

# INFEÇÃO CUTÂNEA E PULMONAR POR *MYCOBACTERIUM AFRICANUM*

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**RESUMO** – A tuberculose cutânea é uma doença incomum, constituindo 1,5% de todas as formas de tuberculose. Na doença pulmonar e cutânea, as infeções causadas por *Mycobacterium africanum* e *Mycobacterium tuberculosis* podem ser clinicamente indistinguíveis.

Um rapaz de 6 anos da Guiné-Bissau foi hospitalizado devido a uma úlcera pré-auricular direita com evolução de dois anos e linfadenopatia regional. O teste tuberculínico foi positivo e a radiografia de tórax revelou um nódulo hipotransparente no lobo pulmonar direito, com características sólidas na TAC. As biópsias da úlcera e da linfadenopatia revelaram infiltrado linfocítico com reação granulomatosa; o exame cultural e a PCR confirmaram infeção por *Mycobacterium africanum*. Foi realizado tratamento antibacilar durante 6 meses, com redução significativa da lesão. Nos países desenvolvidos é importante lembrar as várias formas de tuberculose cutânea, que se pode apresentar isoladamente ou em associação com outras formas de infeção. Nos doentes provenientes de áreas endémicas, um teste tuberculínico positivo deve levantar a suspeita desta entidade.

**PALAVRAS-CHAVE** – Tuberculose cutânea; Tuberculose pulmonar; *Mycobacterium africanum*; Criança.

## CUTANEOUS AND PULMONARY INFECTION BY *MYCOBACTERIUM AFRICANUM*

**ABSTRACT** – Cutaneous tuberculosis is an uncommon disease, accounting for 1.5% of all types of tuberculosis. In pulmonary and cutaneous disease, infections caused by *Mycobacterium africanum* and *Mycobacterium tuberculosis* can be clinically indistinguishable.

A six-year-old boy from Guinea-Bissau was hospitalized due to a right pre-auricular ulcer with two-year evolution and regional lymphadenopathy. Tuberculinic test was positive and the thoracic radiography showed a hypotransparent node on the right lower pulmonary lobe, with solid characteristics in CT scan. Skin ulcer and lymphadenopathy biopsies revealed lymphocytic infiltrate with a granulomatous reaction; the culture and PCR confirmed *Mycobacterium africanum* infection. Antibacillary treatment was supplied for six months, leading to significant reduction of the lesion.

In developed countries it's important to remind the several forms of cutaneous tuberculosis, which can present solely or in association with other forms of infection. In patients from endemic areas, a positive tuberculinic test should rise the suspicion of this entity.

**KEY-WORDS** – Tuberculosis, cutaneous; Tuberculosis, pulmonary; *Mycobacterium* infections; Child.

## Caso Clínico

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*The authors declare that the patient gave written informed consent for the use of its photos in this article.*

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### INTRODUCTION

Cutaneous tuberculosis (CT) is a rare disease, nearly inexistent in industrialized countries. It accounts for about 1.5% of all forms of tuberculosis (TB)<sup>1</sup> and 0.1-1% of all cutaneous pathologies<sup>2,3</sup>. However, since the eighties, the disease has become more frequent, as for pulmonary TB.

Cutaneous infections results from direct inoculation, inhalation of the mycobacteria (leading to pulmonary infection and dissemination) or contiguity with lesions from nearby organs, such as lymph nodes, bone, digestive tract, pleura and lung<sup>3,4</sup>.

There are several forms of CT: tuberculous chancre, TB verrucosa cutis, lupus vulgaris, scrofuloderma, gumous TB, miliary TB, TB cutis orificialis and tuberculids<sup>4</sup>.

