Case report

Atypical mycobacterial infection resembles sporotrichosis in elderly patient

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Abstract

Atypical mycobacterial (AM) infection is caused by Mycobacterium species other than M. tuberculosis. AM skin infection has clinical manifestations that resemble M. tuberculosis infection and deep fungal infection. Laboratory workup is necessary to confirm the diagnosis.

An 83-year-old female came with a painful lump and swelling on her right lower extremity since three months before admission. Physical examination revealed a plaque consisting of multiple erythematous and hyperpigmented papules and nodules, diffuse erythematous lesion, and shallow ulcers partially covered with pus and crust. Histopathological features showed tuberculoid granuloma. Direct test and periodic acid-Schiff (PAS) staining of the skin biopsy found no fungal element nor acid-fast bacilli (AFB). Culture and polymerase chain reaction (PCR) of M. tuberculosis were negative. The working diagnosis was atypical mycobacterial infection and treatment with 450 mg rifampicin and 100 mg minocycline daily were administered accordingly. In two months observation following the treatment, the pain was no longer exist, the ulcers were completely healed, and some nodules were in the process of healing.

Among other Mycobacterium spp, M. marinum is the most common cause of AM infections. Clinical manifestation of M. marinum infection may present as solitary or multiple nodules on the hands, feet, elbows and knees with sporotrichoid spreading pattern. The diagnosis of AM was established based on clinical and laboratory examination. The diagnosis was also confirmed by good clinical response to minocycline and rifampicin.

Keywords: atypical, mycobacterium, minocycline, rifampicin.

Abstrak

Infeksi mikobakterium atipik (MA) merupakan infeksi yang disebabkan oleh spesies Mycobacterium selain M. tuberculosis. Infeksi MA pada kulit memberikan gambaran klinis menyerupai infeksi M. tuberculosis sehingga dibutuhkan pemeriksaan penunjang untuk menegakkan diagnosis.

Seorang wanita berusia 83 tahun datang dengan benjolan yang nyeri dan bengkak di tungkai bawah kanan sejak 3 bulan lalu. Pada pemeriksaan fisis terdapat papul, nodus eritematosa sampai hiperpigmentasi multipel, lesi eritematosa difus, ulkus dangkal, sebagian terisi pus, sebagian tertutup krustu. Gambaran histopatologis menunjukkan granuloma tuberkuloid, abses yang tersusun atas sel radang berupa limfosit, histiosit, eosinofil dan sel polimorfonuklear (PMN). Dari pemeriksaan langsung dan pewarnaan periodic acid-Schiff (PAS) pada biopsi kulit tidak ditemukan elemen jamur maupun bakteri tahan asam (BTA). Hasil biakan M. tuberculosis dari jaringan dan pemeriksaan polymerase chain reaction (PCR) M. tuberculosis menunjukkan hasil negatif. Ditegakkan diagnosis kerja infeksi...
mikobakterium atipik sehingga diberikan terapi rifampicin 450 mg/hari dan minosiklin 100 mg/hari. Pada pengamatan hari ke-21 pascaterapi tampak ulkus menutup, tidak ada pus, beberapa nodus mengalami resolusi, dan nyeri yang sudah tidak dirasakan.

Infeksi MA pada kulit banyak disebabkan oleh M.marinum. Manifestasi klinis infeksi M.marinum dapat berupa nodus soliter atau multipel pada tangan, kaki, siku, dan lutut. Diagnosis infeksi MA pada kasus ini ditegakkan berdasarkan anamnesis, pemeriksaan fisik, dan pemeriksaan penunjang. Diagnosis juga didukung dengan respons yang baik terhadap terapi minosiklin dan rifampisin yang merupakan terapi pilihan pada infeksi MA.

Kata kunci : mikobakterium, atipikal, minosiklin, rifampisin.

Introduction

Atypical mycobacteria (AM) or Mycobacterium other than tuberculosis (MOTT) are a group of Mycobacterium species other than M. tuberculosis and M. leprae. AM is ubiquitous in the environment, both in soil and water. It can infect various organs and manifests as multiple disease entities; being the most common are pulmonary disease, lymphadenitis, skin disease and a disseminated form infection. The exact prevalence of AM is unknown, but a national data survey in the United States of America on isolation of AM species between 1970 and 1980 estimated that there were 1.8 cases per 100,000 population; while data between 2005 and 2006 showed that there were 7.2 cases per 100,000 population. Lung cases ranked the highest with 5.6 cases per 100,000 population, which was followed by skin as the most common extra pulmonary case with 0.9 case/ 100,000 population.

AM is classified into four groups based on the growth rate and pigmentation pattern; three groups are slow grower while one is rapid grower. All groups can cause skin diseases and systemic infections.

