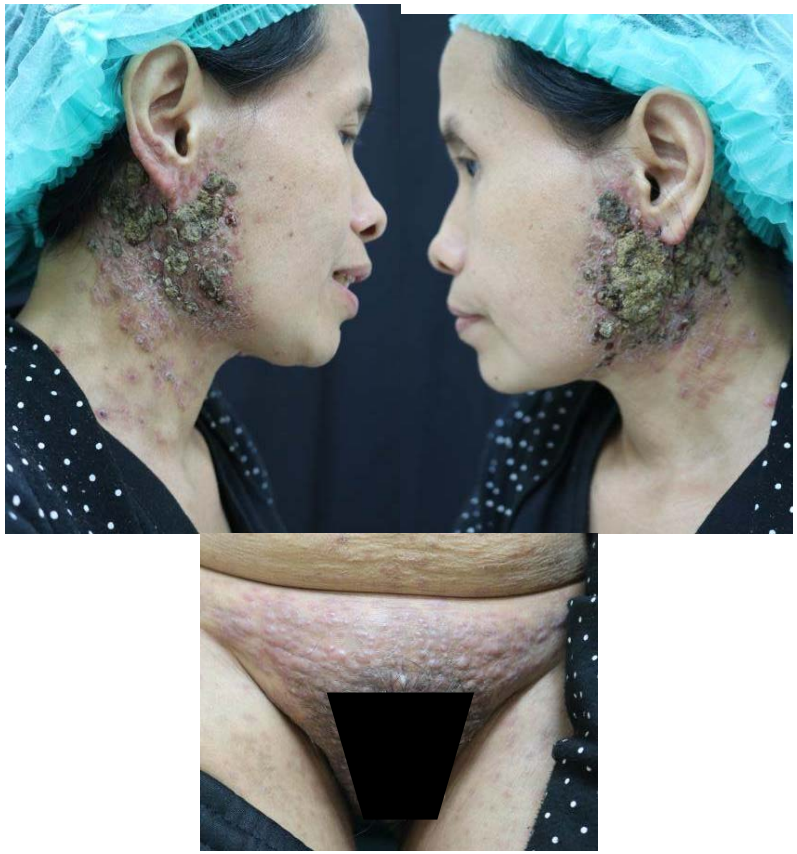
Case 22
A 44-year old Thai woman from Uttaradit

Chief complaint: Multiple brownish keratotic papules in pubic area for one week



(Fig. 22.1)

Present illness:

The patient noticed a few asymptomatic bumps on both sides of neck one year earlier.

There were thick yellow-brown scaly crusts in mandibular areas on both sides, which gradually extended to her neck on the next 7 months, so she went to a nearby hospital and had lymph node biopsy for two consecutive times with a 2-month interval. She was diagnosed with acute lymphadenitis and received a course of antibiotic treatment without clinical improvement. She denied neither fever, weight loss, or fatigue.

Additionally, there were multiple brownish keratotic papules in her pubic area one week earlier. These brought the patient to Ramathibodi Hospital.

Past history:

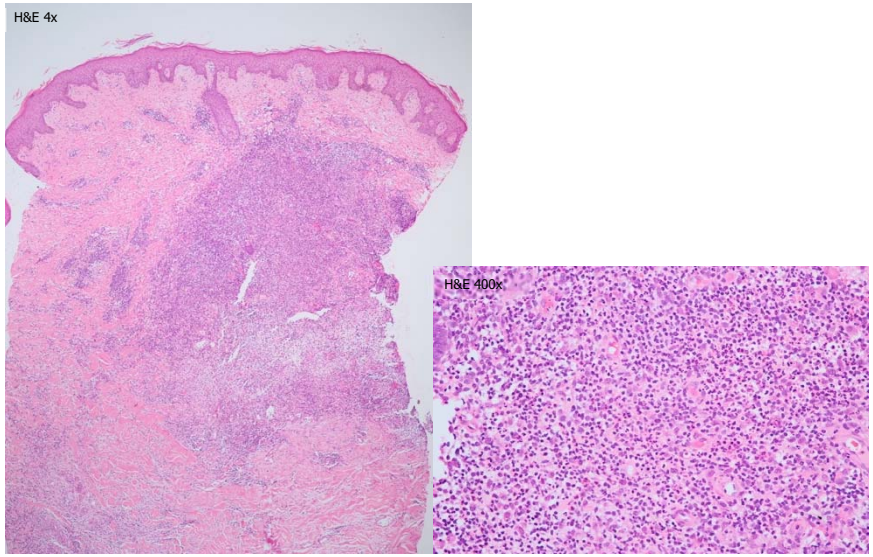
- She had no other underlying diseases.
- She had never experienced any trauma in these areas.

Physical examination:

V/S: T 37.2°C, P 80 beats/min, RR 20/min, BP 128/83 mmHg
HEENT: no pale conjunctivae, anicteric sclerae
Lymph nodes: A few enlarged cervical lymph nodes, bilaterally
Other systems: unremarkable

Dermatological examination: (Fig. 22.1)
Multiple erythematous scaly papules confluent to form plaques with yellow-brown keratotic crusted scales in mandibular areas bilaterally, extending to neck, and on mons pubis.

