Sporotrichoid cutaneous infection by *Mycobacterium haemophilum* and *kansasii* in an IgA-deficient man

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Abstract

Background
The prevelance of infections by nontuberculous mycobacteria has steadily increased over the past decades, especially in immunocompromised patients.

Case presentation
We present a patient with IgA-deficiency and a mixed cutaneous infection by Mycobacterium (M.) haemophilum and M. kansasii.

Discussion
Cutaneous M. haemophilum infections are most often the result of HIV or transplantation-associated immunosuppression. Rarely, M. haemophilum may infect healthy patients or iatrogenically immunosuppressed patients without transplantation. M. kansasii is one of the best known nontuberculous mycobacteria and large awareness exists about its involvement in diseases both of immunocompetent and immunocompromised patients. Diagnosis relies on skin biopsy, histopathologic examination, and microbiological cultivation.
Background

IgA-deficiency is the most common primary antibody deficiency. Although many affected individuals have no apparent symptoms, selected patients suffer from recurrent mucosal infections, allergies, and autoimmune diseases [1].

NTM are ubiquitous in the natural environment [2]. Infections by nontuberculous mycobacteria (NTM) are becoming an increasing complication, particularly among immunocompromised patients. *Mycobacterium (M.) haemophilum* is an established cause of cutaneous lesions in immunocompromised hosts [3]. The most common clinical manifestations of *M. haemophilum* are cutaneous lesions with a preference for cooler body sites such as extremities, while the development of sporotrichoid nodular lymphangitis is exceptional.

*M. kansasii*, with its several subtypes, are one of the most frequent NTM and involved in diseases of both immunocompetent and immunocompromised patients [3]. Clinically, *M. kansasii* presents in a manner most resembling tuberculosis and here most commonly as tuberculosis-like pulmonary disease [4]. Cutaneous infections due to this slow growing mycobacterium are rare and may resemble cellulitis or sporotrichosis. *M. kansasii* should be included in the differential diagnosis of skin infections with an indolent course and lack of response to antibiotics [5]. Inoculation of the NTM into the host usually occurs during disruption of the skin barrier.

Patients commonly show a history of fish tank cleaning, oyster shucking, swimming, or other aquatic activities [6], and thus, *M. kansasii* is can cause infections of the hand.
**Case presentation**

A 48-year old man presented with multifocal nodules of variable size arranged in a sporotrichoid manner on the right arm, the dorsum of the digit IV, the left arm, the right side of his back, the knees and a partly sharp marginated erythematous plaque on his back (Figure 1 A, B, C, D). The lesions persisted for 2 months, without any other symptom. Skin biopsies were initiated that revealed caseating epitheloid cell granuloma in the dermis with a marginal zone of lymphocytes and a subepidermal lympho-histiocytic infiltrate with perivascular accentuation (Figure 1 E, F). By PAS-, Fite- and Auramin staining no acid fast bacilli were detected. Microbiological cultures showed twice growth of *M. haemophilum* from a lesion on the right hand. In addition, *M. kansasii* was recovered from another lesion on the elbow. Tuberkulin skin test was negative. Interestingly, our patient’s history revealed an IgA-deficiency. A broader immunodeficiency excluded. There was no clinical evidence of a systemic mycobacterial infection. A triple treatment with clarithromycine 2x500 mg/d, rifabutine 1x300 mg/d and ethambutol 1x20mg/kg body weight/d was initiated. This regime was given for 6 months, while a complete clinical remission was seen within 4 months.

**Material and methods**

Clinical specimens were subjected to mycobacterial culture. For the detection of mycobacteria from skin biopsies, Ziehl-Neelsen microscopic examination and mycobacteria specific culture were performed by using the automated BACTEC MGIT 960 system (Becton Dickinson) at 36°C and Lowenstein-Jensen Agar (LJA) at 36°C, 24°C and 30°C. LJA at 30°C was supplemented with hemin discs in order to detect *M. haemophilum*, which was generally performed in case of skin biopsies. Growth of acid fast bacilli was detected from LJA at 30°C surrounding the hemin discs. The culture isolate was then identified as nontuberculous mycobacterium due to the absence of a amplicon by a mycobactaerium tuberculosis specific gyrB PCR [7] and then verified for further species identification by GenoType Mycobacterium DNA strip assay (Hain Lifescience, Nehren, Germany) [8]. The GenoType Mycobacterium CM/AS assays (CM, common mycobacteria; AS, additional species) were performed as recommended by the manufacturer. The GenoType Mycobacterium CM assay enables the simultaneous identification of species, including the most relevant *M. tuberculosis* complex and e.g. members of the *M. avium* complex, *M. abscessus*, *M. kansasii* and *M. chelonae* etc. Additionally, the AS test provides the identification of rarely found species, such as *M. simiae*, *M. hemophilum*, and *M. mucogenicum*.

