Acute Hearing Loss Due to Scrub Typhus: A Forgotten Complication of a Reemerging Disease

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We describe 6 patients with scrub typhus who presented with acute hearing loss, a forgotten complication of this reemerging disease. They were admitted with fever of 10–14 days' duration and had clinical evidence of deafness and pneumonitis. Five patients had eschars, which prompted the diagnosis of typhus fever and led to early institution of treatment. Deafness has been described as a clue to the diagnosis of scrub typhus; awareness of this symptom facilitated early diagnosis in 4 of 5 patients who recovered. Acute hearing loss or hearing impairment in a febrile patient should arouse strong suspicion of scrub typhus.

Rickettsial diseases are prevalent throughout the world. Recent reports of outbreaks of scrub typhus suggest that the disease is reemerging in Southeast Asian countries [1–4]. Variable but adequate literature on clinical manifestations and complications of this disease can be obtained from past records [5]. However, most rickettsial infections and their complications have been forgotten, either because they are absent because of wide use of effective antibiotics, such as chloramphenicol and tetracycline, or because they remain undiagnosed because of a lack of proper investigative facilities.

We have recently encountered several outbreaks of scrub typhus infection in Sri Lanka. These outbreaks occurred from the late through the early months of the year (November–May), primarily during the nonrainy periods (personal experience of R.P., T.G.A.N.C., A.S.D., and H.J.dS.). The infections were diagnosed on the basis of clinical signs: the presence of high fever, lymphadenopathy, and an eschar [6]. The clinical diagnosis was supported by the observation of rapid defervescence within 24–48 h after initiation of appropriate treatment [7]. However, no proper investigative facilities were available for disease confirmation. A recent study done in the hilly central areas of Sri Lanka provides evidence of a reemergence of infections due to *Orientia tsutsugamushi* (scrub typhus), *Rickettsia* species in the spotted fever group, and *Rickettsia typhi* [8].

The available literature on scrub typhus suggests that the most common clinical features are intermittent fever with headache, conjunctival injection, and lymphadenopathy [9]. Approximately 48%–82% of individuals develop an eschar [10] at the site of the bite of the vector, the larvae of *Leptotrombidium* species mites (chiggers). However, the detection of an eschar requires careful examination of the patient. Patients with scrub typhus may also develop lymphadenopathy and hepatosplenomegaly, and about one-third of patients with scrub typhus are known to develop deafness, which is considered to be a diagnostic feature [5]. Other complications include pneumonitis, myocarditis, vasculitis, encephalitis, and, rarely, acute renal failure [11].

During the most recent outbreak of scrub typhus in Sri Lanka (from November 2003 to May 2004) 32 patients were suspected of having scrub typhus; several patients who presented after 9–10 days of clinical illness exhibited pneumonitis, myocarditis, hearing impairment or deafness, and encephalitis. A delay in diagnosis was thought to have resulted in these complications. We describe 6 patients with hearing impairment or deafness (6 [19%] of 32) who were admitted to the professorial medical unit at North Colombo Teaching Hospital, Ragama, Sri Lanka, over a period of 8 months, and highlight the importance of suspecting scrub typhus in patients who present with fever and altered hearing of acute onset, a forgotten predictor of a reemerging disease.

Case reports. Patient 1 was a 47-year-old schoolteacher was admitted to the hospital with a 2-week history of intermittent high fever, with a temperature that varied from 38.5°C to 41°C. She had clinical evidence of pneumonitis and myocarditis. After 2 days, she complained of hearing impairment, and she developed complete deafness during the next 24 h. Later, she became delirious and restless. She had hepatomegaly (liver palpable 3 cm below the costal margin) but had no papilledema. Extensive investigation, including MRI of the brain, revealed no apparent cause of her illness. She did not respond to empirical treatment with ceftrioxone, parenteral quinine, or acyclovir. A careful clinical examination revealed an eschar on the

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Table 1. Summary of clinical and serological findings for 6 patients with scrub typhus and hearing loss.

Patient	Duration of fever in days	Type of hearing loss (no. of days since onset)	Clinical signs and symptoms present				Serum antibody titers[a]			
							Acute phase		Convalescent phase	
			Eschar	Pneumonitis	Myocarditis	Encephalitis	IgM	IgG	IgM	IgG
1	12	Deaf (~14)	Yes	Yes	Yes	Yes	1024	2048	512	8192
2	11	Deaf (~10)	Yes	Yes	No	No	4096	512	…	…
3	10	Deaf (~9)	Yes	Yes	No	No	128	64	2048	2048
4	13	Tinnitus (~11)	Yes	Yes	No	No	4096	2048	…	…
5	12	Tinnitus (~11)	Yes	Yes	No	No	2048	128	2048	512
6	14	Deaf (~9–11)	No	Yes	Yes	Yes	8192	2048	…[b]	…[b]

[a] Serological examination for scrub typhus was performed using indirect fluorescent antibody assay with the Karp strain of *Orientia tsutsugamushi* as the antigen. Titers are reported as the inverse of the last dilution at which a positive reaction was seen.

