Case Report

Oral Sarcoidosis with Pulmonary Involvement: A Case Report with Literature Review

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Abstract:

Sarcoidosis is an uncommon granulomatous disorder which rarely presents with intraoral lesions. We report a case of 26-year-old Thai male presented with solitary whitish to yellowish painless ulcerated and indurated plaque on the lower labial mucosa for 1 year. Histopathology revealed non-caseating granulomatous inflammation with multinucleated giant cells. Other granulomatous diseases were excluded prior to the diagnosis. Abnormal chest X-ray was detected by pre-employment screening. The patient was diagnosed as smear-negative pulmonary tuberculosis. Neither cutaneous lesion nor chest imaging had been changed after 5 months of standard anti-TB treatment. Tissue biopsy from right upper lung exhibited non-caseating granuloma with negative AFB, GMS stains. Culture for Mycobacterium tuberculosis and fungal cultures were also negative. The overall clinicopathology findings are compatible with oral sarcoidosis with pulmonary involvement.

Keywords: ● *Non-caseating granuloma* ● *Oral sarcodosis* ● *Pulmonary lesion*

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รายงานผู้ป่วย

โรคซาร์คอยด์ในช่องปากและระบบทางเดินหายใจ

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บทคัดย่อ

โรคซาร์คอยด์เป็นโรคในกลุ่มการอักเสบแบบแกรนูโลมาที่พบได้ไม่บ่อย โดยเฉพาะอย่างยิ่งการมีรอยโรคบริเวณช่องปากซึ่งมีรายงานการพบน้อยมาก รายงานฉบับนี้เป็นการนำเสนอผู้ป่วยชายไทย อายุ 26 ปี มีผื่นสีเหลืองขาวลักษณะนูนหนาที่เยื่อบุริมฝีปากล่างเป็นเวลา 1 ปี ผลทางพยาธิวิทยาพบ non-caseating granulomatous inflammation with multinucleated giant cells ในชั้นหนังแท้ ผู้ป่วยได้รับการตรวจเพิ่มเติมเพื่อวินิจฉัยแยกโรคอื่นๆ ในกลุ่มแกรนูโลมา และได้ทำเอกซเรย์ทรวงอกก่อนเข้าทำงานซึ่งพบมีความผิดปกติ โดยได้รับการวินิจฉัยเป็นวัณโรคปอด หลังจากได้รับการรักษาวัณโรคเป็นเวลา 5 เดือน ไม่พบการเปลี่ยนแปลงของรอยโรคที่เยื่อบุริมฝีปากล่างและภาพรังสีทรวงอก จึงได้รับการตัดชิ้นเนื้อที่ปอด พบลักษณะเป็น non-caseating granuloma ทำการย้อม AFB และ GMS ไม่พบเชื้อก่อโรค รวมทั้งเพาะเชื้อไม่พบเชื้อวัณโรคและเชื้อรา จากอาการและผลทางพยาธิวิทยาดังกล่าว ผู้ป่วยรายนี้จึงได้รับการวินิจฉัยโรคซาร์คอยด์ในช่องปากและทรวงอก

คำสำคัญ: ● *แกรนูโลมา* ● *โรคซาร์คอยด์ในช่องปาก* ● *รอยโรคที่ปอด*

เวชสารแพทย์ทหารบก 2561;71:291-6.

Introduction

Sarcoidosis is a rare multisystemic disorder which predominantly involves lungs. Skin, eyes, liver, heart, kidneys, central nervous system and bones are less frequently affected. Cutaneous involvement is accounted for 15-20% of all cases of sarcoidosis[1]. Cutaneous lesion usually presents with papules, plaques or nodules which rarely ulcerate[2]. Incidence of sarcoidosis is typically among young adults and elderly around 60 years of age[3]. The etiology is unknown and histopathology shows non-caseating granulomas.

Oral sarcoidosis is a rare condition. Only about 70 cases have been reported in worldwide[4,5]. Affected sites include buccal mucosa, gingiva, palate, tongue and lip[5-8]. According to previous reports, various presentation of oral lesions were granulomas, gingivitis, gingival hyperplasia, gingival recession, masses and swelling[9].

Case report

A 26-year-old Thai male presented with a whitish to yellowish painless ulcerated and indurated plaque on lower labial mucosa for 1 year (Figure 1). The lesion was painless and gradually enlarged. He had initially been treated as chronic aphthous ulcers with 10 mg/day of prednisolone for 2 weeks, 0.6 mg/day of colchicine for 4 months and topical corticosteroid. The lesion did not significantly improve. Histopathology showed non-caseating granulomatous inflammation with multinucleated giant cells (Figure 2,3). Special stains (AFB,GMS), *Mycobacterium tuberculosis* culture, fungal culture, and PCR for *Mycobacterium tuberculosis* were all negative. Diagnosis of oral sarcoidosis was suggested. An

