetra allergic)
 - good efficacy
- Ciprofloxacin – poor response
- Other broad-spectrum abx ineffective

Take home message

- Very difficult to diagnose during acute stage
- Heightened clinical suspicion
 - epidemiological data
 - history of exposure to vectors or reservoir animals
 - travel to endemic areas
 - rash and Eschar
 - low platelets, hypernatremia, elevated liver enzymes.
- Such suspicion should prompt empirical treatment with doxycycline