Tick Borne Relapsing Fever Imported into the United Kingdom

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**SUMMARY:** A case of tick borne relapsing fever contracted in Cyprus and imported into England is reported. This is the first report of the diagnosis being established by finding the organism in the bone marrow.

**Case Report**

A 24 year old soldier was admitted to the Cambridge Military Hospital, Aldershot, with a two-day history of fever, vomiting, headache and backache of abrupt onset. He had had a similar episode which lasted three days and ended five days before the start of his current illness. He had recently returned directly to England from Cyprus, where he had spent three weeks on exercise. In the last week of this exercise, and seven days before he first became ill, he spent the night in a cave, and on waking noted the presence of ticks on his legs.

On examination his temperature was 38.3°C. The liver was palpable, but not tender, 2cms below the right costal margin. The spleen was palpable 3cms below the left costal margin. A fading haemorrhagic lesion, possibly an insect bite, was present over the Achilles tendon of the left leg and there were no other abnormal findings.

Investigations showed Hb 10.4g/dl, MCV 90fl, PCV 0.34, MCHC 30g/dl, MCH 30pg. The white cell count was 7.7 x 10^9/l with 25 per cent polymorphs, 65 per cent lymphocytes and 7 per cent monocytes. The platelet count was 97 x 10^9/l. The erythrocyte sedimentation rate (ESR) was 90mm/hour.

Three hours after admission his temperature rose to 41°C and he had a rigor. The following tests were negative — cultures of urine, sputum and blood; repeated examination of the peripheral blood for malarial parasites; Weil Felix and Widal tests and serological tests for syphilis, glandular fever, psittacosis, Q fever, toxoplasmosis, cytomegalovirus, leptospirosis, brucellosis and hepatitis B. Liver function tests, urea and electrolytes, prothrombin time and immunoglobulins were normal apart from IgM which was 5.53g/1 (normal 0.45-1.8) consistent with acute infection. A chest X-ray, electrocardiogram and ultrasound of the liver and biliary tract were normal.

After one day he became apyrexial and asymptomatic and remained thus for three days, following which there was recurrence of symptoms and fever up to 41°C for two days. There was then an apyrexial asymptomatic period of five days followed by a recurrence lasting two days. Physical signs remained unchanged throughout this period, at the end of which Hb was 9.6g/dl with a normochromic normocytic film. The white cell count and differential platelet count, liver function tests and urea and electrolytes were normal. The ESR was 66mm/hour. A specimen of bone marrow was obtained by sternal puncture. This showed normoblastic erythropoiesis and the presence of organisms of the genus *Borrelia*. These were also present, though in sparser number, in a Giemsa stained peripheral blood smear taken at the same time.

The patient was given 30mg of prednisolone orally followed 24 hours later by a single oral dose of 200mg of doxycycline. Two hours after this he felt nauseous and his pulse rate rose from 80 to 100 per minute, and remained thus for two hours. He remained otherwise well and there was no change in blood pressure or temperature.

He stayed in hospital for a further 16 days and was discharged 39 days after admission, at which time neither the spleen nor the liver was palpable. At discharge Hb was 13.4g/dl and white cell count, platelets and ESR were normal.

Two weeks later he was readmitted with symptoms and signs, similar to, but of a milder nature than his other relapses. *Borrelia* were not found on a peripheral blood smear. It was assumed that he had suffered a further relapse and he was given a one week course of tetracycline 250mg q.d.s. without ill effect. There was no further relapse over a period of six months follow up. The course of events is show in Figure 1.

