

Case 22

A 73-year-old female from Samut Prakan

Chief complaint: Multiple discrete papules and pustules on face, right thigh and right leg.



Present illness:

The patient presented with progressive dyspnea and fever. She was diagnosed with lobar pneumonia. During hospitalization for bronchoscopy, she developed multiple erythematous papules and pustules on her face, right thigh and right leg.

Past history:

Her underlying disease is minimal change disease with relapsing proteinuria and has been receiving 60 mg/day of prednisolone for 2 months.

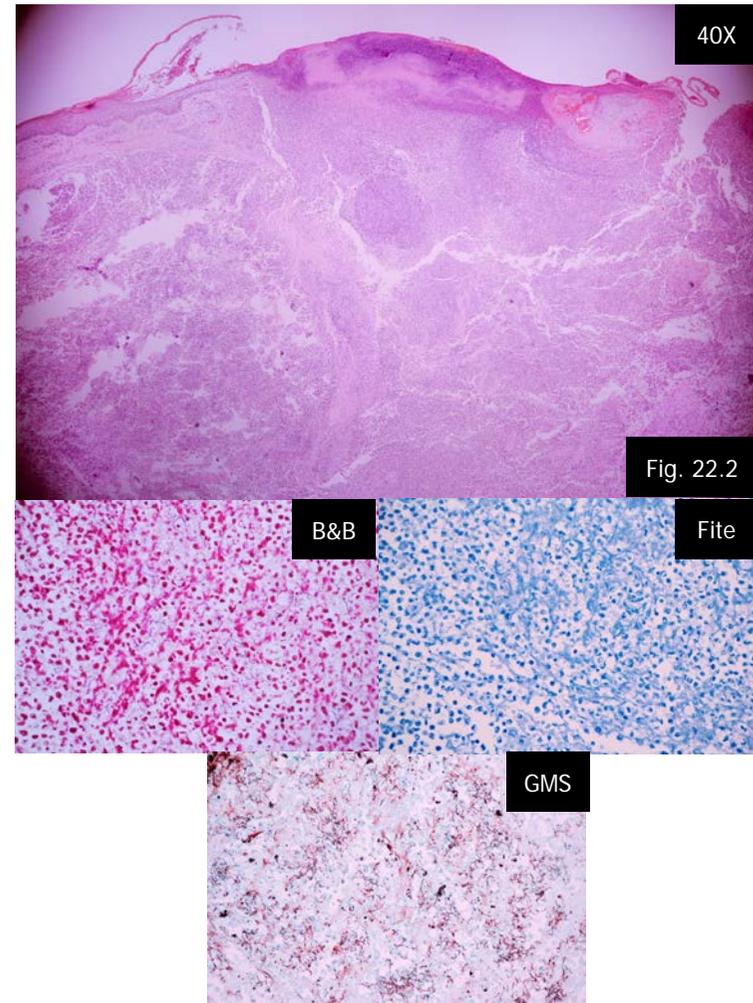
Physical examination:

- HEENT: Oral thrush
- Lungs: Decrease breath sound at left lower lung
- CNS: Motor grade IV all, impaired finger to nose test
- Others: Normal

Dermatological examination: Several discrete erythematous papules and pustules on nose, right thigh and right leg. (Fig 22.1)

Histopathology: (S19-000302, right thigh)

- Suppurative dermatitis with neutrophils (Fig. 22.2)
- Numerous branching filamentous gram positive bacteria highlighted by Brown-Brenn (B&B), Fite and GMS staining
- Negative PAS and AFB staining



Investigations:

- CBC: Hb 12 g/dL, Hct 39%, Plt 305,000 /cumm, WBC 17,300 /cumm (N 97.3%, L 1.8%, M 0.8%, B 0.1%)
 - LFT: AST/ALT 40/15 U/L, ALP/GGT 95/69 U/L, TB/DB 0.6/0.3 mg/dL
 - BUN/Cr: 30/0.73 mg/dL
 - CT lung: Patchy consolidation at basal and lateral basal segment of left lower lung
 - CT brain: 6-mm non-enhancing hypodensity lesion at cerebellar vermis without surrounding edema
- Skin tissue:
- Gram stain: Numerous polymorphonuclear cells, no organism seen
 - GMS stain: Positive branching filamentous bacteria
 - Modified acid fast stain: No organism seen
 - Aerobe culture: *Nocardia spp.*
 - Mycobacterium culture: *Nocardia spp.*
 - 16S-rRNA: Target not detected
 - 18S-rRNA: Target not detected

Bronchoalveolar lavage:

- Modified acid fast stain: No organism seen
- GMS stain: No organism seen
- Aerobe culture: *Nocardia spp.*
- Fungus culture: *Aspergillus spp.*
- Mycobacterium culture: no growth
- 16S-rRNA: *Nocardia brasiliensis*
- 18S-rRNA: Target not detected

Hemoculture: no growth

Diagnosis: Disseminated nocardiosis

Treatment:

- Intravenous trimethoprim/sulfamethoxazole plus imipenem/cilastatin

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Discussion:

Nocardia spp. is aerobic, gram-positive, partially acid fast filamentous bacteria. This organism contains mycolic acid in the cell wall, so they are closely related to Mycobacterium.¹ They usually can be found as saprophytic germs in soil, rotten plants, dust, or water.^{2,3} Normally, they can infect human via skin inoculation or respiratory inhalation. Therefore, most common infected sites are lung, skin and soft tissue respectively.⁴

Cutaneous nocardiosis composes of two groups. The first group is primary cutaneous nocardiosis, of which primary infected site is skin. This certain group usually occurs in immunocompetent patients who have history of traumatic wound.³ Primary cutaneous nocardiosis can be divided into acute and chronic forms, The acute form consists of lymphocutaneous infection and superficial skin infection which either can present with various clinical presentations such as nodulo-pustular lesion, ulcerative bullous lesion, cellulitis, sporotrichoid distribution, linear keloid-like lesion or abscess.^{1,2} While chronic form shows as mycetoma.^{4,5} Second group is disseminated nocardiosis with skin involvement spreading from other organ, especially lung. It commonly manifests as pustule, nodule, or abscess. Immunosuppressive status is major risk factor of this group. Other associated factors comprise of chronic lung disease, organ transplantation, HIV infection and malignancy.^{1,4,6,7} Mortality rate in this group is considerably high (44-85%) and prognosis can be worsen in CNS involvement condition.^{4,8}

As for the pathogenesis, primary cutaneous nocardiosis mostly caused by *Nocardia brasiliensis* whereas disseminated nocardiosis mostly caused by *Nocardia asteroides*.⁹

Laboratory tests considered useful including direct examination of clinical specimens and culture. For direct examination, gram stain shows gram-positive right angle branching filamentous bacteria and acid fast stain demonstrates weakly positive acid fast branching filamentous bacteria. Although direct examination is useful to

diagnose, definitive diagnosis of nocardiosis can only be made when the isolation of *Nocardia* species is accomplished in culture.⁹ Moreover, the isolation should be kept under observation for 2 to 3 weeks due to its slow growing property.^{5,9} Therefore, routine culture media can allow bacterial overgrowth. Nowadays, the RNA sequencing on 16S ribosomal RNA is the best tool and has become the gold standard for identification of *Nocardia* species.⁹ Thus, it allows more precise selection of adequate antimicrobial agent, especially disseminated nocardiosis which tend to be resistant to various antimicrobial drugs.¹⁰

Standard treatment of cutaneous nocardiosis are trimethoprim/sulfamethoxazole. Treatment duration of disseminated nocardiosis should be extend for 6-12 months. Besides, if patient has CNS involvement or immunosuppressive status, like our patient, the treatment should be extended up to 1 year. As mentioned above, due to disseminated nocardiosis tend to have drug resistant, combined antimicrobial agents should be considered for example, trimethoprim/sulfamethoxazole plus imipenem.⁴ Initial treatment should be started with intravenous form for 3-6 weeks, then switch to at least two combined oral drugs for 1 year.¹¹

Our patient is 73 year-old female with immunosuppressive status from prolong steroid usage. She presented with multiple discrete papules and pustules on face, right thigh and right leg during hospitalization for bronchoscopy from lobar pneumonia. Bedside pus gram stain and Wright stain failed to demonstrate organism, then incisional skin biopsy was performed and revealed numerous branching filamentous bacteria in GMS, Brown Benn and Fite stain. Nine days later, *Nocardia spp.* was identified in aerobe subculture from right thigh tissue. 16S-rRNA of bronchoalveolar lavage fluid showed *Nocardia brasiliensis* and also found *Aspergillus spp.*, which was considered as co-infection. CT brain was performed due to impaired finger to nose test and revealed a hypodensity lesion at cerebellar vermis suspected cerebral nocardiosis. Finally, she was diagnosed as disseminated nocardiosis. As mentioned before, our

patient was treated with trimethoprim/sulfamethoxazole combined with imipenem/cilastatin. Moreover, her prednisolone was tapering off to 20 mg daily. After treatment, the lesions decreased in size.

References:

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