

Mycobacterial Skin Infections: Comparison between Histopathologic Features and Detection of Acid Fast Bacilli in Pathologic Section

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Background : Detection of acid fast bacilli (AFB) in chronic granulomatous inflammation is an important clue for mycobacterial infection.

Design : A retrospective review of 104 pathologic sections (from 1994 to 2001) of suspected cases of mycobacterial (tuberculous and nontuberculous) skin infections to study histopathologic features and the correlation with the presence of AFB in the section was performed.

Results : All cases showed granulomatous inflammations that can be categorized into 4 types: mixed cell, suppurative, tuberculoid and palisading granuloma. AFB was found in 32 sections (30.77%). Ninety five specimens from 104 specimens were simultaneously cultured. AFB positive cases yielded higher positive cultural results, 17 from 29 cases (58.62%) compared to the AFB negative group, 23 from 66 cases, (34.85%). Mixed cell granuloma was the most common histologic feature, but suppurative granuloma was the most common histological feature (56.25%) in which AFB could be found, which was statistically significantly different from other types of granuloma. Tuberculoid granuloma was more common in the AFB negative group (20.83%) compared to the AFB positive group (9.37%) but the difference was not statistically significant. In cases that AFB could not be found, the inflammation tended to be located in the upper half of the dermis.

Conclusion : AFB can be more frequently detected in suppurative granuloma that might be located in any portion of the dermis. This finding was not species specific.

Keywords : Mycobacterial skin infections, Histopathologic features and detection, Acid fast bacilli

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A diagnosis of mycobacterial infections can be made by detection of characteristic histopathologic features with the presence of acid fast bacilli (AFB) in clinical specimens. Detection of AFB plays a crucial part in the diagnosis because granulomatous inflammation can be found in various conditions and diseases other than mycobacterial infections, such as foreign body reaction, fungal infection and sarcoidosis⁽¹⁾. Detection of AFB is one of the rapid and cost-effective ways to confirm mycobacterial

infection. Though this method is not sensitive, not specie-specific and requires a skillful interpretator, it will provide very useful information for the clinician in planning the appropriate management according to the clinico-pathologic correlation.

The aim of this study was to investigate the histopathologic features of cutaneous lesions, which suspected mycobacterial infections and to determine the difference between those in which AFB could and could not be found in pathological sections.

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Material and Method

A retrospective study (from 1994-2001) of 104 pathologic sections from a skin biopsy of suspected

mycobacterial, tuberculous (TB) and nontuberculous (NTM), infections was performed. Data were recorded from the out-patient skin clinic, Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. All of these cases had a single or a few chronic skin lesions which were usually asymptomatic and slow progressive. Clinical manifestations ranged from ulcers, papules, indurated plaques, hyperkeratotic verrucous plaques (tuberculosis verrucosa cutis-like), nodules, sporotrichoid lesions and tumefaction with draining sinus. Skin biopsy was performed in each case for histopathologic study and culture. Specimens for histopathologic study were processed by conventional formalin-fixed, paraffin embedded method, staining with hematoxylin-eosin and Ziehl-Neelsen for AFB. Histopathologic features and the presence of AFB was evaluated blindly by two independent observers for each biopsy specimen. In cases with discordant findings, biopsy specimens were reexamined by the two observers together in order to come to an agreement.

Results

The histopathologic features were recorded in terms of types of granulomatous inflammation, depth of infiltration and presence or absence of AFB in the pathologic section.

Acid fast bacilli (AFB) were found by the staining method in pathologic sections in 32 cases (30.77%), in the remaining 72 cases (69.73%) AFB was not found. Among those 104 specimens, mycobacteria were identified by the cultural method in 40 cases (42.10%); only 7 cases were *Mycobacterium tuberculosis*, the remaining 33 cases were NTM (*M. marinum*, *M. chelonae*, *M. fortuitum*, *M. avium*, *M. terrea* and *M. szulgai*).

Those in which AFB were found in the pathologic section yielded higher positive cultural results (17 from 29 cases, 58.62%) compared to the group in which AFB was not found (23 from 66 cases, 34.85%)

Granulomatous inflammation was found in all cases and could be categorized into 4 types as mixed cell granuloma, suppurative granuloma, tuberculoid granuloma and palisading granuloma. The difference between mixed cell and suppurative granuloma was the aggregation of neutrophils to form microabscesses within granulomas (Fig. 1) which was definitely found in suppurative granuloma, whereas diffusely interspersed with other kinds of inflammatory cells in

mixed cell granuloma (Fig. 2). Small and poorly formed tubercles were found in mixed cell and suppurative granuloma in contrast to tuberculoid pattern.