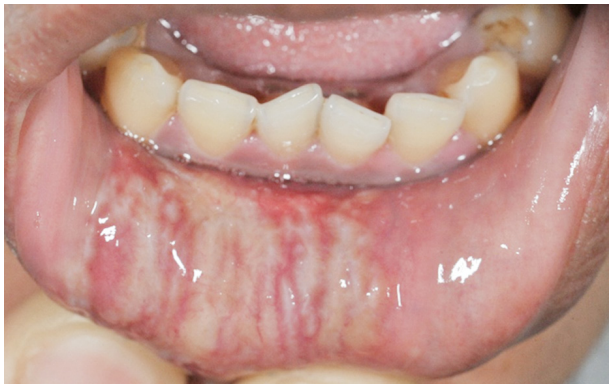

Figure1 Localized solitary well-defined whitish to yellowish painless ulcerated and indurated plaque 4 cm. x 2 cm. in size on lower labial mucosa

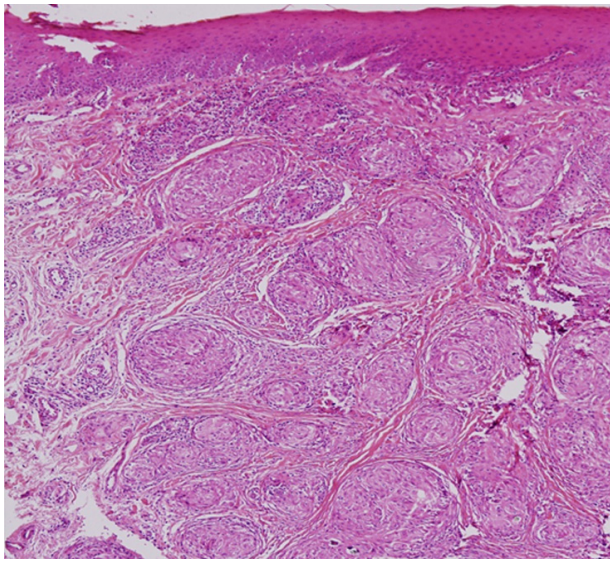

Figure 2 Histopathology examination shows acanthotic epidermis with hyperkeratosis. Dermis shows several packed naked granulomas. (H&E, 10X)

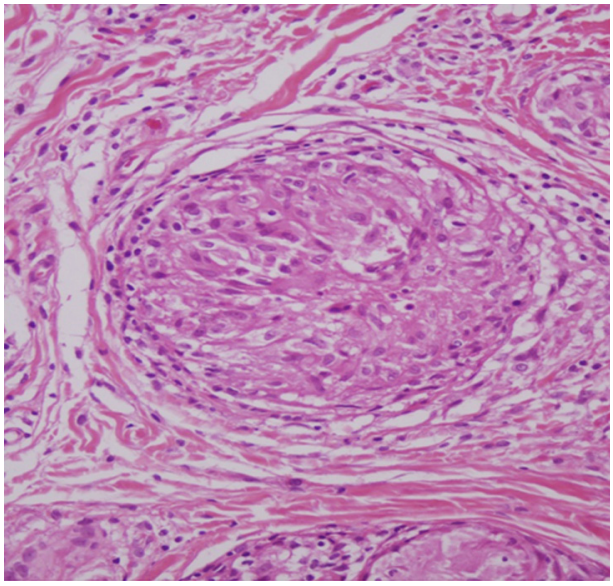

Figure 3 Histopathology examination shows packed naked granulomas characterized by histiocytic aggregates with multinucleated giant cells in dermis. Stroma is fibrotic with less lymphocytic infiltration. (H&E, 40X)