The etiologic agents of CT are bacteria from the *Mycobacterium tuberculosis* complex, including *Mycobacterium tuberculosis*, *Mycobacterium bovis*, *Mycobacterium africanum* and *Mycobacterium microti* and several other mycobacteria which don't usually cause disease among humans. *Mycobacterium africanum*, which is less frequent in Europe and North America, may be responsible for infections clinically indistinguishable from *Mycobacterium tuberculosis*, including pulmonary TB and CT. In the past, two biovariants of *Mycobacterium africanum* were described, *West African Mycobacterium africanum* and *East African Mycobacterium africanum*; the latter is now grouped with *Mycobacterium tuberculosis sensu strictu*. *West African Mycobacterium africanum* has actually two variants: *Mycobacterium africanum* type 1 and *Mycobacterium africanum* type 2<sup>5</sup>.

By its rarity we report a case of CT by *Mycobacterium africanum* in a child, which we didn't find previously described in literature.

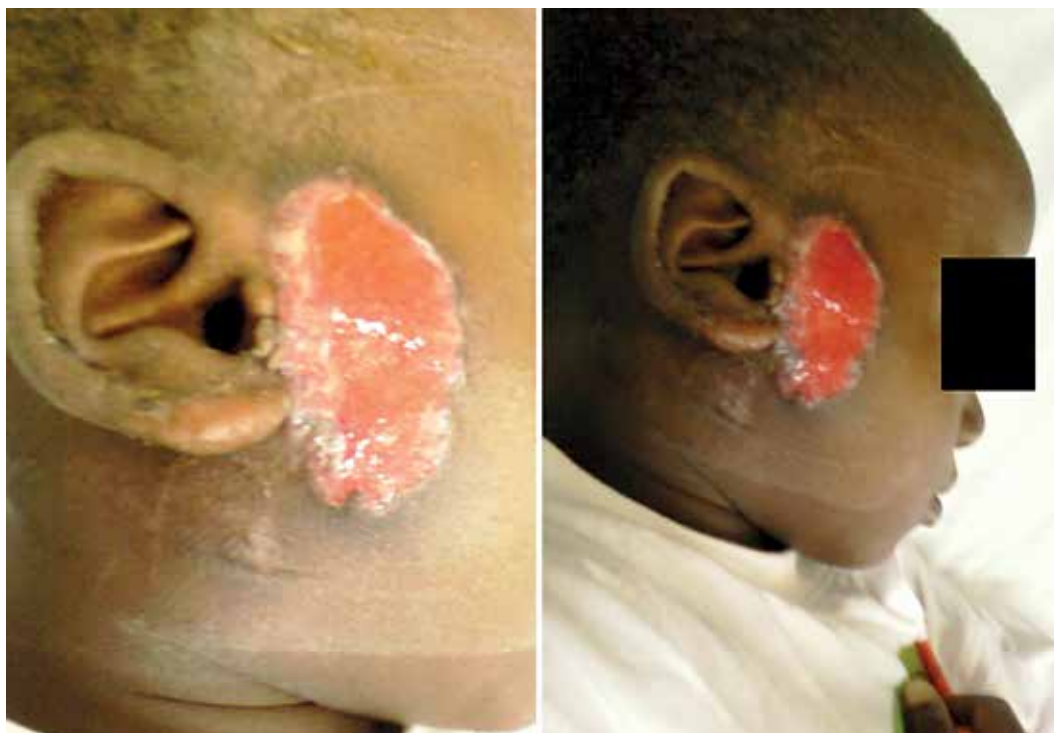
### CASE REPORT

A six-year-old boy, natural from Guinea-Bissau, was brought to Portugal for diagnostic evaluation and treatment of a chronic ulcer on his right pre-auricular area, with 2 years of evolution. In Guinea he had previously been treated with non-specified systemic and topic antibiotics, which haven't lead to any clinical improvement. The patient had no other symptoms, namely fever, loss of weigh or cough. There was no relevant epidemiologic history regarding contacts with TB patients.

Upon admission the child had a good general health status. In the right pre-auricular region he had a 12x6cm ulcer, with regular and well-defined edges and an erythematous even bottom partially covered by a purulent exudate (Fig. 1). In the right posterior cervical region a 5x6cm, tender, painless and non-adherent lymphadenopathy was palpable. There were no other alterations on physical examination.

