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Clinical presentation of louse-borne relapsing fever among Ethiopian refugees in northern Somalia

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Louse-borne relapsing fever (LBRF) is still endemic among Ethiopian populations. In order to assess the clinical presentation of LBRF in an Ethiopian refugee camp in northern Somalia, a referral system was organized for all pyrexias of unknown origin. Among the 134 patients referred, 37 showed *Borrelia* in fresh and stained blood smears. Common clinical features were: high fever (above 39°C in 73% of the cases), headache and general body pain (88%), liver tenderness (62%), petechia (54%), nausea and vomiting (46%), chills and rigors (30%) and epistaxis (11%). Jaundice was absent. No fatalities were observed. The clinical picture was less severe than in previous studies on LBRF. This difference might be due to the fact that the present study was community-based as opposed to the previous studies which were hospital-based.

Ethiopia is an historic focus of louse-borne relapsing fever (LBRF) (Robinson, 1942; Bryceson *et al.*, 1970). The recent concentration of large Ethiopian populations in refugee camps has created highly favourable conditions for the development of louse infestation and transmission of LBRF. In such camps, so-called pyrexias of unknown origin are a daily problem for practitioners. Therefore, in the absence of laboratory facilities, the identification of clinical criteria for the diagnosis of LBRF is of prime practical importance. This was the first objective of the present study, carried out in September 1986 in the Tugwajale B refugee camp located in northern Somalia. Study of patients recruited like ours at a community level might give a more accurate picture of the disease than hospital-based studies previously carried out in Khartoum (Salih *et al.*, 1977; Ahmed *et al.*, 1980) and Addis Abeba (Bryceson *et al.*, 1970).

BACKGROUND

The Tugwajale B camp, which contains 32 000 refugees, is located in northern Somalia 70 km east of Hargeisa, the regional capital, and 5 km west of the Ethiopian border. The camp area is a semi-desert highland at an altitude of about 4500 ft. At the time of the survey (September 1986), the temperature ranged from 10–28°C, but a minimum temperature of about 0°C is common in winter. Most of the refugees reached the camp during the first three months of 1986, having originated from the neighbouring Harargue province in Ethiopia. This population was rural-based or semi-nomadic. A camp survey conducted in September 1986 showed that 52% of the population belonged to the Somali ethnic group and 45% to the Oromo group. Most of the refugees (86%) lived under tents given by the relief organizations, while the others had built traditional huts. A mean of five persons lived in each tent, which measured 2 × 4 m.

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Refugees were cared for by the relief agencies Médecins sans Frontières, Save the Children Fund and Somalian Red Crescent under the responsibility of the Somalian Refugee Health Unit (RHU). Health structures included outpatient departments with adult and maternal–child health clinics. Severe illnesses were referred to the Medical Observation Unit, which was a hospital under tents. 'Home visiting' activities were also carried out by the health team with the help of refugee community health workers. Despite repeated insecticide campaigns, louse infection remained heavy, favoured by the lack of personal hygiene and the crowded life in the tents. In early 1986, limited blood smear examinations had shown that LBRF occurred in the population and, at first, pyrexia of unknown origin was currently treated as such.

POPULATION AND METHODS

The present study was carried out from 18–28 September 1986. During this period all patients from the camp with pyrexia of unknown origin (fever over 38°C, 100·4°F, without obvious cause) were referred to the Medical Observation Unit from the outpatient departments and by 'home visiting' teams. Symptoms and signs were recorded on charts drawn up with the physicians and nurses of the camp. A field laboratory for standard staining, microscopic examination and centrifugation had been set up.

Each patient with pyrexia of unknown origin had blood taken by finger-tip puncture. A microscopic examination of fresh samples was performed. Thin blood smears were dried, stained by the Diff Quick technique (Harleco) and read in the field (BL). Thick smears were dried for 12 hours, dehaemoglobinized, fixed with methanol and then stained with 3% Giemsa solution. On return to Paris all the stained smears were re-read independently by two investigators (B.L., J.J.R.).

In addition, each patient had blood taken by venepuncture and/or onto filter paper using a calibrated microtube. A second blood sample was obtained ten to 15 days later from 45% of the patients. Serology was performed on serum or on the eluate obtained from the filter paper for *Rickettsia prowasecki* and *R. mooseri*, using a Dot ELISA technique at a 1/100 and the immunofluorescence technique (Lennette and Schmitt, 1984). IF tests were considered as positive when the dilution was equal to or higher than 1/80. The criteria for a recent infection was an initial titre higher than 1/160 or a four-fold increase in titre between the first and the second sample.

