

CASE REPORT

A case of post-partum borderline tuberculoid leprosy complicated by a median nerve abscess, peptic ulceration and rifampicin-induced haemolytic renal failure

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Summary We report a case of borderline tuberculoid leprosy complicated by a median nerve abscess, acute renal failure secondary to rifampicin-induced haemolysis and duodenal ulceration secondary to steroid use. Rifampicin induced haemolysis is a rare and probably under-reported complication of leprosy multi-drug therapy. It should be considered when patients complain of flu-like symptoms after taking their monthly rifampicin.

A 31-year-old Indian woman from Mumbai presented 3 weeks after a full-term delivery in September 1999, with a history of numbness on the lateral border of the right thumb. Over the next 2 weeks, she developed swelling of her wrist, loss of sensation over the thumb and reduced grip strength. A week later, a papular erythematous eruption appeared at the same site. Neurophysiological studies confirmed lack of sensory conduction within the digital nerve affecting the thumb and a skin biopsy showed a granulomatous dermatitis with epidermal erosion. Leprosy was considered but a provisional diagnosis of cutaneous sarcoid was made.

She was commenced on prednisolone 40 mg once daily. After 3 weeks, the skin rash had resolved, the wrist swelling and grip strength had improved, but the anaesthetic patch on the lateral border of her thumb remained unchanged. The rash recurred when the prednisolone dose was reduced to 20 mg and the swelling returned when the dose was further reduced to 2.5 mg.

At this point, she moved house and presented for the first time in June 2000 to Kings College Hospital, 10 months after her original symptoms. There was absence of light touch, pinprick and temperature on the lateral border of the thumb. The right radial cutaneous nerve was thick and non-tender, the median nerve was positive for Tinel's sign and the right abductor pollicis brevis had reduced power. A group of violaceous papules forming a plaque over the thumb were present. A skin biopsy showed oedematous confluent granulomas in the dermis with associated nerve destruction. No mycobacteria were seen. The HLA-DR

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epidermal stain was strongly positive, indicating an active inflammatory process. She was reviewed at the Hospital for Tropical Diseases. These clinical features and neurophysiological findings in combination with the histology were consistent with post-partum borderline tuberculoid leprosy in reaction complicated by median nerve damage.

She was treated with the World Health Organisation (WHO) recommended regimen for paucibacillary leprosy, rifampicin 600 mg monthly together with dapsone 100 mg daily and prednisolone 40 mg daily for the management of the neuritis.

Three weeks later, she developed acute abdominal pain secondary to an acute perforated duodenal ulcer and required an emergency laparotomy. The perforated duodenal ulcer was oversewn with an omental patch. She was rapidly weaned off prednisolone and commenced on cyclosporin 100 mg daily as alternative immunosuppression. She made a good post-operative recovery. Endoscopy performed 3 weeks later showed a mild residual duodenitis and antibody to *Helicobacter pylori* was detected. In addition to the lansoprazole 30 mg twice daily started postoperatively, she was treated for 2 weeks with amoxicillin 1 g twice daily and clarithromycin 500 mg twice daily.

Three weeks later, her haemoglobin dropped to 10.2 g/dl (normal range 11.5–16.0 g/dl) with a raised reticulocyte count of $183 \times 10^9/l$ (normal range $25-100 \times 10^9/l$). The only new finding was a low-grade fever of 37.8°C. The anaemia was attributed to dapsone, which was then discontinued. Three weeks later, the haemoglobin had returned to 12.3 g/dl with a reticulocyte count of $146 \times 10^9/l$. Her G6PD levels were normal and she was recommenced on dapsone at a dose of 100 mg daily.

In November 2000, she developed a tender 1 cm fixed nodule over the right thenar eminence (Figure 1). MRI of the wrist and hand showed abnormal thickening with heterogeneous increased signal intensity within the median nerve (Figure 2) with an area of reduced T1 weighted signal intensity at the centre of a nodule suggestive of a fluid nidus



Figure 1. There is a papular violaceous eruption over the medial aspect of the right thumb. In addition, a tender 1 cm fixed nodule over the right thenar eminence is noted, corresponding to the underlying median nerve abscess.