AM infection is treated with systemic antibiotics. In some conditions, however, surgical intervention is necessary. Combined systemic antibiotics treatment is recommended to prevent bacterial resistance. Antibiotics of choices are rifampicin, minocycline, clarithromycin, doxycycline, ethambutol, isoniazid, ciprofloxacin and trimethoprim-sulfamethoxazole.

Treatment duration is ranging from four to 38 weeks, depends on the clinical response. Treatment is continued for another four weeks after the lesion has resolved to prevent recurrence.

Diagnostic criteria for AM include clinical, microbiological and histopathological manifestations. The gold standard for diagnosis of AM is mycobacterial culture to identify the AM species. Non-specific microbiologic test including Acid-Fast Bacilli (AFB) test can also be carried out.

We report a case of suspected atypical mycobacterium infection in an 83-year-old female patient. To our knowledge AM is rarely found and limited number of cases has been reported.

Case

An 83-year-old woman came to outpatient clinic at Department of Dermatology and Venereology dr. Cipto Mangunkusumo National Hospital, complains of a painful lump, wound and swelling of the right lower extremity since three months before admittance. The lump started as multiple vesicles on her right foot. The vesicles developed pus and formed a lump. Within a month, the lump became bigger and wider, ascending to the right lower extremity. She noticed the lump became tender. Before she came to dr. Cipto Mangunkusumo National Hospital, she was treated using wet dressings and combined prescribed topical agent, but there were no improvement. There was a history of fever when the lesion was swollen. A history of injury was not obtained the patient; however, before the symptoms appeared, there was an activity of cleaning a fish pond and gardening. A history of chronic cough or pulmonary tuberculosis was denied. The patient denied keeping any furry pets or taking medicine before symptoms appeared, and had no medical or food allergies. The history of diabetes mellitus, hypertension, kidney, heart, and liver diseases was also denied. There was no similar illness in the family members.
Vital sign and general condition were within normal limits. The nutritional status was adequate. Other examination showed normal limits. The dermatological status of the right lower extremity region showed that on the dorsal of the right foot, there were lesions of varying lenticular and nummular sizes, consist og papules, multiple erythematous to hyperpigmented nodules with diffuse erythematous plaque and shallow ulcer; some of them contained with pus and covered with shallow brownish crust (figure 1).

Figure 1. On first visit, (1A) and (1B) papules, multiple erythematous to hyperpigmented nodes, lenticular and nummular, diffuse erythematous lesions, multiple shallow ulcers, some containing pus and covered brownish yellow crusts.

The Gram stain examination, showed a lot of leukocytes, a moderate amount of Gram-positive cocci and a large amount of Gram-positive bacilli. Based on the history, physical examination and laboratory workup, the working diagnosis for the patient was carbuncle and pyogenic ulcer.

The initial treatment, was clindamycin 3 x 300 mg/day and wound care. After 2 weeks of treatment, there was no clinical improvement; therefore, a possibility of atypical mycobacterium was considered along with other differential diagnoses such as skin tuberculosis, sporotrichosis and mycetoma. Other laboratory work up were biopsy, AFB test, culture and PCR were done.

Results of laboratory test showed a leukocyte count of 4520/µL, Hb level of 12.3 gr/dL, hematocrit of 37.5 %, platelet count of 164000/µL, AST level of 66 U/L, ALT level of 48 U/L, ureum level of 22.5 mg/dL, creatinine level of 0.5 mg/dL and fasting blood glucose of 91 mg/dL. Results of the chest X-ray were still within normal limits. Results of histopathological examination showed that in the epidermis, mild acanthosis and, hypergranulosis; were existed while in the dermis, there was edema and abscesses which consisted of inflammatory cells such as lymphocytes, histiocytes, eosinophil, polymorphonuclear cells, necrotic nuclear dusts, Langhans giant cells, and fibrosis of sub-dermis (figure 2). PAS staining of skin biopsy did not reveal any fungal element. AFB test showed negative result and there was no growth of M.tuberculosis in the culture. The M. tuberculosis PCR test showed negative results. Culture and PCR for identifying AM species could not be performed as these facilities were not available.

Diagnosis of atypical mycobacterial infection was made based on history, physical examination and laboratory work up. The treatment for this patient included wound care, 1x450 mg /day of rifampicin and 1 x 100 mg/day of mynocycline, which planed or 3 months. On 2 month observation following the treatment, the ulcer was closed, the nodes had undergone resolution, erythematous lesion became hyperpigmented without pain (figure 3).

Discussion

AM skin infection can occur as a primary infection by direct inoculation of AM on non-intact skin or through hematogenous dissemination from other primary source, particularly the lungs.1 Risk factors for infection are injury, water-associated activity such as cleaning of aquariums, swimming, contact with fish and soil.1,5 In this case, there were risk factors of water-associated activity. Cleaning a fish pond and gardening.
The patient had no recollection of any injury; however, considering that the patient was 83 years old, with reduced skin barrier function, a condition which can facilitate the development of skin infections. Disseminated distribution from the lungs can also be excluded since there were no history of chronic cough, or pulmonary tuberculosis. The chest X-ray results were within normal limits.