RESULTS

During the observation period, 134 patients with pyrexia of unknown origin were referred to the Medical Observation Unit. Recent infection with *R. prowaseki* was diagnosed in one case. No recent infection with *R. mooseri* was recorded. Low titres of antibodies to *R. prowasecki* were found in 36% of the patients by Dot ELISA and/or IF. *Plasmodium falciparum* was found in three patients, and *P. vivax* in one.

Louse-borne relapsing fever was diagnosed in 37 patients. The age of the 37 borrelia cases ranged from three to 35 years (median: 14), with 84% of cases under 25 years of age. The male: female ratio was 0·94. Fifteen cases belonged to the Somali ethnic group, 21 to the Oromo. Most of the LBRF patients had been in the camp for six to eight months. The distribution of the LBRF cases throughout the camp sections was homogeneous. The patients consulted on average four days after the appearance of the first symptoms.

A temperature of above 39°C was observed in 27 patients (73%). Chills and rigors were reported in 30% of the patients. Severe headache and general body pain were reported in 88% of the cases; general body pain was usually muscular or joint pain, and abdominal pain. Cough was reported in 66%. Nearly half (46%) had nausea or vomiting, and 32% had watery diarrhoea.

Most of the patients looked apathetic and were silent on admission. Tachycardia was commonly above 120 beats per minute. Conjunctivitis was reported in eight patients (21%). Jaundice was absent. Liver tenderness was the most common sign and occurred in 62% of the cases. Spleen tenderness was present in 38%. The liver was palpable in 13%, and the spleen in 5% of the cases. Petechial spots were found in 20 patients (54%). Epistaxis occurred among 11% of the patients. No other type of skin involvement such as rash or ecchymosis was noticed. Bleeding gums were present in 16% of the patients. Neurologic signs were never observed. No significant auscultatory signs were recorded. Among those with diarrhoea, one reported having seen blood in the faeces.

Patients were treated with IM procaine penicillin (300 000 international units) on the first day of admission, followed by oral doxicyclin 200 mg on the second day (adult regimen) according to RHU recommendations. Patients were discharged after 48 hours if they had improved. No Herxeimer reaction and no deaths were recorded during the period of hospitalization.

Among the 37 patients, four were pregnant women in the last three months of pregnancy. All four had a severe attack with fever of around 39·5°C. Two of them, in their ninth month of pregnancy, delivered still births at the time of the relapsing fever attack.

DISCUSSION

The present work confirms the persistence of LBRF in a population originating from an historic focus of the disease, and indeed from an area where outbreaks have been reported since 1937 (Bryceson *et al.*, 1970). This raises the question of the mode of persistence of *B. recurrentis* in its endemic focus.

Of the 37 cases, 31 (84%) occurred in subjects under 25 years of age. This age distribution is clearly quite different from that in the camp population. A previous survey in the same population showed that the prevalence rate of louse infestation (about 60%) does not vary according to age (unpubl. data). This suggests that older people might have developed immunity through previous infection. A serological test for diagnosing past infections of *B. recurrentis* is not yet available.

In the present study, the clinical picture of LBRF showed marked differences between patients, but was less severe than that reported in investigations previously carried out in Ethiopia and Sudan (Bryceson *et al.*, 1970; Salih *et al.*, 1977; Ahmed *et al.*, 1980). Indeed, our study confirms the favourable prognosis of LBRF when treatment is given at an early stage. However, we did not observe any case of jaundice, whereas this sign was present in 16% of the patients studied by Bryceson *et al.* (1970), 41% of those studied by Ahmed *et al.* (1980) and 46% of those studied by Salih *et al.* (1977). We observed epistaxis in only 11% of our cases as compared with 35–40% in reports by the same authors. The lesser severity in our group of patients might by related to the fact that the other authors conducted hospital-based studies, whereas our study was community-based. Therefore, our patients were recruited independently of the severity of illness. In addition, our study was conducted after the main nutritional problems in the camp had been resolved; the importance of nutritional status in the severity of LBRF has been underlined by others (Bryceson *et al.*, 1970).

When the camp was newly set up, a higher mortality associated with pyrexia of unknown origin was reported than during our period of observation. In addition to the improvement in nutritional status, this might be related to the delay in treatment while the camp was being organized and to possible variations in the prognosis of LBRF according to the stage of outbreaks. Since there were no permanent laboratory facilities, the occurrence of other causes of fever associated with a higher mortality (e.g. typhus, as shown by the prevalance rate of residual antibodies) cannot be excluded.