[b] Patient 6 died within 48 h after admission to the hospital; no convalescent-phase serum was available for testing.

right axilla, which led to the diagnosis of scrub typhus. She was treated with intravenous chloramphenicol and oral doxycycline and had a rapid and complete recovery. An indirect fluorescent antibody assay was used to test acute-phase and convalescent-phase serum samples for the presence of both IgG and IgM antibodies against *O. tsutsugamushi*. The assay was performed using the *O. tsutsugamushi* "Karp" strain as antigen, and antibodies were detected using goat antihuman γ-specific IgG or μ-specific IgM antibodies labeled with FITC (Kirkegaard & Perry Laboratories). A 4-fold rise in IgG titer between acute-phase and convalescent-phase serum samples was detected, which confirmed the clinical diagnosis of scrub typhus. There was complete recovery of hearing, confirmed by audiometry, in 6 months.

Patients 2–5 were women aged 57–58 years who presented with clinical illnesses similar to that of patient 1 but without features of myocarditis or encephalitis. They presented on days 12–15 of their illness. At the time of admission to the hospital, all had variable hearing impairment, ranging from tinnitus to reduced hearing. Because of our recent experience, we examined the 4 patients carefully for eschars, which we detected under the left breast, in the right groin area, on the left buttock, and on the left axilla, respectively. The patients responded rapidly to treatment with oral tetracycline. Indirect fluorescent antibody assay results revealed that 2 of these patients had >4-fold increase in IgG titer against *O. tsutsugamushi* between acute-phase and convalescent-phase serum samples and that 2 patients had high IgM titers in the acute-phase samples (convalescent-phase serum samples were not available); these findings were consistent with the diagnosis of scrub typhus. Objective hearing improvement was noted in 2 weeks to 3 months.

Patient 6 was a 52-year-old mother of 5 children who was transferred from a district hospital in the northwestern region of the country with a 14-day history of high fever and confusion. Her fever pattern was similar to the previously-discussed patients. On admission, she was confused and had hearing loss. She had abnormal movement in all 4 limbs, and her eyes rapidly oscillated in all directions. She also had clinical evidence of pneumonitis and myocarditis. This patient had been treated with intravenous quinine, intravenous ceftrioxone, and intravenous acyclovir. We entertained a diagnosis of scrub typhus because of our recent experience with febrile patients who had hearing impairment. Although we could not locate an eschar on this patient, we administered chloramphenicol and tetracycline in addition to the previously-mentioned drugs. This patient did not show any improvement, and she died within 48 h of admission. On inquiry from the hospital from which she was transferred, we learned that she had complained of tinnitus on about day 9 of her illness, prior to starting treatment with intravenous quinine, and she had developed impaired hearing 2 days later. A serum sample collected at the time of admission to our hospital revealed a high titer of IgM against *O. tsutsugamushi* (table 1), a finding consistent with the clinical diagnosis of scrub typhus infection.

Discussion. In Sri Lanka, we consider scrub typhus in the differential diagnosis of patients admitted with pyrexia of unknown origin. However, in patients with clinical features suggestive of multiorgan involvement following an acute febrile illness, the differential diagnoses typically include diseases such as leptospirosis, atypical pneumonia, falciparum malaria, and typhoid. If there is no improvement with treatment, the cases are investigated to exclude the diagnoses of connective tissue disorders and infections such as miliary tuberculosis. We sometimes commence empirical treatment for these illnesses, pending investigation results, if the patient presents with severe illness. Although such an approach may not be acceptable in developed countries, lack of facilities for confirmatory investigations and/or the deterioration of the patient's condition compel us to employ this type of patient management.

With regard to the patients described here, when the patients' initial presentations were considered, it could be argued that if the eschars had been detected at the beginning of the illness,

many or all the complications could have been prevented. However, it should be noted that the early stages of eschars frequently go unnoticed in dark-skinned people. Furthermore, the patients are usually unaware of the bite, the eschar is painless and does not itch, and the bite may be in a location that is difficult to examine, such as the groin [11]. The eschar is not easily detectable until the scab falls off, after 10–12 days, leaving a crater with a yellow base. Moreover, the eschar may mimic another wound, or it may be very small.

The other problem with rickettsial diseases is that there is no readily available test that confirms the diagnosis at an early stage of the disease. The Weil-Felix test, which was previously used for diagnosis, is nonspecific and has a low sensitivity. It is no longer recommended for the diagnosis of rickettsial infections [12]. The more appropriate tests, such as indirect fluorescent antibody assay, use antigen from in vitro cultivation of rickettsial agents, and are available only at reference centers. The only other clue to clinical diagnosis is the rapid clinical improvement of a patient who receives appropriate treatment [7]; this is retrospective and nonspecific.

Therefore, we stress the importance of suspecting rickettsial infections in patients who present with pyrexia of unknown origin, especially with complications that were previously documented in the literature. We believe that, if the relationship between scrub typhus and hearing impairment had been considered, we could have prevented the costs incurred in the investigations and treatment in patient 1 and the death of patient 6.

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