THE DIAGNOSIS OF SCRUB TYPHUS: AN EVALUATION

M. RAMANATHAN
MOHD NOORDIN BIN ZAINAL ABIDIN
VENUGOPAL BALACHAND

SUMMARY

Scrub typhus is an endemic problem in Malaysia. Yet its diagnosis appears to depend heavily on the Weil-Felix test as the more sophisticated diagnostic procedures are not available routinely.

We therefore reviewed our experience with scrub typhus patients treated at the Melaka General Hospital from 1983 to April 1986, to identify those clinical features which are diagnostic of this rickettsial illness.

Based on the clinical presentation of our patients and the dramatic response of scrub typhus to Doxycycline, we propose a clinical approach to diagnosis until more specific and cheap diagnostic procedures become available in our laboratories. Otherwise, this rickettsial illness will continue to be under-recognised.

INTRODUCTION

Scrub typhus is an endemic problem in the rural parts of our country. Its diagnosis appears to depend heavily on the Weil-Felix test as the more sophisticated procedures are still not available in our clinical laboratories, particularly in the rural settings.

M. Ramanathan, MRCP(UK)
Consultant

Mohd Noordin bin Zainal Abidin, MBChB (Cairo)
Medical Officer

Venugopal Balachand, MBBS (Madras)
House-Officer

Department of Medicine
General Hospital, 75400 Melaka, Malaysia

The Weil-Felix test at its best could only be taken as an indirect evidence of this rickettsial illness. This test has certain problems: (1) only 40 – 60% of scrub typhus patients develop the OXK agglutinins.[1] Therefore a negative Weil-Felix reaction does not exclude scrub typhus infection; (2) false positive reactions can occur with sera from patients with urinary tract infections due to proteus organisms, leptospirosis, and relapsing fevers.[2]

The more sensitive and specific diagnostic procedures which are still confined to the research laboratories include: indirect immunofloures-cence technique; the enzyme-linked immuno-sorbent assay (ELISA); indirect immunoperoxi-dose technique.

Due to the limitations of the Weil-Felix test and the lack of more sensitive facilities in our laboratory, we set out to identify those clinical features which are diagnostic of this notifiable illness by reviewing the experience with scrub typhus patients at the Melaka General Hospital from 1983 to April 1986.

PATIENTS AND METHOD

The case notes of the patients who had been treated for scrub typhus were reviewed. Those who had been treated as "scrub typhus" but in whom the clinical notes were not convincing were excluded from the study. We were able to identify 25 patients with scrub typhus over the four-year study period.

RESULTS

The duration of fever with which these patients were admitted to the hospital varied from one to

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TABLE I
PREVALENCE OF SYMPTOMS IN 25 CASES OF SCRUB TYPHUS

Symptoms	Prevalence (%)
Fever	100
Chills	84
Rigours	84
Headache	56
Vomiting	28
Joint pains	16
Cough	8
Loss of appetite	24
Photophobia	8
Change in bowel habits	16
Deafness (transient)	4

TABLE II
PREVALENCE OF SIGNS

Signs	Prevalence (%)
Eschar	40
Lymphadenopathy	60
Hepatomegaly	36
Splenomegaly	36
Jaundice	12
Rash	28

15 days. Seven patients were febrile for less than five days, and nine patients had fever for more than two weeks. The mean was eight days. The prevalence of symptoms and signs are presented in Tables I and II, respectively.

The routine haemoglobin and total white cell counts of these patients were very variable and were not helpful in the diagnosis of scrub typhus.

Weil-Felix test

Fourteen patients had positive OXK titres to single serum specimen and 11 patients were negative; the range of titres varied from 1/50 to 1/4,000.

Outcome of treatment

Doxycycline was used to treat 17 patients, tetracyclines for five, and chloramphenicol for five patients. It is interesting to note that those who were on doxycycline took less than 48 hours to become afebrile, while others took more than 72 hours to do so.

DISCUSSION

We compared our findings with larger series published earlier: a series of 200 cases from American troops in World War II as reported by Sayen *et. al.*, in 1946. At that time no specific therapy was available for scrub typhus;[3] a series of 87 cases from American troops in Vietnam reported by Berman and Kundin in 1973.[4]

A comparison of the salient clinical features between the above two series and ours is given in Table III. However, a few of these signs and symptoms merit special mention. While the prevalence of headache and lymphadenopathy in our series was lower than the two previous series, our patients had higher incidence of hepatomegaly. The prevalence of an enlarged spleen was comparable to the two earlier series.

Eschar

This has always been considered the characteristic of the disease so much so earlier workers virtually excluded the diagnosis of scrub typhus in the absence of an eschar.

However, subsequently a number of workers have proved this assumption to be incorrect.

TABLE III
COMPARISON OF THE PERCENTAGE PREVALENCE OF THE SALIENT CLINICAL FEATURES

Feature	Sayen *et al*[3]	Berman *et al*[4]	Our series
Headache	–	100	56
Chills	–	80	84
Cough	–	45	8
Loss of appetite	–	–	24
Lymphadenopathy	90	85	60
Rash	71	34	28
Eschar	60	46	40
Hepatomegaly	20	13	36
Splenomegaly	35	43	36
Jaundice	–	1	12

Moreover, the incidence of eschar in Asian people has been shown to be low.[5] The presence of eschar in only 40% of our patients appears to support this claim.

There are certain features of the eschar which needs to be pointed out. Firstly, most textbooks describe the eschar as a punched-out ulcer covered with a thick black scab. However, in our patients often the black scab was missing, leaving behind only a punched-out ulcer.