Signs other than jaundice and epistaxis were observed with a similar frequency in our work and in that of others (Bryceson *et al.*, 1970; Salih *et al.*, 1977; Ahmed *et al.*, 1980). In particular, the liver tenderness present in 50–60% of cases indicates frequent occurrence of hepatic involvement. In our study, when the 37 LBRF cases were compared to the 97 patients with pyrexias of unknown origin which were not due to *Borrelia*, liver tenderness was the only discriminatory sign (23/37 *v.* 37/97, $\chi^2=6{\cdot}25$, $P<0{\cdot}01$). The difference was borderline for spleen tenderness (14/37 *v.* 27/97), but a similar percentage was found in LBRF *v.* non-LBRF pyrexia of unknown origin for petechia (54% *v.* 62%) and cough (66% *v.* 77%). Therefore, these signs which were common in the LBRF we diagnosed had no discriminatory value. In the literature, the frequency of petechia varies from zero (Salih *et al.*, 1977) to 17% (Bryceson *et al.*, 1970) and 60% (Greaves *et al.*, 1945). The frequency of cough reaches 53% in some studies (Bryceson *et al.*, 1970). As we did not identify discriminatory symptoms or groups of symptoms which could be used in practice for diagnosing LBRF on clinical grounds, laboratory diagnosis of LBRF should be performed in the field. Refugee camps cannot be equipped with sophisticated laboratories, but *Borrelia* can be identified easily in fresh blood smears and after standard staining.

The fact that two of the four LBRF pregnant women delivered still-born babies is consistent with previous reports on the adverse effects of LBRF on the foetus (Bryceson *et al.*, 1970; Goubau, 1984).

From our limited experience, the procedure for treatment and early follow-up of LBRF cases in Tugawale B camp appears to be adequate. In fact, the main difficulty is prophylaxis. Despite the four de-lousing campaigns which preceded our study, LBRF was still a problem in the camp. The resistance of lice to insecticides had been correctly tested but major difficulties had been encountered in implementing the dusting campaigns. This was mostly due to difficulty in spraying very large populations, and to cultural factors which deterred the subjects, especially the women, from undergoing individual body treatment. In addition, knowledge about the mode of transmission and prevention of LBRF was notably insufficient, as shown by a survey we conducted during the period of our clinical investigation on a random sample of the camp population. For instance, less that 50% of the population related the lice to fever, and only 65% knew why de-lousing dustings were performed. Based on these observations, culturally targetted health messages are currently being distributed in Tugwale B camp to promote this prevention.

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An investigation of the coagulant activity of the venom of the saw-scaled viper (*Echis carinatus*) from Saudi Arabia

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Unlike the venom of *Echis carinatus* from India, Pakistan, Nigeria, Kenya, Iran and Oman, Saudi Arabian *E. carinatus* venom is a poor activator of prothrombin. However, it possesses similar defibrinogenating activity to the other venoms. This is because the venom from Saudi Arabian snakes contains a calcium-dependent factor X activator. It is suggested that in future studies of the coagulant activity of venoms, the determination of plasma coagulant activity should be carried out in the presence of added calcium ions. This applies particularly to those venoms which do not act on plasma or fibrinogen, but which do cause *in vivo* defibrinogenation.

The coagulant properties of the venom of the saw-scaled or carpet viper, *Echis carinatus* (ECV), originating from Saudi Arabia, were investigated in an attempt to explain why it causes powerful *in vivo* defibrinogenation in the absence of significant *in vitro* coagulant action on plasma (Theakston and Reid, 1983).

MATERIALS AND METHODS

Venom

A pool of lyophilized venom from six adult Saudi Arabian specimens of *E. carinatus* maintained at the Liverpool School of Tropical Medicine was used. Venom was reconstituted in physiological solution immediately before use.

Plasma Coagulant Activity

Four healthy human volunteers were bled from the cubital vein and 25 ether-anaesthetized mice were bled by cardiac puncture. The pooled blood from each was collected in citrate (nine parts blood: one part 3·8% sodium citrate) and platelet-poor plasma was prepared by centrifuging at 1500 ***g*** for 15 minutes, at 4°C. Two different methods were used to study plasma coagulant activity:

(1) Venom (50 µl of a 250 µg ml^{-1} solution), or saline, was added to 0·2 ml of plasma and 0·1 ml of different calcium chloride concentrations (3·125–25 mM) at 37°C. The clotting times were recorded following addition of the venom.
(2) Fifty microlitres of different venom concentrations (final concentrations ranging from 1000–1·8 µg ml) was added to 0·2 ml of human or mouse plasma and 0·1 ml of 12·5 mM $CaCl_2$/37°C, and the clotting times recorded. The minimum coagulant dose on plasma (MCD-P) was estimated using the method of Theakston and Reid (1983). The MCD-P is defined as the minimum amount of venom which clots the plasma in 60 seconds.

Prothrombin Activation

Bovine prothrombin was prepared according to the method of Miletich *et al.* (1980). Briefly, 800 ml citrated bovine plasma was precipitated by addition of 43·2 ml 1 M barium chloride,

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