Pott Disease in a 14-year-old Girl Affected by Congenital Lamellar Ichthyosis Type 3 and Diabetes Mellitus

Maria Elena Cucuzza1, Flavia La Mendola1, Angela D’Ambra1, Pierluigi Smilari1, Filippo Greco1, Agata Fiumara1, Andrea D Praticò1,2

1Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy, 2Maurice Wohl Clinical Neuroscience Institute, King’s College London, London, UK

Abstract

Extrapulmonary manifestations of tuberculosis (TB) are particularly frequent during childhood, and usually involve the lymph nodes and the skull. They are related to predisposing immunosuppression conditions. A patient affected by diabetes mellitus type 1 (DMT1) and congenital lamellar ichthyosis type 3 came to our attention with a 4-year history of recurrent parotitis and severe back pain and inferior limb hypomobility, which had lasted for 6 months. A diagnosis of chronic TB parotitis combined with Pott disease was performed after a suggestive spinal magnetic resonance imaging, and positive culture and polymerase-chain reaction examination. Surgical aspiration of the fluid collection and a 12-month antitubercular treatment resulted in complete resolution of the symptomatology. This is the first report of a Pott disease in a patient affected by the two co-occurrences of two immunosuppression diseases such as DMT1 and congenital lamellar ichthyosis type 3

Keywords: Congenital lamellar ichthyosis type 3, diabetes mellitus type 1, extrapulmonary tuberculosis, Pott disease, spinal tuberculosis

INTRODUCTION

Extrapulmonary manifestations of tuberculosis (TB) occur in 20% of infected patients and are particularly frequent in childhood. In particular, spinal TB, also known as Pott disease, is caused by the localization of mycobacteria in the vertebrae. It is particularly rare (2% of all TB cases), but it may account for 15% of the total extrapulmonary and 50% of skeletal manifestations of TB. In particular, in childhood, it represents the most common extrapulmonary involvement, after lymph nodes.

Pott disease usually presents in patients affected by predisposing causes such as overcrowding, malnutrition, alcoholism, diabetes mellitus, HIV, and other immunosuppressive conditions. Congenital lamellar ichthyosis type 3 is characterized by the loss of acylceramide, an important component of the epidermal barrier and connective tissue. Such condition could ideally be a predisposing factor for the development of extrapulmonary manifestations of TB, including Pott disease or parotitis, even if, by now, this association has never been observed in the same TB patient.

We herein report a girl, aged 14 years, affected by diabetes mellitus type 1 (DMT1) and congenital lamellar ichthyosis type 3, who came was diagnosed with tubercular parotitis and Pott disease.

CASE REPORT

We describe the case of a 14-year-old girl from Sri Lanka, born at full term, after an uneventful pregnancy, by consanguineous parents. At the age of 2, she had been diagnosed as affected by congenital lamellar ichthyosis type 3: this diagnosis had been made by a multigene panel for ichthyosis, with mutations involving TGM1 gene (one missense, L366P, and one nonsense, Q124X). Three years later, DMT1 occurred.

She came at our attention because she had suffered, for the last 4 years, of recurrent episodes of parotitis, complicated in the last 6 months by severe back pain. At admission, her general conditions were fair, as she presented remarkable back pain. A diagnosis of chronic TB parotitis combined with Pott disease was performed after a suggestive spinal magnetic resonance imaging, and positive culture and polymerase-chain reaction examination. Surgical aspiration of the fluid collection and a 12-month antitubercular treatment resulted in complete resolution of the symptomatology. This is the first report of a Pott disease in a patient affected by the two co-occurrences of two immunosuppression diseases such as DMT1 and congenital lamellar ichthyosis type 3

Address for correspondence: Dr. Andrea D Praticò, Department of Clinical and Experimental Medicine, University of Catania, Via S. Sofia 78, Catania, Italy. E-mail: andrea.pratico@unict.it

How to cite this article: Cucuzza ME, Mendola FL, D’Ambra A, Smilari P, Greco F, Fiumara A, et al. Pott disease in a 14-year-old girl affected by congenital lamellar ichthyosis type 3 and diabetes mellitus. J Global Infect Dis 2018;10:166-8.
pain resulting in significant motor limitations and paresthesia in both legs. Routine laboratory examinations showed anemia (Hb 9.9 g/dl), with normal ferritin levels (56 mg/dl), high erythrocyte sedimentation rate (ESR) (43 mm), and C-reactive protein (21 mg/dl). Immunoglobulins (IgAs) level was in the normal range for her age. HBA1AC levels were 9% (normal values <6%).

