

Enlarging plaque on the face with enlarged supraorbital nerve

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Case report

A 38-year-old Nigerian man, who had been living in Italy since 2008, presented with an annular lesion on the right temporal and frontal region that appeared two months prior to his visit. He reported a slow centrifugal enlargement of the lesion. The man complained about headache and pain radiating to the right frontal region. He was not taking any drugs. Physical examination disclosed an annular plaque of almost 10 x 8 cm in diameter (Figure 1). The margins were raised and slightly edematous, while the skin in the center was not infiltrated but dry and anaesthetic. Edema was observed around the right orbit. The supraorbital nerve was thickened and palpable (Figure 1, white arrow).

Skin biopsy showed a multifocal superficial and deep granulomatous dermatitis with epithelioid granulomas (Figures 2 and 3) with perineural distribution. The granulomas were also focally "touching" the epidermis (Figure 4). Multinucleated giant cells, discrete edema within the granulomas, and dilated superficial vessels were also observed. PAS and



Figure 1. Annular anesthetic plaque with raised margins on the right temporal and frontal region. [Copyright: ©2013 Massone et al.]

Grocott stains were negative. Fite-Faraco stain did not show *Mycobacteriae*. Polymerase chain reaction (PCR) for *Mycobacteriae* was not performed.

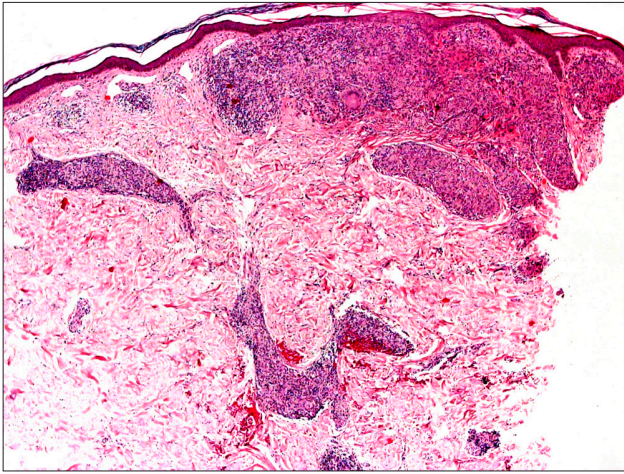


Figure 2. Multifocal superficial and deep granulomatous dermatitis with epithelioid granulomas (hematoxylin and eosin, original magnification 40x). [Copyright: ©2013 Massone et al.]

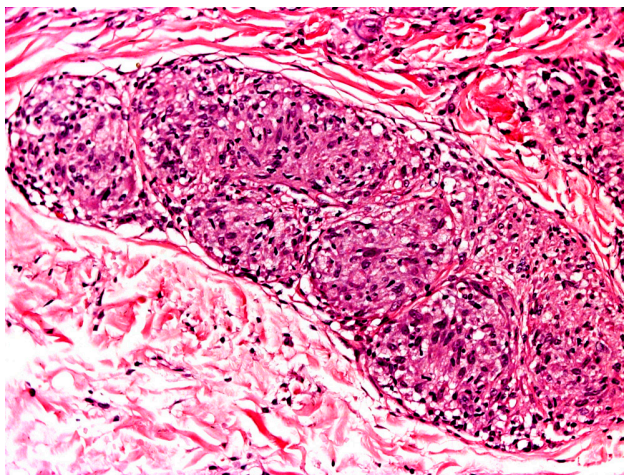


Figure 3. Epithelioid granulomas without necrosis (hematoxylin and eosin, original magnification 200x). [Copyright: ©2013 Massone et al.]

Routine laboratory investigations were within normal limits and a HIV test was negative. Chest X-ray was normal. Ophthalmological consultation was unremarkable. Neurological consultation confirmed an enlargement of the supraorbital nerve without any neurological deficit. Magnetic resonance (MR) confirmed edema of the supraorbital nerve that was compressed at the *frontal notch*, explaining the origin of the unilateral headache and pain. A nerve biopsy was not performed.

What is your diagnosis?

Answer: Tuberculoid leprosy with reversal reaction (also called “reactional tuberculoid leprosy” or “low resistant tuberculoid leprosy”).

Discussion

Leprosy or Hansen disease is a human chronic infectious disease associated with damaging inflammatory lesions in the skin and peripheral nerve caused by *Mycobacterium leprae*

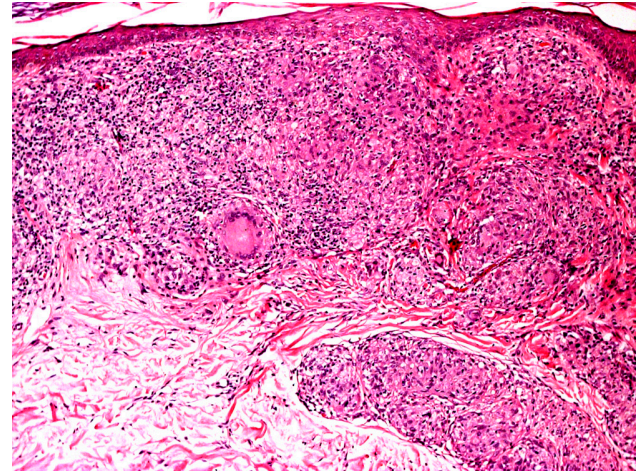


Figure 4. The granulomas are focally “touching” the epidermis. Moreover, multinucleated giant cells and slightly intra-granuloma edema are observed (hematoxylin and eosin, original magnification 100x). [Copyright: ©2013 Massone et al.]