Laboratory workup showed normal hemogram, a reactive C protein of 3.72mg/dL and sedimentation rate of 80mm/sec. Immunologic study, namely immunoglobulin level and lymphocytary populations, was normal, and ELISA for HIV 1 and 2 were negative. Tuberculin test was positive, with a 15mm area of induration.

## Caso Clínico



**Fig 1** - Patient at admission, with a cutaneous 12x6cm ulcer, with regular and well-defined edges and an erythematous even bottom partially covered by purulent exudate and a right posterior cervical lymphadenopathy.

Thoracic radiograph showed a nodular hypotransparency on the right lower lobe. Face and lung computed tomography scan revealed densification of the subcutaneous tissue underneath the ulcer and a 23mm solid node on the right lung base (Fig. 2). Bronchoscopy was normal and gastric aspirate negative for mycobacteria.



**Fig 2** - Pulmonary computed tomography scan showing a 23mm node on the right lung base.

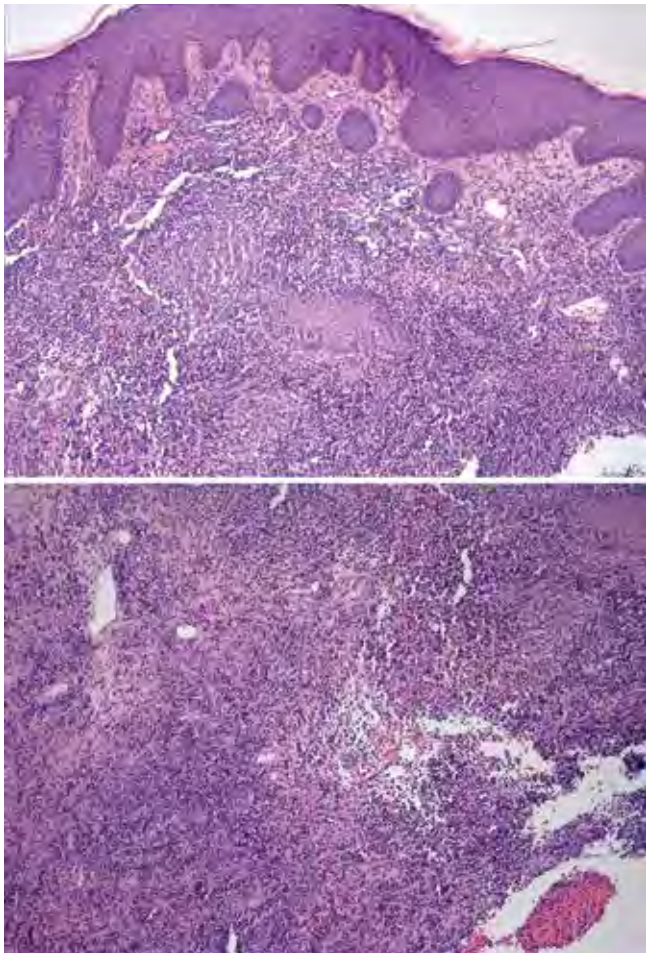
At this point, the differential diagnosis included Buruli ulcer disease, skin cancer, leishmaniasis and actinomycosis; therefore, skin and ganglionic biopsies were performed. Both exams have shown a lymphocytic infiltrate with granulomas (Fig. 3), but Ziehl-Neelsen staining was negative. Cultural exam and subsequent amplification allowed for the identification of *Mycobacterium africanum* by polymerase chain reaction (PCR). *Staphylococcus aureus* and *Streptococcus pyogenes* were identified as co-infectant microorganisms.

Isoniazid, rifampicin and pyrazinamid were started, with significant reduction of cutaneous and pulmonary lesions after three months of treatment, and this response was maintained for six months, leading to full recovery.