Ultrasound examination of the neck showed a uniformly enlarged parotid glands with multifollicular aspect, resembling a chronic recurrent parotitis. Thorax X-ray did not show signs of active tubercular infection. Magnetic resonance imaging (MRI) of the column showed from L5 to S2, a spondylodiscitis with a prevertebral abscess, anteriorly located, with intraforaminal and epidural-intracanalicular extension [Figure 1]. The following days she underwent to partial left L5-S1 laminectomy and drainage of the paravertebral intracanal and retroperitoneal abscess. The cytology of the abscess showed numerous epithelioid confluent granulomas with central caseous necrosis, multinucleated giant Langerhans-type cells: these findings were suggestive of chronic TB granulomatous inflammation. *Mycobacterium tuberculosis* was identified by acid-fast bacilli culture and confirmed by polymerase chain reaction.

For these finding, therapy with rifampicin, ethambutol, isoniazid, and pyrazinamide for the first 2 months, followed by isoniazid and rifampicin for the next 10 months. Despite this, an MRI control after about 1 month showed an initial increase in volume of the prevertebral abscess, which was then further drained, while a new examination at 3 months showed a clear volume reduction. In the same time, an appreciable clinical improvement has been noticed, together with an overall normalization of the blood test (last Hb was 12.5 g/dl, with normal values of RCP and ESR). In the last follow-up examination, at 6 months, the abscess was remarkably reduced and the patient does not show any neurological sequelae.

### Discussion

In a period of 4 years, the present patient has developed two extrapulmonary localizations of TB: parotitis, and Pott disease, being affected by two predisposing factors: DMT1 and congenital lamellar ichthyosis type 3. This last is an autosomal recessive condition caused by mutation of the gene *CYP4F22* (located on 19p13.12), which encodes a member of the cytochrome P450 superfamily of enzymes involved in the metabolism of fatty acids to their omega hydroxyl derivatives. *CYP4F22* mutations are quite rare and the disease typically occurs in consanguineous families. The most important product of *CYP4F22* enzyme is acylceramide, an important component of epidermal barrier; its reduction causes a barrier damage and a consequent immunosuppressive state, as in our patient. In her case, such lack of defenses was exacerbated by the co-occurrence of DMT1, which is known to predispose patients to immunosuppression. Probably for this reason, the patient developed a severe and disseminated form of TB, manifesting in the early phases with recurrent parotitis, and in the later stages as a Pott disease.

TB of the parotid is extremely rare because of the presence, in the gland, of thiocyanate ions and proteolytic enzymes such as lysozyme, which confer antibacterial action. Clinical presentation usually consists in a progressive swelling of the parotid over months or years, without other specific symptoms. In the absence of an active pulmonary infection (75% of cases), the diagnosis is histological.

In a second phase, our patient developed a symptomatic spinal TB with neurologic deficit in the lower limbs and pain. Spinal TB is one of the most common extrapulmonary manifestations of TB in childhood. It can be caused by the spreading of infectious secretions through the gastrointestinal and respiratory tracts, or by lymphatic and/or hemat disemination. Spinal TB usually involves two contiguous vertebrae but up to more than five vertebrae may be affected. It usually affects the vertebral body and then progresses to the disc, which is highly vascularized; regarding the bone tissue, the lamina is commonly involved followed by pedicles, articular processes, spinous processes, and transverse processes. Contrarily to the present patient, spinal TB most commonly affects the upper lumbar and lower thoracic spines, followed by middle thoracic and cervical vertebrae (3%–5%) and atlantoaxial articulation (<1%). Disc disruption and kyphosis, intraosseous and extraosseous abscesses, bone displacement, vertebral collapse spinal cord damage, and spinal artery thrombosis are the most severe complication.