Histopathology (S17-4964A, Pubis) (Fig. 22.2)



(Fig. 22.2)

- Nodular inflammatory cell infiltrates of lymphocytes, admixed with histiocytes, plasma cells and neutrophils, some of those forming suppurative granuloma
- Negative Fite, AFB, Brown-Brenn, GMS, and PAS staining

Laboratory investigations:
- CBC: Hb 9.7 g/dL, Hct 31.4%, WBC 12,230 cells/µL (N 46%, L 45%, Mo 3%, Eo 5%, B 1%), Platelet 428,000 cells/µL
- Anti-HIV: Negative
- CXR: focal opacity in right apical zone
- Tissue PCR for *Mycobacterium* spp.: Negative
- Tissue culture for *Mycobacterium* spp.: *Mycobacterium abscessus*
- Tissue culture for fungus: No growth
- Anti-inteferon (IFN)-γ antibody: Positive

Diagnosis: Disseminated *Mycobaterium abscessus* infection in anti-IFN-γ autoantibody patient

Treatment:
- Oral ciprofloxacin 500 mg twice daily
- Oral clarithromycin 500 mg twice daily
- Oral doxycycline 100 mg twice daily
- Plan to continue the antibiotics until the lesion completely resolved

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Discussion:

Mycobacterium abscessus (*M. abscessus*) is an acid-fast bacillus classified as a pathogenic "rapid growing" nontuberculous mycobacteria[1] (Table 1) which is a ubiquitous environmental organism.[2] Its infection was first described in 1953 by Moore and Frerichs in a woman with chronic osteoarthritis who developed a gluteal abscess.[3] It can also cause skin and soft tissue infections after trauma or surgical procedures, pulmonary infections, central nervous system infections, ocular infections, disseminated diseases or even bacteremia[4] especially in immunocompromised patients.[5]

Cutaneous infections with rapidly growing mycobacteria can manifest in a variety of ways, including ulceration, abscesses, draining sinuses, nodules,[6] and sporotrichoid pattern.[7, 8] The pathogenesis could be direct contact with contaminated material or

water through traumatic injury, surgical wound, environmental exposure, or secondary involvement of skin and soft tissue during disseminated disease.[9] The most commonly involved sites were the lower extremities (48%), upper extremities (31%) and trunk (14%), respectively.[10]

Table 1 Classification of atypical mycobacteria

Group I	Photochromogens	Yellow pigment	*M. marinum* *M. kansasii* *M. simiae*
Group II	Scotochromogens	Yellow-orange pigment	*M. scrofulaceum* *M. szulgai*
Group III	Nonchromogens		*M. avium-intracellulare* *M. ulcerans* *M. haemophilum*
Group IV	Rapid growing		*M. fortuitum* *M. chelonei* *M. abscessus*

Adapted from Bhambri S et al. Atypical mycobacterial cutaneous infections. Dermatol clin 2009;27:63-73.

The gold standard for diagnosis is based on microbiological investigation in which mycobacterial culture at 28–30°C yields non-pigmented colonies resistant to most anti-mycobacterials, including tetracyclines, fluoroquinolones, and sulfonamides, unlike *Mycobacterium chelonae*. 16S rDNA sequencing with other molecular methods can also differentiate *M. abscessus* from other species.[11]

Drug sensitivity testing should be performed according to international guidelines. In general, *M. abscessus* is a species naturally sensitive to amikacin and macrolides (Table 2).[11] Thus, the treatment of serious *M. abscessus* complex disease usually involves initial combination antimicrobial therapy with a macrolide (clarithromycin 1,000 mg daily or 500 mg twice daily, or azithromycin 250–500 mg daily) plus intravenous agents for at least 2 weeks to several months, followed by oral macrolide–based therapy. For skin and soft tissue infection, the antibiotics should be prolonged for at least 4 months.[12]

The general principles for treatment is surgery with draining of abscesses, removal of necrotic tissue and removal of all foreign bodies such as wood splints, silicone implants or other non-biological materials.[11]

Table 2 Interpretation of MIC-values of antimycobacterial drugs, and in vitro drug sensitivity for *M. abscessus*

		MIC, µg/mL		
		Susceptible	Indeterminate	Resistant
Amikacin	S	≤16	32	≥64
Cefoxitin	V	≤16	32-64	≥128
Ciprofloxacin[a]	R	≤1	2	≥4
Clarithromycin[b]	S	≤2	4	≥8
Doxycycline	R	≤1	2-8	≥16
Imipenem	V	≤4	8	≥16
Sulfamethoxazole	R	≤32		≥64
Linezolid	S	≤8	16	≥32
Tigecycline[c]	S	≤4		

[a] Represents all fluouroquinolones
[b] Represents also azithromycin
[c] Definite breakpoints are not determined.
S=sensitive, R=resistant, V=variable.

Adapted from Petrini B. *Mycobacterium abscessus*: an emerging rapid-growing potential pathogen. APMIS 2006;114:319-28.

In this patient, ciprofloxacin 500 mg twice daily, clarithromycin 500 mg twice daily plus doxycycline 100 mg twice daily were prescribed. Investigation for immunocompromised status revealed positive anti-IFN-γ antibody. Anti-IFN-γ autoantibodies are increasingly recognized as a cause of adult-onset immunodeficiency and increase risk for infections with intracellular pathogens, including nontuberculous mycobacteria, nontyphoidal *Salmonella* spp, *Burkholderia* spp, varicella-zoster virus, cytomegalovirus,

Cryptococcus neoformans, *Histoplasma capsulatum*, and *Talaromyces marneffei*. A high titer of neutralizing anti-IFN-γ autoantibodies blocks IFN-γ activation and, in consequence, restrains IFN-γ interleukin-12 pathway. There were reported cases treated with rituximab plus methylprednisolone.[13]

At 6-month follow-up, her lesions gradually resolved by disappearance of hyperkeratotic crusts and decrease in number of erythematous papules. Anti-IFN-γ antibody titer is being awaited for planning of treatment.

References:

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