The eschar should be specifically looked for in a suspicious case as they are very often found in areas which are normally missed during a cursory examination.

The site of the eschar is variable and our series did not point towards any particular site. In three of our patients, it was in the axilla while in the remaining seven patients, the location ranged from the thighs to the neck.

Only six of our patients had an eschar with a positive Weil-Felix test. In 12 patients, the eschar was not seen in spite of a positive OXK titre; on the other hand, in seven patients with eschar this agglutination test was negative.

It is obvious from Table III that the incidence of the cardinal features of the disease namely — eschar, lymphadenopathy, hepatosplenomegaly and rash — are generally much lower in our series as compared to other workers. The possible explanations for this are: Sayen's work was carried out during World War II when no specific therapy was available — therefore his patients would have gone through the natural course of the illness with all its manifestations; it is generally accepted that partially immune people do not exhibit the florid features of scrub typhus; prompt treatment with doxycycline and tetracyclines may abort a full blown attack of scrub typhus; the incidence of eschar in Asian people with scrub typhus is usually low.[5]

The Weil-Felix test

Ideally, a four-fold or greater rise in OXK titre in paired sera collected a minimum of three days apart[7] should be demonstrated to diagnose scrub typhus. However, the collection of paired sera has certain practical problems. Firstly, if scrub typhus is diagnosed promptly and treated with doxycycline, patients become afebrile within 48 hours or so. Therefore it is not possible to hospitalise the patient further for the sole purpose of taking a second serological specimen. Secondly, the cost of this procedure is prohibitive at times. Therefore we normally do only a single serological test.

When does this become significant? "The probability of diagnosing scrub typhus in Malaysian patients whose single serum specimen has an OXK titre of 1:320 is 0.79".[7]

Thus, if we use 1:320 as the cut-off point, then only 40% of our patients can be taken to have a positive Weil-Felix. This is well within the accepted limitations of 40 — 60% positivity for this serological test in scrub typhus.

The present state of notification of scrub typhus

In Peninsular Malaysia alone, results of serological tests show that as many as 5 million cases per year may occur mostly in the oil palm and rubber estates.[6]

The intensity of this problem was clearly demonstrated by Brown *et. al.*,[5] who showed that 23% of febrile patients admitted to Mentakab District Hospital, Pahang, had scrub typhus. The same study also showed that 80% of oil palm estate workers admitted with fever suffered from scrub typhus.

Yet it cannot be denied that this rickettsial illness is undernotified. It is obvious from our own series in Melaka, which may be considered to be a semi-rural area, that only 25 cases were recognised over a period of three-and-a-half years.

The possible causes for undernotification

Firstly, there is a low index of clinical suspicion. Even in our own series, only 32% were provisionally diagnosed to suffer from scrub typhus. The rest were initially considered to suffer from viral fever (40%) and a host of other illnesses (Table IV).

Secondly, an undue dependence on a positive Weil-Felix test before notifying a case as scrub typhus.

TABLE IV
TENTATIVE DIAGNOSIS ON ADMISSION

	Weil-Felix Test (No. of patients)	
	Positive	Negative
Viral fever	5	5
Typhus	3	5
Typhoid	–	3
Viral hepatitis	1	–
Urinary tract infection	–	1
Guillain Barre Syndrome	–	1
Malaria	1	–
	10	15

Thirdly, even in the Weil-Felix negative patients, too much dependence is placed on the presence of an eschar.

Lastly, unlike in typhoid and malaria, no specific, simple, reproducible and cheap test is available at the moment to diagnose scrub typhus.

Diagnosis of scrub typhus based on clinical criteria

Based on our study, we propose as illustrated in Figure 1 a set of clinical criteria to diagnose scrub typhus.

A febrile patient with a negative screening for typhoid and malaria may tentatively be diagnosed as a cause of scrub typhus even if Weil-Felix test is negative if he has four or more of the following clinical features: chills; eschar; lymphadenopathy; rash; hepatomegaly; and splenomegaly.

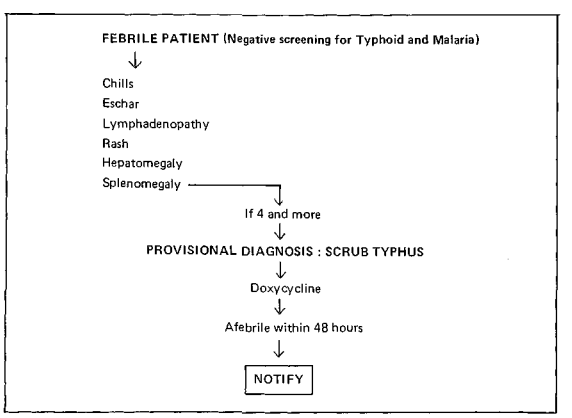

Fig. 1 A clinical approach to the diagnosis of scrub typhus.

The patient should then be put on a therapeutic trial of doxycycline. If he responds within 48 hours, it should be notified as scrub typhus.

We strongly believe such a scheme is justified until when a simple, cheap, definitive and rapid test is available to diagnose scrub typhus, especially in the rural areas. Otherwise we will continue to underdiagnose, undertreat and underestimate the intensity of this endemic illness.

CONCLUSION

Undue reliance should not be placed on the Weil-Felix test to diagnose scrub typhus. The clinical diagnosis of this rickettsial disease is possible until a specific and cheap diagnostic technique becomes available.

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