Mycobacterium CM assay revealed a banding pattern specific for the *M. haemophilum-M. nebraskense-M. malmoense-M. palustre* group. Further species differentiation was done with
the AS assay that showed positive reaction for *M. haemophilum* and *M. nebraskense* and no reaction for *M. malmoense* or *M. palustre*. Together with the growth requirement for hemin this indicated the differentiation of *M. haemophilum*. However, species identification of *M. heamophilum* was confirmed at the National Reference Center for Mycobacteria in Borstel (Germany). *M. kansasii* was recovered with the Bactec MGIT 960 and identified with the GenoType Mycobacterium CM assay.
Discussion

NTM can be categorized by the growth rate (slowly growing and rapidly growing species), pigmentation (pigmented and nonpigmented species), and optimal growth temperature, which can provide helpful information for a preliminary classification of NTM. *M. marinum*, *M. kansasii*, and *M. avium-intracellulare* are examples of slow-growing mycobacteria. *M. fortuitum*, *M. chelonei*, and *M. abscessus* are examples of rapidly growing mycobacteria [1,2]. Diagnosis relies on skin biopsy, histopathologic examination, microbiological cultivation and molecular detection of mycobacterial DNA.

Strikingly, cutaneous *M. haemophilum* infections are most often the result of HIV- or transplantation-associated immunosuppression. Its most common clinical manifestations are cutaneous lesions with a preference for cooler body sites such as extremities. Rarely, *M. haemophilum* may infect iatrogenically immunosuppressed patients without transplantation or even healthy persons, and the development of sporotrichoid nodular lymphangitis is exceptional [3].

In contrast, *M. kansasii* infection has been reported in up to 20 percent of NT mycobacteriosis in both immunocompetent and immunocompromised patients. Its disseminated type is uncommon but of poor prognosis [9]. The outcome of *M. kansasii* pulmonary infection is good if diagnosed and treated early. In one report, *M. kansasii* infection occurred on the hand and forearm, with carpal tunnel syndrome complicated by concomitant pulmonary *M. tuberculosis* [6], and in another as cellulitis in a patient with systemic lupus erythematosus [4].

As the only comorbid condition, our patient showed an immunoglobulin (Ig) A deficiency. IgA-deficiency is the most common primary antibody deficiency. However, many affected individuals have no apparent symptoms, selected patients suffer from recurrent mucosal infections, allergies, and autoimmune diseases [1].

Sustained, very low levels of IgA, IgG, or IgM, as found in primary immunodeficiency syndromes, are associated with significantly increased risks of infections, primarily respiratory tract infections of bacterial origin. Generally, IgA deficiency appears better tolerated. IgA is the main protein of the mucosal immune system. Due to the large surface area of the human mucosa of up to 400 m2, the role of IgA in the defense of this surface from harmful agents of the environment is extremely essential. Any changes connected with a lack or an overproduction of this Ig can manifest as variable clinical diseases [10]. Strikingly, this is the first report about a correlation of IgA deficiency and a disposition to infections with NTM.
Conclusions
According to our knowledge this is the first report of a mixed cutaneous infection by *M. haemophilum* and *M. kansasii* in a patient with IgA-deficiency. The patient was working as a scaffolder and had contact with diverse environmental habitats while touring around Europe. Although the definite relevance of his IgA-deficiency remains unclear, this immunological imbalance may contribute to the patient's vulnerability towards NTM.
Patient’s informed consent
We obtained a written informed consent from the patient for publication of this article and accompanying images. A copy of the written consent is available for the review by the Editor-in-Chief of this journal.

Competing interests
The authors declare that they have no financial and non financial competing interests.

Authors’ contributions
VB and MH conceived the project and drafted the manuscript. AB and TR helped for drafting the manuscript. MF interpreted the histological specimens. All authors read and approved the final manuscript.

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References


Figure 1 legend

Clinical and histological findings. On the right arm (A) erythematous nodules (B) were found in a sporotrichoid manner. On the back (C) a sharply margined erythematous plaque (D) was seen. Histopathology of the skin revealed in the dermis disseminated caseating partly epithelioid cell granulomas with a marginal zone of lymphocytes and a subepidermal lympho-histiocytic infiltrate with perivascular accentuation (E). By PAS-, Fite- and Auramin staining no acid fast bacilli were detected. (F) Close up of an epithelioid cell granuloma.
Figure 1
Additional files provided with this submission:

Additional file 1: Bekou_et_al-mykobak-3-2010-bmc-dermat_end.doc, 49K
http://www.biomedcentral.com/immedia/1113065411377019/supp1.doc