Suppurative granuloma was the most frequent pattern found in the AFB positive group and was statistically significantly different from the other group by chi square test (Table 1). Numerous AFB could frequently be found in both suppurative and mixed cell pattern in contrast to the tuberculoid pattern; a few bacilli could only be found. Mixed cell granuloma was the most common pattern. Tuberculoid pattern was obviously more frequent in the AFB negative group but not statistically significantly different from the others. Palisading granuloma was found in only one case in the AFB negative group and mycobacteria could not be recovered by cultural method in this case.

In terms of depth of infiltration, the infiltrate tended to involve the upper dermis instead of the lower dermis or diffuse infiltration in the AFB negative group (Table 2), in contrast to the AFB positive group in which there was no specific site of predilection in the dermis. Epidermal changes such as acanthosis and pseudoepitheliomatous hyperplasia could be detected

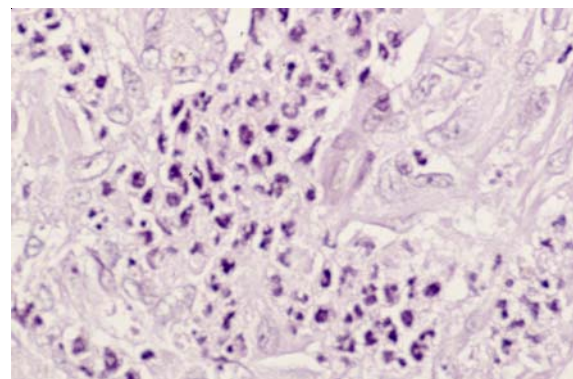


Fig. 1 Suppurative granuloma

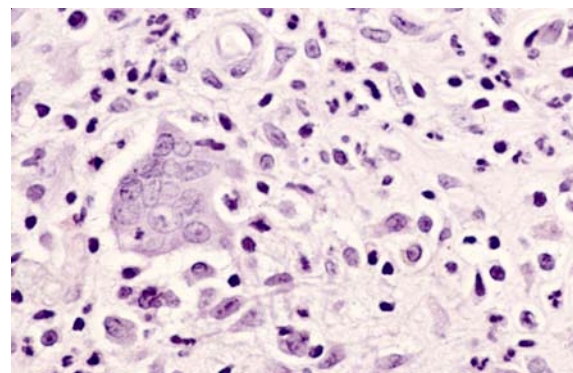


Fig. 2 Mixed cell granuloma

Table 1. Comparison between type of granuloma and AFB stain result

	AFB+ (%)	AFB- (%)
Mixed cell	11 (34.38)	35 (50.00)
Suppurative	18 (56.25)*	21 (27.78)
Tuberculoid	3 (9.37)	15 (20.83)
Palisading	0 (0)	1 (1.39)
Total	32 (100.00)	72 (100.00)

**p* = 0.01

Table 2. Comparison between depth of inflammation and AFB stain result

	AFB+(%)	AFB-(%)
Upper half	13 (40.63)	47 (65.28)
Lower half	13 (40.63)	16 (22.22)
Diffuse	6 (18.74)	9 (12.50)
Total	32 (100.00)	72 (100.00)

in cases that granuloma was involved in the upper dermis.

Discussion

Mycobacterial skin infections present variable clinical and histopathologic features^(2,12). These features were determined by the pathogenicity of the infecting strain, route of infection, and host cellular immunity⁽²⁾. Detection of AFB in granuloma confirmed the diagnosis of mycobacterial infections⁽¹⁻³⁾. Cultural identification of mycobacteria from clinical specimen remains the gold standard for diagnosis and specie specific^(2,3). In the present report, detection of AFB in the pathologic section correlated well with the rate of detection by the cultural method. Though the sensitivity of the staining method seemed to be less than the cultural method, it provided more rapid and cost effective.

The histopathologic changes are not specie specific and range from acute suppurative process to typical granulomatous inflammation^(5,11). The time of evolution was another factor other than host immune status could influence histopathologic changes^(1,2,11). An early lesion showed a predominantly neutrophilic response and long standing lesions showed more prominent granulomatous reactions. The dynamic nature of the disease was more clearly demonstrated in immunosuppressed patients infected with NTM⁽¹¹⁾. Though the well established histopathologic

features of cutaneous TB is tuberculoid granuloma with or without caseous necrosis, this feature is constantly seen only in lupus vulgaris^(2,13). In primary infected cases (tuberculous chancre) or infection in immunocompromised host (acute military TB and tuberculosis cutis orificialis), histopathologic features may be nonspecific acute inflammation, neutrophilic abscess, and poorly formed tubercle that can be seen in the late state. Histopathologic features of NTM infections can mimic those caused by TB. Features that have been reported were neutrophilic response that may form abscesses^(5,8) with mild granulomatous reaction, lymphohistiocytic infiltration^(5,7), non specific chronic inflammation^(1,5), various kinds of granuloma such as tuberculoid^(1,2,5,11), mixed cell^(3,8), suppurative^(3,11), and palisading granuloma^(5,11) and panniculitis^(5,11). Suppurative granuloma was the most characteristic feature that was previously reported in cutaneous NTM infections. In the present report, suppurative granuloma ranked the second most common pattern subsequent to mixed cell granuloma and these findings were not specie-specific. In previous reports AFB could easily be found in hosts with lowered cellular immunity^(2,11) and the histopathologic features that have been reported in these cases are neutrophilic response and abscess formation. In the present report, AFB were most frequently found in suppurative granuloma but the relationship with host immune status was not studied.