Figure 2. An MRI (post-contrast and T1 weighted) of the wrist and hand showing abnormal thickening with heterogenous increased signal intensity within the median nerve that lies within the thenar eminence.

and consistent with a nerve abscess (Figure 3). She was restarted on a reducing course of oral prednisolone initially at 40 mg daily and the median nerve abscess spontaneously discharged. After 1 month (prednisolone 20 mg daily), the median nerve was less tender and the skin lesions were less erythematous.

She continued to make good progress, but in February 2001 she developed diarrhoea, vomiting, jaundice and rapidly became anuric. She was admitted in acute renal failure, creatinine $600 \mu\text{mol/l}$ (normal range $70\text{--}120 \mu\text{mol/l}$), haemoglobin 8.5 g/dl and a raised reticulocyte count of $212 \times 10^9/l$. The rifampicin was discontinued. She was treated supportively and the prednisolone was increased to 60 mg daily. Her urine output increased over the next 48 h and her creatinine reduced to $450 \mu\text{mol/l}$. Anti-rifampicin antibodies were demonstrated within the serum, suggesting a diagnosis of rifampicin-induced haemolysis complicated by acute renal failure. By June 2001, the renal function had normalized whilst

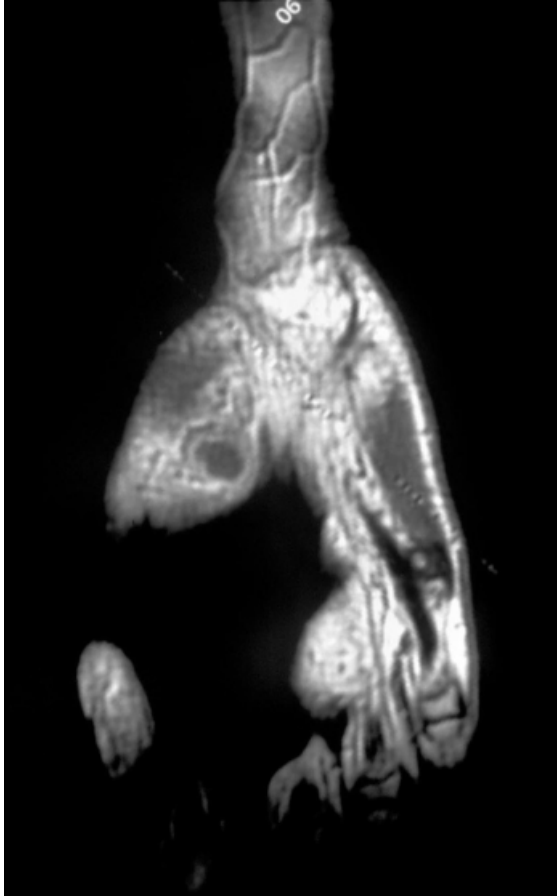


Figure 3. An MRI (T1 weighted) showing reduced signal intensity within the centre of the nodule, which is suggestive of a fluid nidus and consistent with a nerve abscess.

the cutaneous and neurological symptoms continued to settle on a reducing course of prednisolone.

Discussion

This patient illustrates the classical presentation of post-partum borderline tuberculoid leprosy in reaction. The case was complicated by a perforated duodenal ulcer, the development of a median nerve abscess and rifampicin induced haemolysis, which are all rare in isolation, let alone in the same patient.

The development of a post-partum type 1 reaction, in patients with established disease is well documented.¹ In pregnancy, a state of relative immunosuppression occurs with the maternal immune response being directed away from cell-mediated immunity to humoral activity. With restoration of full cell-mediated immunity in the immediate post-partum period, previously sub-clinical symptoms may become manifest. Our patient developed an

erythematous plaque 6 weeks after delivery and this is typical of other reported cases.² In these patients, rapid and severe nerve damage was a prominent feature. The severity of this reaction may be explained by the presence of previously unrecognized antigen within the peripheral nerves. This is supported by the demonstration that live but dormant *Mycobacterium leprae* may persist in peripheral nerves.³