AM skin infection mostly caused by *M. Marinum*, *M. fortuitum*, *M. abscessus*, *M. Cheloneae* and *M. ulcerans*. Clinical manifestation of AM infection varies depending on the species of etiological agents. The development of abscess and cellulitis at the site of injury, particularly due to sharp pointed contaminated puncture wounds are most commonly caused by species of fast growers mycobacteria, i.e. *M.cheloneae, M.fortuitum* and *M.abscessus*. Skin disease caused by *M.marinum* is usually developed due to contact with contaminated water, fish fin or fish bites. The disease is commonly found in workers who have water-associated activity, both in salt-water and fresh-water, such as fishermen or fish ponds workers. *M. marinum* causes chronic granulomatous skin infection. The initial lesion takes the form of papules, particularly on the elbows, knees, feet and hand, which usually have contact with water, and then may developed into nodes, plaque; and can be suppurate and ulcerate, in a sporotrichoid-like disseminated distribution of lesions or simply following the lymph flow. Small-sized superficial lesions can heal spontaneously, while large lesions persist for months to years.

In this case; on right lower extremity and right dorsal foot, multiple lesions were found in the form of papules, suppurative nodes as well as ulcers, which disseminated according to the lymphatic channel. The patient reported that at the beginning, there was only a small lump resembling a vesicle on her foot. It was assumed that there was an injury, which became the inoculation site and then

![Image](attachment:image1.png)

**Figure 2.** Histopathologic features with hematoxylin and eosin staining. (2A) (magnification, x 40), Edema appears on dermis, abscesses composed of inflammatory cells such as lymphocytes, histiocytes, eosinophils, polymorphonuclear cells, dust core. (2B) (magnification, x 400), Inflammatory infiltrate. (2C) (magnification, x 400), Tubercles consist of Langhans giant cells surrounded by epithelioid cells.

![Image](attachment:image2.png)

**Figure 3.** After 2 months therapy using combination of rifampicin and minocycline. (3A) and (3B) all ulcers healed, nodes and erythematous lesions improved become hyperpigmentation and scarring.
disseminated following the lymphatic channel to the lower extremity.

The diagnosis of AM infection was established based on clinical manifestation, which was then confirmed with microbiological and histopathological examination of the skin tissue. The microbiological examination can be performed by AFB test, but the examination was non-specific while the gold standard of examination is for identifying Mycobacterium species still culture.1,8 Histopathological feature varies depending on the lesion; it can be tuberculoid granuloma, the development of abscess, infiltrate of diffuse histiocytes, paninculitis, non-specific chronic inflammation, sarcoid granuloma and rheumatoid-like nodule.8 Other laboratory work up, such as PCR can also be utilized to differentiate various species of AM.1,2 Differential diagnosis of AM infection varies depending on clinical manifestation.1,2,8 In this case, the dominant clinical manifestation were nodes with sporotrichoid-like dissemination with some of being ulcerative and located at the injury site; therefore the differential diagnosis were sporotrichosis, skin tuberculosis and mycetoma.

The histopathological feature depends on the form of lesion and host immunity. There are 7 patterns of histopathological features for AM infection; tuberculoid granuloma, development of abscess, infiltrate of diffuse histiocyte, paninculitis, non-specific chronic inflammation, sarcoid granuloma and rheumatoid-like nodule.8 In this case, the differential diagnosis of deep mycosis including sporotrichosis and mycetoma can be excluded as the direct test showed no fungal element; and, skin biopsy with PAS staining did not reveal any fungal element. The other differential diagnosis, i.e. skin tuberculosis can also be excluded since there was atypical clinical manifestaton and the PCR result for M. tuberculosis showed negative result and no M. tuberculosis growth was found on the skin culture.

The supporting facts for diagnostic criteria of were clinical manifestation, histopathological features of tuberculoid granuloma, abscess, histiocytes infiltrate and non-specific chronic inflammation. The diagnostic criteria of microbiological test using culture as the gold standard and PCR examination could not be performed since the facilities of such specific laboratory work up for identifying the AM species were not available. In addition, clinical response to combined therapy of 450 mg daily of rifampicin and 100 mg daily of minocycline have also supported establishing the diagnosis of AM infection.

The treatment for this case were combination of systemic antibiotics rifampicin minocycline. Both have bactericidal properties and many have reported that they are effective, both as monotherapy or as a combination.2,7 For AM infection, a combined therapy and longer duration of treatment is preferable in order to prevent resistance.2 The respond to the combined treatment was excellent. In 2 months following treatment, the ulcers closed, with the resolution of nodes, no new lesion appeared and the pain subsided. The treatment for the patient was continued for 4 weeks after the lesion resolved to prevent recurrence.

References

