Tuberculosis (TB) is caused by *Mycobacterium tuberculosis*, an acid-fast bacillus, which is usually transmitted through the respiratory tract (1). The lungs are the most commonly infected site, but the skin, among many other organs, may also be affected (1). Cutaneous TB (CTB) is a rare form of TB, comprising only 1–1.5% of cases of extrapulmonary TB (2). CTB is often classified by the route of propagation: haematogenous dissemination, TB from exogenous source, or TB from endogenous source (2, 3). Clinical manifestations of CTB include lupus vulgaris, tuberculosis verrucosa cutis, scrofuloderma, miliary tuberculosis, orificial tuberculosis, tuberculous chancre, gumma and metastatic tuberculosis (2, 3). In addition to “true” CTB, tuberculids (i.e. erythema induratum of Bazin, papulonecrotic tuberculid and lichen scrofulosorum) are skin manifestations of underlying TB infection where *M. tuberculosis* may not be found from the lesion itself, but is considered the cause of the skin symptom and is treated successfully with TB treatment (2–4).

**CASE REPORT**

A 61-year-old Caucasian female was referred to the Department of Dermatology for an ulcer in her face, which had been present for 1.5 months. She was using bisoprolol for dysrhythmia and had been diagnosed with rheumatoid arthritis 5 years earlier. Since then, she had been taking hydroxychloroquine and sulfasalazine for rheumatoid arthritis, and adalimumab had been added to the antirheumatic therapy 5 months previously. Screening for hepatitis B and HIV, interferon gamma release assay (IGRA) for *M. tuberculosis*, and chest X-ray were performed, with normal results, before initiating adalimumab. In the late summer, the patient was bitten by a mosquito near an eyebrow and noticed a blister afterwards. The lesion became crusted, expanded and ulcerated. Adalimumab was suspended because of the suspected infection. When the patient developed adenopathy of the neck and reported having fever for several weeks, a general practitioner suspected ulceroglandular tularemia (Fig. 1A). However, the ulcer expanded during 2 weeks of treatment with doxycycline and the patient was referred to a dermatologist.

In the consultation, an ulcer surrounded by oedema located medially to the eyebrow was identified. Except for adenopathy of the neck on the same side, physical examination was unremarkable. The laboratory findings are listed in Table I. Tularemia was still considered the most probable diagnosis, since the area of Oulu University Hospital is endemic for tularemia, and late summer or early autumn is the typical season for tularemia in Finland. Moreover, the results for *Franciella tularensis* antibodies were not yet available. However, when, after 2 weeks of treatment with ciprofloxacin, the ulcer was still expanding (Fig. 1B), biopsies for histological examination and mycobacterial and fungal culture were taken from the ulcerative lesion.

The biopsy revealed granulomatous inflammation and necrosis. Ziehl-Neelsen stain showed acid-fast bacilli suggestive of mycobacterial infection. Fungal and routine bacterial culture was negative; no PCR test for *M. tuberculosis* was taken. The patient was referred to the Department of Infectious Diseases for further investigation.

Full-body computed tomography (CT) scan revealed enlarged lymph nodes in the abdomen and neck, and suspected tuberculosis lesions in the lungs and spleen. PCR test for *M. tuberculosis* was positive from the cervical lymph node and sputum and, later, the culture from the facial ulcer also showed *M. tuberculosis*. IGRA (using QuantiFERON-TB Gold-in-tube assay, DiaSorin, Saluggia

| Laboratory analysis | Result | Reference range |
|---------------------|--------|----------------|
| B-haemoglobin, g/l  | 123    | 117–155        |
| B-leucocytes, 10⁹/l | 5.6    | 3.4–6.2        |
| B-thrombocytes, 10⁹/l| 406    | 150–360        |
| B-erythrocyte sedimentation rate, mm/h | 45 | <20 |
| P-C-reactive protein, mg/l | 27 | <10 |
| P-alkaline phosphatase, U/l | 108 | 35–105 |
| P-alanine aminotransferase, U/l | 17 | <35 |
| P-bilirubin, µmol/l | 9 | <25 |

B: blood; P: plasma.

**Fig. 1.** (A) Facial ulcer at the time of the general practitioner appointment. (B) One month later at the dermatology consultation when the biopsies were taken.
Italy) was now > 4 IU/ml (reference range <0.35 IU/ml). Due to COVID-19 restrictions, the patient had recently had very limited contact with others, and no contacts with active TB were detected. Instead, the patient found out that she had been in contact with a person with active TB in very early childhood, and therefore her condition was considered a reactivation of latent tuberculosis infection (LTBI). Treatment with pyrazinamide 1,500 mg/day, rifampicin 600 mg/day, isoniazid 300 mg/day and ethambutol 1,200 mg/day was initiated for 9 months, and the patient was discharged in good condition.

**DISCUSSION**

It has been estimated that, globally, 1 out of every 3 people is latently infected with *M. tuberculosis* (5). However, only a minority of TB infections manifest as active disease. In an individual with LTBI, the lifetime risk of active TB infection is 5–15%, but some subpopulations, such as immunocompromised individuals and those with HIV, are at increased risk (6). Treatment with tumour necrosis factor (TNF)-α inhibitors also poses such a risk because of the important role of TNF in the defence against *M. tuberculosis* (7, 8). Systematic screening for LTBI is therefore recommended before initiating anti-TNFα therapy (6). The available methods to test LTBI are tuberculin skin test (TST) and IGRA, both of which can be used according to the WHO’s recommendations (6). Many guidelines regarding immunosuppressed patients also recommend chest X-ray and detailed clinical history of risk factors (travelling or migration from endemic areas, exposure to individuals with active TB) in addition to TST or IGRA, some recommend concurrent TST and IGRA testing, and some guidelines suggest recurrent testing during long-term medical immunosuppression (9).

Our patient was screened for LTBI by IGRA and chest X-ray before initiating adalimumab. However, she had been taking 10 mg prednisolone daily for a week before the IGRA sample was taken, and during the preceding weeks she had also had several intra-articular corticosteroid injections, which may have systemic effects (10). Immunosuppression may affect the reliability of LTBI screening (11). The estimations of IGRA sensitivity for LTBI vary and are somewhat conflicting. A sensitivity of approximately 80–90%, depending on the method used, has been suggested in countries with low incidence of TB (12). In another meta-analysis, sensitivity of 52% was estimated in immune-competent adults, and in immunocompromised individuals the sensitivity was even lower (13). In meta-analyses, specificity of IGRA and TST for LTBI is 93–100% and 88–100%, respectively, but BCG vaccination significantly reduces the specificity of TST (12–14).

Screening for LTBI is important before initiating biological agents, especially TNF-α inhibitors. However, the limitations of LTBI screening must be observed and it is necessary to remain vigilant for symptoms and signs of TB, even though the initial screening shows normal results. Recurrent LTBI testing should be considered, particularly if the patient develops unexpected new clinical signs.

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