In terms of depth of involvement, the infiltration tended to involve the upper dermis in some types of cutaneous TB in immunocompetent hosts such as lupus vulgaris and tuberculosis verrucosa cutis⁽²⁾ but these features were not well documented in NTM infections⁽³⁾. Bartralot et al reported that the more prevalent histologic finding in immunosuppressed host was abscess formation that tended to involve diffusely deep dermis and subcutaneous tissue⁽¹¹⁾. In the present study, AFB could predominantly be found in some types of granuloma but with no specific site of predilection in contrast to AFB negative cases in which the inflammation tended to be located in the upper dermis.

Conclusion

AFB can be more frequently detected in suppurative granuloma. Tuberculoid granuloma that tends to be located in the upper dermis was the pattern in which AFB was rarely found. Detection of AFB in the pathologic section and histopathologic feature can reflex cell-mediated immune status of the host.

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การติดเชื้อกลุ่มวัณโรคที่ผิวหนัง: การเปรียบเทียบระหว่างลักษณะทางจุลพยาธิวิทยากับการตรวจพบเชื้อติดสีทึบกรดในชิ้นเนื้อที่ตัดจากรอยโรค

พรรณแห มไหสวริยะ, เจน มโนกุล, ศุภกานต์ เข็มเงิน, อังคณา ฉายประเสริฐ

การติดเชื้อกลุ่มวัณโรคที่ผิวหนัง มีอาการทางคลินิกที่ไม่จำเพาะเจาะจงเพียงพอที่จะให้การวินิจฉัยได้โดยไม่ต้องมีการตรวจเพิ่มเติมทางห้องปฏิบัติการ การตรวจทางจุลพยาธิวิทยามักจะเป็นแบบ *granulomatous inflammation* ซึ่งอาจจะเกิดได้จากการติดเชื้ออื่น เช่นการติดเชื้อราชนิดลึกที่ผิวหนัง แต่หากตรวจพบเชื้อติดสีทึบกรดในแกรนนูโลมาด้วย จะเป็นการช่วยบอกว่าเป็นการติดเชื้อกลุ่มวัณโรคจริง แม้ว่าจะบอก species ไม่ได้ คณะผู้รายงานได้ทำการศึกษาย้อนหลัง ตั้งแต่ปี พ.ศ. 2537-2544 จากสไลด์ทางจุลพยาธิวิทยาจำนวน 104 แผ่น ของผู้ป่วยที่สงสัยว่าจะมีการติดเชื้อกลุ่มวัณโรคที่ผิวหนัง ที่มารับการตรวจรักษาที่คลินิกแกรนนูโลมา แผนกผู้ป่วยนอก ภาควิชาตจวิทยา คณะแพทยศาสตร์ศิริราชพยาบาล พบว่าทุกสไลด์มีลักษณะทางจุลพยาธิวิทยาเป็น *granulomatous inflammation* ซึ่งแบ่งเป็นกลุ่มย่อยได้ 4 แบบ คือ แบบ *mixed cell*, *suppurative*, *tuberculoid* และ *palisading* พบเชื้อติดสีทึบกรดในพยาธิสภาพจำนวน 32 ราย (ร้อยละ 30.77) เมื่อเปรียบเทียบกับการเพาะเชื้อขึ้น พบว่ากลุ่มที่ตรวจพบเชื้อติดสีทึบกรดเพาะเชื้อขึ้นได้บ่อยกว่า กลุ่มที่ตรวจไม่พบเชื้อ พยาธิสภาพแบบ *mixed cell granuloma* เป็นชนิดที่พบบ่อยที่สุด (ร้อยละ 56.25) แต่จะตรวจพบเชื้อติดสีทึบกรดได้บ่อยที่สุดในพยาธิสภาพแบบ *suppurative granuloma* พยาธิสภาพแบบ *tuberculoid granuloma* มักจะตรวจไม่พบเชื้อติดสีทึบกรด และในกลุ่มที่ตรวจไม่พบเชื้อ พยาธิสภาพมักจะมีอยู่ในชั้นตื้นของหนังแท้ แต่การตรวจพบเชื้อติดสีทึบกรดจะสามารถตรวจได้ในทุกระดับของหนังแท้ที่มีพยาธิสภาพแบบ *suppurative*.