(*M. leprae*). Leprosy’s clinical manifestations are determined by a dynamic interactionary process between *M. leprae* and cell-mediated immunity (CMI) of genetically predisposed subjects. According to Ridley and Jopling, leprosy patients are placed into a spectrum of clinico-pathological manifestations with polar tuberculoid (TT), lepromatous (LL) and intermediate types of borderline tuberculoid (BT), mid-borderline (BB) and borderline lepromatous (BL) leprosy. The spectrum is characterized by the balance between CMI and mycobacterial load: high CMI response means low number of bacilli (paucibacillary leprosy: TT and part of BT). Low CMI response means high number of bacilli (multibacillary leprosy: LL, BL, BB and part of BT) [1-6]. As Ridley wrote: “the spectrum is uninterrupted and there may be patients with an intermediate position among two groups” [5].

Anesthetic unilateral single lesions characterize TT leprosy, while bilateral asymmetrical distribution of lesions (macules, papules and plaques) characterize BT leprosy. Multiple symmetrically arranged macules and small or large nodules and plaques characterize BL and early LL. Loss of sensation is typical in TT and BT lesions, while it appears only late in BL and LL lesions. Early damage to autonomic nerve fibers impairs sweating and causes dry skin in TT and BT leprosy [1].

Leprosy reactions, divided into *type 1* (called also reversal reaction or RR) and *type 2* (called also erythema nodosum leprosum or ENL) reactions, are severe acute episodes that are common in immunologically unstable borderline patients, and involve an up-regulation of the host response to *M. leprae* antigens. RR is more frequent in BT patients during treatment and are due to an improvement of CMI against *M. leprae* (so-called upgrading RR) [1,7,8].

During RR, all three components of the peripheral nervous system are affected: sensory, motor and autonomic.

Sensory loss causes anesthesia, analgesia and inability to discriminate hot and cold. Motor deficit causes muscle weakness, paralysis and atrophy with irreversible nerve damage, leading to impairments and permanent disability [1].

The most common nerves involved in RR are the median, radial and ulnar nerves, the sural, posterior tibial and perineal nerves, great auricular and the facial nerve. In all leprosy patients, accurate neurological examination includes testing for loss of sensation on skin lesions, palpation of commonly involved peripheral nerves, evaluation of sensory function, and muscular strength. When involved, nerves appear enlarged at palpation [1,2].

Nerve involvement can be confirmed using electrophysiology and echography or MR. RR has to be immediately treated with steroids before nerve damage occurs. Moreover, nerve involvement may be caused by compression due to edema, and the granulomatous inflammation affecting the nerve and can be treated surgically by opening the anatomic tunnel and performing an external neurolysis [1,9].

Concerning our patient, the clinical differential diagnosis included, among others, mainly sarcoidosis, skin lymphoma, granuloma annulare, tinea faciei, discoid lupus erythematosus and lupus vulgaris. A centrifugally enlarging anaesthetic plaque with dry skin in a subject coming from an endemic area favors leprosy. A single unilateral anaesthetic lesion is typically seen in TT. The presence of multifocal epithelioid granulomas without necrosis but with perineural distribution confirmed leprosy and excluded tuberculosis and the other differential diagnosis. According to Ridley and Jopling the patient was classified as TT. The negative Fite-Faraco stain is not surprising because in more than 50% of TT patients *M. leprae* are not seen in TT biopsies because the CMI has already eliminated the pathogens. For the same reason, also PCR is unremarkable in more than 50% of TT patients, and it was not performed by us because a negative PCR does rule out the diagnosis [1,10].

The presence of multinucleated giant cells on histopathology, discrete edema within the granulomas, and dilated superficial vessels were histopathologic signs of RR [11], are compatible with the clinical enlargement of the supraorbital nerve and the headache reported by the patient. The supraorbital nerve is a branch of the frontal nerve, it is a pure sensitive nerve that is not frequently involved in leprosy. When enlarged it is palpable on the forehead slightly lateral to the midline. Its involvement produces minimal clinical damage to the patient. The supraorbital nerve can rarely cause headache and pain in the orbital cavity [1,12].

TT is a stable form of leprosy with a stable CMI against *M. leprae*. In contrast with borderline patients (BT, BB and BL), TT patients usually do not suffer from RR and do not shift to another form of the disease [1,8]. RR occurs more frequently in BT or BB and has been only rarely reported in TT

[1,13-15]. Our case is interesting because the patient presented classic clinical and histopathological TT but also developed an RR of the supraorbital nerve. These cases have been previously reported as “reactional tuberculoid leprosy” or “low resistant tuberculoid leprosy.” This unusual form of leprosy is represented by a solitary TT lesion with signs of RR (edema of the lesion and enlargement of the nerve) and can be explained by a changing of the CMI, in particular with decrease of CMI against *M. leprae* and development of RR [1,13-15]. If not promptly and correctly diagnosed and treated, our patient probably would have progressed in the spectrum of the disease and shifted to BT with the development of more lesions and maybe even more extensive nerve damage.

Multidrug therapy as recommended by the WHO for paucibacillary leprosy was started and the patient received rifampicin 600 mg/month, and dapsone 100 mg/day. Dapsone was subsequently substituted by minocycline 100 mg/day because of the onset of anemia. The therapy was continued for 6 months. Prednisone 30 mg/day (for 3 months with progressive tapering) was added to treat the concomitant RR. Because the headache and pain did not improve with the corticosteroid therapy, surgical enlargement of the *frontal notch* was performed with improvement of the pain. The therapy was well tolerated, and at 10-month follow-up the plaque disappeared and the supraorbital nerve was not enlarged anymore.

Leprosy patients have to be categorized correctly before starting therapy: during RR, multidrug therapy and steroids are needed, in order to control the disease and prevent irreversible nerve damage.

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