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Case Report

Scrofuloderma and granuloma annulare-like lesions: Challenges of diagnosing cutaneous tuberculosis in developed countries

András Bánvölgyi ^{a,*,1}, Pinar Avci ^{a,1}, Norbert Kiss ^a, Fanni Adél Meznerics ^a, Antal Jobbágy ^a, Luca Fésűs ^a, Judit Hársing ^a, Enikő Kuroli ^{a,b}, Ágota Szepesi ^b, Márta Marschalkó ^a

^a Department of Dermatology, Venereology and Dermatooncology, Semmelweis University, H-1085 Budapest, Hungary

^b First Department of Pathology and Experimental Cancer Research, Semmelweis University, Budapest, Hungary

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ABSTRACT

Tuberculosis remains a global health concern, as the increasing levels of urban poverty, higher number of immunodeficient patients and the development of drug resistance threaten the overall efforts made to induce a downward trend for the disease. Scrofuloderma, also known as tuberculosis cutis colliquativa is a subtype of cutaneous tuberculosis. Here we detail a case of a 70-year-old female patient presented with unilateral, left-sided, multiple palpable, painful, ulcerated and purulent cervical nodules, accompanied by persistent generalized erythematous popular granuloma annulare-like skin lesions on the upper extremities. Based on the result of the PCR assay, culture, imaging and histopathological findings, the diagnosis of scrofuloderma was established.

To achieve prompt diagnosis and early treatment, it is crucial to include scrofuloderma in the differential diagnosis of ulcerated lesions in developed countries as well, and also be aware of the additional clinical symptoms, such as granuloma annulare-like lesions, possibly accompanying cutaneous tuberculosis.

1. Introduction

Tuberculosis remains a global health concern, as the increasing levels of urban poverty, higher number of immunodeficient patients and the development of drug resistance threaten the overall efforts made to induce a downward trend for the disease [1,2].

2. Report of a case

A 70-year-old female patient presented with unilateral, left-sided, multiple palpable, painful, ulcerated and purulent cervical nodules (Fig. 1<u>A</u>), accompanied by persistent generalized erythematous papular granuloma annulare-like skin lesions on the upper extremities (Fig. 1<u>C</u>, <u>D</u>). Both the cervical nodules and the papular lesions appeared one year prior to her admission to the clinic.

Personal history of tuberculosis was negated, however, the patient reported that her mother had pulmonary tuberculosis when the patient was a child. However, at the time of the patient's symptoms appeared we could not confirm her mother's status as she had already passed away. The socioeconomic background and the negative anamnesis of household members have not previously raised suspicion of tuberculosis.

Elevated inflammatory marker levels were recorded, while serology for syphilis, human immunodeficiency virus, bartonellosis, brucellosis and tularemia was negative. QuantiFERON-TB-2G an interferon-gamma (IFN- γ) release assay for *Mycobacterium tuberculosis* was negative.

Chest X-ray revealed unilateral residual hilar calcification, further confirmed by Computed Tomography (CT). CT images also showed bilateral pulmonary fibrosis in the lower lobes and a supraclavicular conglomerate infiltrating the surrounding area. Moreover, magnetic resonance imaging (MRI) of the head and neck showed generalized skin and soft tissue lesions extending from the neck to the apex of the left lung (Fig. 1B).

The histological examination of an excised cervical lymph node demonstrated necrotizing granulomatous lymphadenitis with several

¹ First two authors contributed equally to this manuscript.

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^{*} Corresponding author at: Department of Dermatology, Venereology and Dermatooncology, Faculty of Medicine, Semmelweis University, 41 Mária utca, Budapest H-1085, Hungary.

E-mail addresses: banvolgyi.andras@med.semmelweis-univ.hu (A. Bánvölgyi), pavci81@gmail.com (P. Avci), kiss.norbert@med.semmelweis-univ.hu (N. Kiss), meznerics.fanni@stud.semmelweis.hu (F.A. Meznerics), jobbagy.antal@phd.semmelweis.hu (A. Jobbágy), fesus.luca@med.semmelweis-univ.hu (L. Fésűs), harsing.judit@med.semmelweis-univ.hu (J. Hársing), kuroli.eniko@med.semmelweis-univ.hu (E. Kuroli), szepesi.agota@med.semmelweis-univ.hu (Á. Szepesi), marschalko.marta@med.semmelweis-univ.hu (M. Marschalkó).



Fig. 1. Clinical and MRi images A) Multiple ulcerated, purulent lesions on the left side of the neck B) MRI image of the head and neck region showing generalized skin and soft tissue lesions extending from the neck to the apex of the left lung C, D) Disseminated, infiltrated, granuloma annulare-like 3–6 mm papules and papulonodules on the left arm.

typical Langhans-type giant cells and caseous necrosis (Fig. 2<u>A, B</u>). Ziehl-Nielsen staining for acid-fast bacilli, Grocott methamine silver and periodic acid-Schiff (PAS) stainings were negative (Fig. 2<u>C</u>). The biopsy of the lesions on the extremities revealed features resembling granuloma annulare (Fig. 2**D**).