Chronic back pain is the most frequent symptom, but presentation may also include malaise weight loss, night sweats, tenderness, stiffness, muscle spasm, and kyphosis. Initially, neurologic symptoms include weakness and numbness, which can progress to complete paraplegia, the most severe complication of spinal TB. The diagnosis is based on a combination of clinical and radiological findings, in particular, MRI and CT scans. In any case, it is mandatory a
confirmation of the disease by biopsy demonstrating acid-fast bacilli on microscopy or isolated culture of the microorganism. Due to the lower amount of lactobacilli in extrapulmonary TB cultures, the diagnosis is usually performed by polymerase chain reaction, which shows a greater sensitivity. Treatment is based on the staging system proposed by the Gulhane Askeri Tip Akademisi and involves surgery (in the more severe cases) \(^{[8]}\) in combination with antimicrobial treatment, which usually includes isoniazid, rifampicin, pyrazinamide, and either ethambutol or streptomycin and can be modified based on susceptibility testing. Duration of therapy ranges from 12 to 24 months.\(^{[9]}\)

**Conclusions**

This is the first report of the co-occurrence of DMT1, congenital lamellar ichthyosis type 3, and a severe extrapulmonary TB infection consisting of recurrent parotitis and Pott disease in the same patient. This underlines, especially in countries with high prevalence of TB infection, the importance of a careful clinical examination, aimed to find the eventual presence of hidden or mild symptoms suggesting an extrapulmonary TB. This is particularly important in children affected by chronic immunodeficiency disorders, in whom, a deeper clinical examination is advisable, as it may show signs of extrapulmonary TB, allowing further examinations and a prompt treatment.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship**

The Authors have not received any financial support or support in the preparation of the manuscript.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Devrim I, Aktürk H, Bayram N, Apa H, Tulunoglu S, Devrim F, et al. Differences between pediatric extra-pulmonary and pulmonary tuberculosis: A warning sign for the future. Mediterr J Hematol Infect Dis 2014;6:e2014058.
2. Moon MS. Tuberculosis of spine: Current views in diagnosis and management. Asian Spine J 2014;8:97-111.
3. Ohno Y, Nakamichi S, Ohkuni A, Kamiyama N, Naoe A, Tsujimura H, et al. Essential role of the cytochrome P450 CYP4F22 in the production of acylceramide, the key lipid for skin permeability barrier formation. Proc Natl Acad Sci U S A 2015;112:7707-12.
4. Sugiuira K, Takeuchi T, Tanahashi K, Ito Y, Kosho T, Saida K, et al. Lamellar ichthyosis in a collodion baby caused by CYP4F22 mutations in a non-consanguineous family outside the mediterranean. J Dermatol Sci 2013;72:193-5.
5. Errami N, Benjelloun A, Tahtah N, Hemmaoui B, Jahidi A, Nakkabi I, et al. Tuberculosis of the parotid gland: Histology surprise. Pan Afr Med J 2015;20:343.
6. Moorthy S, Prabhu NK. Spectrum of MR imaging findings in spinal tuberculosis. AJR Am J Roentgenol 2002;179:979-83.
7. Yusof M, Hassan E, Rahmat N, Yunus R. Spinal tuberculosis: The association between pedicle involvement and anterior column damage and kyphotic deformity. Spine (Phila Pa 1976) 2009;34:713-7.
8. Oguz E, Sehirlioglu A, Altinnakas M, Orturk C, Komurcu M, Solakoglu C, et al. A new classification and guide for surgical treatment of spinal tuberculosis. Int Orthop 2008;32:127-33.
9. Rajasekaran S, Khandelwal G. Drug therapy in spinal tuberculosis. Eur Spine J 2013;22 Suppl 4:587-93.