### DISCUSSION

CT diagnosis is based on clinical exam, histological study and culture of the bacteria, and PCR allows the identification of the species. There may be no systemic manifestations of the disease and clinical signs may overlap other pathologies, such as Buruli's ulcer,

## Caso Clínico



**Fig. 3** - Skin biopsies showing a lymphocytic infiltrate with granulomas.

atypical mycobacteria infection, syphilis, cat-scratch disease, actinomycosis, psoriasis, leishmaniasis, discoid lupus erythematosus and neoplasms. In our patient, the long time of evolution of the cutaneous lesion plus the application of several topics (potentially changing the original features of the ulcer) and the bacterial overgrowth have obscured the clinical picture. In this case, the skin biopsy was critical to the diagnosis.

In CT, histopathology may show a non-specific inflammatory infiltrate, caseating granulomas and, sometimes, bacilli may be seen. Observation of acid-alcohol resistant bacilli (BAAR) is highly suggestive of mycobacteria, even though there are several other microorganisms, like *Corynebacterium* and *Nocardia* sharing this biochemical property. Ziehl-Neelsen staining can also detect mycobacteria, but it is necessary to have a large number of bacilli in the sample ( $>10^4$  bacteria/

milliliter)<sup>3</sup> for the test to become positive. In our patient, Ziehl-Neelsen was negative, which can be due to a small number of mycobacteria in the ulcerated tissue.

Cultures and PCR are the gold standard for isolation of the agent. However, these techniques have a low sensibility: 50-72% for PCR when it is made in samples BAAR negative and 80% for culture<sup>3</sup>. In conclusion, CT is still a challenge in clinical practice, not just because of the large spectrum of differential diagnosis but also due to the complexity and delay of the bacterial isolation.

We were initially surprised by the isolation of *Mycobacterium africanum*, as it is a very rare bacteria in our country. Searching the literature, we found just three cases of CT<sup>6,7</sup>, none of them amongst children. This agent is rarely found in Europe<sup>7-9</sup>, but is common in West and Central Africa, including Guinea-Bissau, from where our patient was from. In these areas *Mycobacterium africanum* is responsible for 50-60% of all cases of pulmonary TB<sup>5</sup>.

*Mycobacterium africanum* may cause all forms of TB, including CT<sup>10</sup>, disseminated<sup>7,10,11</sup>, cerebral TB<sup>9</sup> and orchiepidimitis<sup>12</sup>. From the three cases of CT caused by *Mycobacterium africanum* described in the literature, two were lupus vulgaris<sup>6,7</sup> and the third had multiple cutaneous and visceral lesions<sup>10</sup>. Our patient had a lesion compatible with tuberculous chancre and even though the agent was not isolated in bronchoalveolar lavage and gastric aspirate, we admit that the pulmonary node had also tuberculous origin, due to the concomitance of the lesions, the simultaneous response to antibacillary treatment and the low sensibility of these exams (gastric aspirate is positive in 30-40%<sup>13</sup> of cases and bronchoalveolar lavage is even less sensitive<sup>14</sup>).

Due to the presence of a skin ulcer, lymphadenopathy and pulmonary infection we admit that our patient had disseminated TB. In CT pulmonary involvement occurs in 12-26,5%<sup>15-17</sup> and regional lymphadenopathy is considered an indication of dissemination of the disease<sup>17</sup>. In children, the presence of lymphadenopathy is even more frequently related to disseminated disease than in adults<sup>17</sup>. However, in our case it is not straightforward to define whether the cutaneous lesion was acquired by primary inoculation or by hematogenous dissemination from pulmonary infection, since the child had no respiratory symptoms.

As noted previously, infection caused by *Mycobacterium africanum* is indistinguishable from other mycobacteria<sup>9</sup>; however, is recommendable to identify the species, not only due to epidemiological matters, to detect and control outbreaks<sup>11</sup>, but also because *Mycobacterium bovis* is resistant to pyrazinamid<sup>9</sup>, which has obvious implications in treatment.



## Caso Clínico

In industrialized countries, where CT is extremely rare, is important to remember this entity, which can be found associated with systemic forms or be the only manifestation of the mycobacterial infection. The suspicion index should be high in patients from an endemic area, with immunodeficiencies or a positive tuberculinic test. Diagnostic methodology is essential for diagnosis, allowing to start prompt treatment and avoid development of complications and sequels potentially irreversible.

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