PCR assay and culture targeting *Mycobacterium tuberculosis* from the discharge of the ulcerating nodules of the neck and purified protein

derivative (PPD) skin test proved positive.

Based on the result of the PCR assay, culture, imaging and histopathological findings, the diagnosis of scrofuloderma was established.

A combination therapy with Rifampycin + Isoniazid (300/150 mg q. d.), Ethambutol (500 mg b.i.d.), and Pyrazinamide (500 mg t.i.d.) was initiated and administered for 9 months.

The lesions of the neck resolved, residual scars were left and no new lesions developed during the 2 year follow-up. Granuloma annulare-like lesions also completely resolved. Follow-up CT showed no signs of tuberculosis.

3. Discussion

Cutaneous tuberculosis has been described as a 'Great Imitator', as it is easily misdiagnosed as sporotrichosis, sarcoidosis or hidradenitis suppurativa among others [3]. Scrofuloderma, also known as tuberculosis cutis colliquativa is a subtype of cutaneous tuberculosis [4]. It is one of the most frequently encountered types of cutaneous tuberculosis, presenting with subcutaneous nodules and/or cold abscesses overlying tuberculous lymph nodes [4]. Lesions are usually scattered around the chest, neck and axilla [4]. Ulcers, sinus tracts and purulent discharge are often observed at later stages [4]. Subcutaneous nodules usually occur via spread from the underlying tuberculosis focus, most commonly by direct infiltration from the affected lymph node [4,5]. Although rare, external inoculation, such as bacilli Calmette-Guerin (BCG) vaccination can also be an underlying cause [4]. Presumably due to the immunologic reaction to the tubercular bacilli, cutaneous disorders, tuberculids, such as granuloma annulare-like or lichen scrofulosorum lesions can appear [6-9].

As the routine tuberculosis workup, Ziehl-Nielsen staining, and QuantiFERON-TB assay may fail to detect the presence of *Mycobacterium tuberculosis*, especially in case of low bacteria count, and culture results take several weeks to obtain, multiple diagnostic procedures, including PCR, should be combined in cases of relevant suspicion.

To achieve prompt diagnosis and early treatment, it is crucial to include scrofuloderma in the differential diagnosis of ulcerated lesions in developed countries as well, and also be aware of the additional

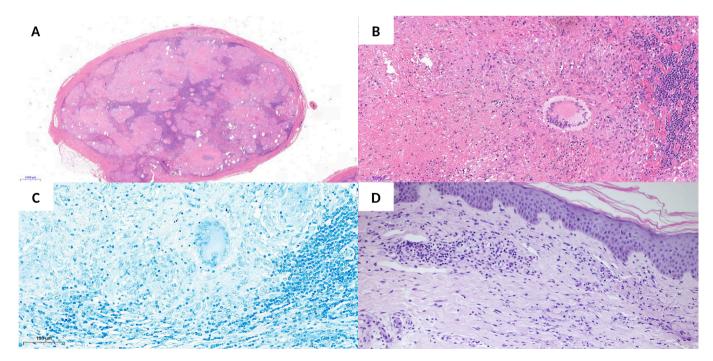


Fig. 2. Histological findings A) Cut surface of the lymph node showing several granulomas (Hematoxylin-eosin (HE), $20 \times$) B) A caseating granuloma with typical Langhans-type giant cells (HE, $200 \times$) C) Cut surface of a cervical lymph node showing a Langhans-type giant cell, no detectable acid fasting bacilli (Ziehl-Nielsen, $200 \times$) D) granuloma annulare-like lesions showing histiocyte and epithelioid cell histologic characteristics (HE, $200 \times$).

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4. Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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CRediT authorship contribution statement

András Bánvölgyi: Conceptualization, Writing – original draft, Writing – review & editing, Supervision. Pinar Avci: Conceptualization, Writing – original draft, Writing – review & editing. Norbert Kiss: Conceptualization, Writing – review & editing. Fanni Adél Meznerics: Conceptualization, Writing – review & editing, Project administration. Antal Jobbágy: Conceptualization, Writing – original draft, Visualization. Luca Fésűs: Conceptualization, Writing – original draft, Writing – review & editing. Judit Hársing: Conceptualization, Writing – original draft, Writing – review & editing, Validation. Enikő Kuroli: Conceptualization, Writing – original draft, Writing – original draft, Writing – review & editing, Validation. Kiting – original draft, Writing – review & editing, Visualization, Writing – original draft, Writing – review & editing, Visualization, Writing – original draft, Writing – review & editing, Visualization, Writing – original draft, Writing – review & editing, Visualization, Writing – original draft, Conceptualization, Writing - review & editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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