**Discussion**

As a disease imported into Great Britain relapsing fever is rarely recognised. Only two cases were notified in the decade 1972-1982.¹ The patient contracted the disease...
after a night spent in a cave in a rural area near Nicosia in Cyprus where he was bitten by ticks. He appears to have had a mild illness and indeed tick borne relapsing fever (TBRF) in Cyprus is rarely severe.\footnote{2} Relapsing fever was first diagnosed in Cyprus in 1939.\footnote{2} It has since been identified in most parts of Cyprus especially in the rural areas around Kyrenia, Famagusta, Nicosia and Larnaca. Several cases were reported in British soldiers in 1945.\footnote{3} All had slept in a cave 8-9 days before becoming ill. The vector was shown to be the soft tick \textit{Ornithodoros tholozani} which lives in caves, holes and rodent burrows.\footnote{2} In Cyprus it prefers rocky shelters and caves with guano floors. It feeds for less than an hour and the bite is rarely painful. Infection occurs by irrigation of the feeding puncture with contaminated saliva or coxal fluid. Ticks can act as the reservoir of infection by the mechanism of transovarial passage.\footnote{4} A presumed rodent reservoir in Cyprus has not been identified.\footnote{7} The disease is infrequently diagnosed in the indigenous population — probably because previous exposure leads to acquired immunity. It is well known that in endemic areas the disease is usually more severe in newcomers.\footnote{5} The causative organism in Cyprus has not been clearly identified — it is either \textit{Borrelia hispanica} or \textit{Borrelia persica} or possibly both.\footnote{2}

The estimated incubation period in this case was 7 days which is the average found in a review of 2073 cases. The average number of relapses in TBRF is 3 with a range of 0-13.\footnote{5} This patient had 4 relapses. Relapses are due to the antigenic instability of the organism.\footnote{7} Relapses stop when the patient develops cumulative immunity to the relapse strains.\footnote{8} The abrupt onset of the initial illness, and of each relapse, whilst feeling well between relapses, which occurred in this patient, are characteristic. Relapses tend to be less severe than the initial illness. In this patient relapses were of equal clinical severity apart from the last relapse which was milder. Apart from splenomegaly, which occurs in 41 per cent, and hepatomegaly (18 per cent) this patient had no other signs of TBRF such as jaundice (8 per cent), rash (28 per cent) and neurological features (8 per cent).\footnote{6} Moderate normochromic normocytic anaemia is common.\footnote{6} The absolute white cell count was normal but there was relative lymphocytosis and an absolute monocytosis. Monocytosis up to 10 per cent of the total white cell count is well documented.\footnote{9} In this case there was an initial thrombocytopenia. Thrombocytopenia occurs in 93 per cent of cases of louse borne relapsing fever (LBRF) but figures for TBRF are not available.\footnote{10} The ESR is markedly variable.\footnote{11}

In this patient \textit{Borrelia} were first found during the third relapse on examination of the bone marrow. Organisms were also present, though in sparse number, in blood films made at the same time as, and for one day after, the bone marrow examination. They were not found on re-examination of earlier peripheral blood films. A literature search suggests this is the first report of finding the organism in the marrow. In all types of relapsing fever the organism is rarely found in the blood in intervals between relapses, although during febrile periods it can be found in 70 per cent of cases. There are, however, some types of relapsing fever where the laboratory diagnosis is hampered by the paucity of organisms in the blood.\footnote{12} In such a case the diagnosis can often be made serologically or by inoculation of blood into young mice.\footnote{12} \textit{Borrelia} may be difficult to detect with Romanovsky stains and a recent study using an acridine-orange stain and fluorescent microscopy has provided a higher diagnostic yield.\footnote{13} It is possible that bone marrow examination will provide an alternative diagnostic method when examination of the peripheral blood is negative. Serological testing for \textit{B. hispanica} and \textit{B. persica} was not possible due to lack of specific antigen.

This patient did not show the characteristic features of a Jarisch-Herxheimer reaction (JHR) after treatment and the small dose of prednisolone he was given was unlikely to have influenced this as much larger doses (3mg/kg) had only a slight effect in modifying the JHR or LBRF whilst naloxone intravenously has recently been shown to diminish or prevent the JHR or LBRF whilst naloxone 30-40mg intravenously had no effect.\footnote{17}

This patient was initially treated with a single oral 200mg dose of doxycycline and had one further relapse 4 weeks later. This dose had been very successfully used in the treatment of LBRF.\footnote{10} TBRF however is known to be more likely to relapse after treatment and trials are needed to compare tetracycline with single dose doxycycline. Until then a prolonged course of tetracycline remains the treatment of choice in TBRF.\footnote{10}

REFERENCES

1. Office of Population, Censuses and Surveys and PHLS Communicable Disease Centre. Series MB2 No 9 Communicable Disease Statistics. 1982; Table 1A.
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