Nerve abscesses are unique to leprosy, more commonly occurring in tuberculoid leprosy⁴ and only rarely in lepromatous leprosy, where they may complicate ENL (erythema nodosum leprosum) reactions.⁵ Affected nerve fasciculi may caseate, forming cold abscesses along the course of the nerve. The caseous material is secondary to destruction of nerve tissue and possesses few or no *M. leprae*, when compared with the numerous *M. leprae* found in the purulent exudate from a lepromatous nerve abscess. Nerve abscesses can affect all cutaneous nerves, but most commonly the ulnar nerve. Involvement of the median nerve is rare, but when it occurs it may be complicated by an acute carpal tunnel syndrome.⁶ Treatments for nerve abscesses include surgical evacuation of the caseous material⁷ and immunosuppression with corticosteroids.⁸

The association between corticosteroid usage and peptic ulceration remains controversial, but is very relevant in leprosy with the frequent usage of corticosteroids to treat leprosy reactions. Evidence from a large meta-analysis suggested that the incidence of corticosteroid related peptic ulceration in 6602 patients was not significantly different to that of a control group.⁹ However a sub-section of patients (where the total dosage of prednisolone exceeds 1000 mg or where it is prescribed for longer than 30 days¹⁰) appear at higher risk of developing steroid-induced ulcers. Further risk factors for peptic ulceration are listed in Table 1. Despite this the literature on the association between corticosteroids and peptic ulcer disease in patients with leprosy was sparse until the recently published TRIPOD trials.¹¹ Analysis of these trials showed no increased risk of major adverse effects (psychosis, peptic ulcer, cataract, glaucoma, diabetes and hypertension) between those patients with nerve function impairment (RFI) treated with prednisolone compared to placebo. In summary whilst the link between corticosteroids and peptic ulcer disease remains unproven,^{9,11,12} standardized regimes of corticosteroids for the treatment of RFI have been shown to be safe in field conditions when a standard pretreatment examination is performed and appropriate risk factors assessed.

Rifampicin induced haemolysis leading to acute renal failure is extremely rare, with only 60 reported cases up until 1998.¹³ Haemolysis occurs because rifampicin-dependent immunoglobulin G (IgG) and IgM antibodies cause red blood cell lysis through interaction with the I antigen on the erythrocyte surface. The I antigen is also expressed on the tubular epithelium and may be the target structure through which rifampicin-antibody complexes

Table 1. Risk factors for peptic ulceration¹⁷⁻¹⁹

Non-steroidal anti-inflammatory drugs

Helicobacter pylori infection

History of peptic ulcer disease

Increasing age

Smoking

Alcohol

Conditions associated with increased gastric acid secretion

lead to tubular cell destruction.¹⁴ A critical level of antigen–antibody complex may be needed to induce the syndrome as these antibodies have been demonstrated in the serum of unaffected patients. Rook *et al.* were unable to demonstrate these antibodies in the sera of leprosy patients receiving intermittent rifampicin in the MRC and WHO THELEP Trials, suggesting that antibody development in these patients is rare.¹⁵

Despite 11.2 million people treated worldwide with the WHO multi-drug therapy regime, there are only two reports of leprosy patients who have developed haemolysis and acute renal failure following rifampicin therapy.¹⁶ Most of the cases reported in the literature are from patients treated for tuberculosis and severe staphylococcal infection. Patients presented with gastrointestinal and ‘flu-like symptoms and signs of intravascular haemolysis (17%), as in our patient.¹³ When our patient’s symptoms were reviewed, it emerged that she had experienced ‘flu-like symptoms for 48 h after taking her monthly rifampicin. Once the haemoglobin transiently dropped to 10.2 g/dl but returned to normal after 3 weeks. At the time this was attributed to dapsone, but in retrospect rifampicin haemolysis was probably occurring at that time.

The frequency of administration of rifampicin is important in causing side effects. Daily administration is associated with minimal side effects. If therapy is intermittent or if the drug is administered after an interruption of treatment, severe adverse reactions (thrombocytopenia, renal failure, and haemolysis) may occur. However, the scarcity of reports of these side effects suggests that they are under reporting by patients and under recognized by doctors.

Finally, leprosy is uncommon in the United Kingdom and this case illustrates the need for increased awareness. Leprosy should always be considered in a patient from an endemic area with unusual skin lesions or peripheral neuropathy, so that early diagnosis and treatment may prevent complications.

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