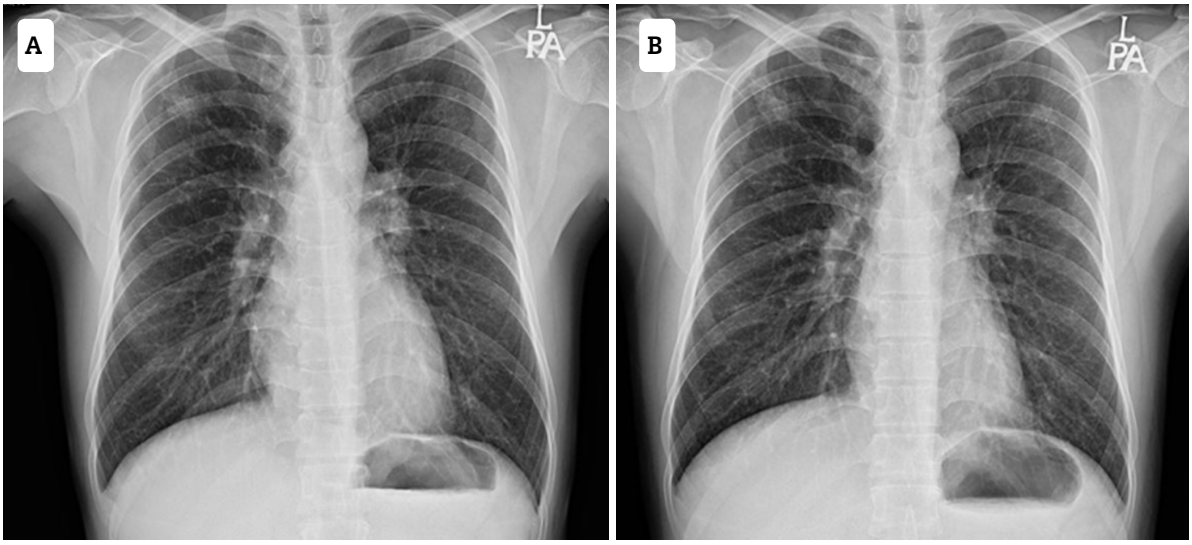

Figure 4 A) Film chest X-ray showed right upper lung reticulonodular infiltration with bilateral hilar lymphadenopathy (Before standard anti-TB treatment). **B)** Film chest X-ray after 5 months of standard anti-TB treatment without significant changes compare.

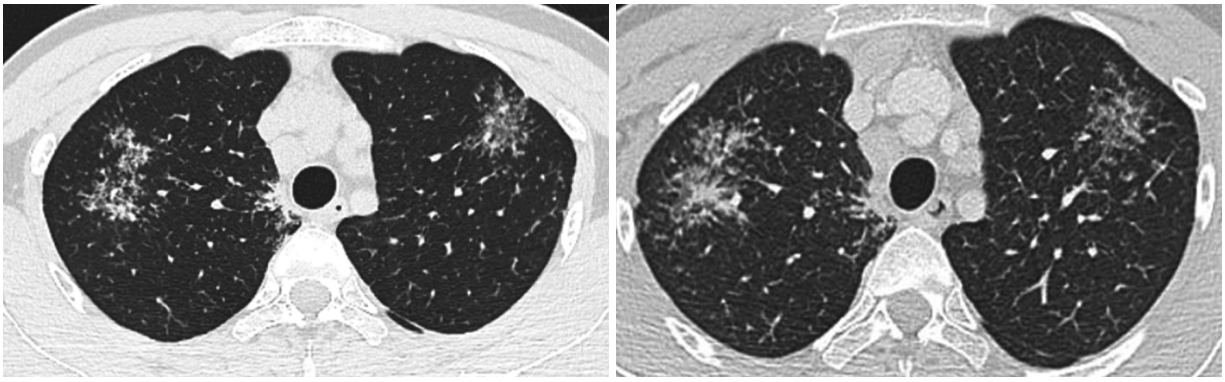

Figure 5 A) High resolution CT lung at 2 months of standard anti-TB treatment **B**) Chest CT at 5 months of standard anti-TB treatment

abnormal infiltration at right upper lung with bilateral hilar lymphadenopathy by chest X-ray was discovered accidentally. There was no chest or systemic symptoms. Sputum AFB was negative for three consecutive days. He was diagnosed as smear-negative pulmonary tuberculosis and had been treated with the standard anti-tuberculosis regimen (IRZE). No significant change of the lip lesion or chest imaging was observed after 5 months of the anti-TB treatment (Figure 4, 5). Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and endobronchial ultrasound-guided sheath were done. Tissue from right upper lung also confirmed non-caseating epithelioid granulomatous pneumonitis. AFB, GMS stains and PCR for *Mycobacterium tuberculosis* were all negative. Further investigations showed no evidence of skin, ocular, joint, abdomen or central nervous system involvement. Gallium-67 scan showed enhancement at bilateral hilar lymph nodes and bilateral pulmonary nodules. All blood tests were normal including serum angiotensin converting enzyme level at 35 (Normal range is 8 to 53). Serum Quantiferon-TB Gold was negative.

The patient was diagnosed as oral sarcoidosis with pulmonary involvement. The treatment is systemic corticosteroid dosage 20 mg/day.

Discussion

Sarcoidosis is a chronic non-caseating granulomatous disorder which affects multiple organs predominantly pulmonary system[10]. The etiology is unknown. Head and neck are also involved in approximately 15% of cases which mostly affect parotid gland or cervical lymph node[2].

Oral sarcoidosis is rare. About 70 published cases have been reported by review of literatures[4,5]. Oral lesion is typically asymptomatic, well-circumscribed, erythematous to brownish or violaceous papules and nodules which ulcerate occasionally[4,6]. Sites of oral sarcoidosis previously reported include buccal mucosa, gingiva, palate, tongue and lip. Oral involvement usually be seen in patients with known sarcoidosis. But there are also reports of oral sarcoidosis as the initial lesion[5-8].

Diagnosis is established by clinical features and histology with other granulomatous diseases excluded. Any suspected case should be confirmed by skin biopsy. Histopathologic evidence is a non-caseating granuloma but this is not pathognomonic for sarcoidosis[11-13]. Differential diagnoses of oral sarcoidosis including tuberculosis, syphilis, deep fungal infection, other mycobacterial infection, Crohn's disease, foreign body granuloma and granulomatosis with polyangiitis must be excluded[4,14,15]. Additional investigation such as staining, culture and tuberculin test are often required.

Clinical and compatible histopathologic findings are the most important evidence for diagnosis. No biomarkers or specific tests can be reliably used for definitive diagnosis of sarcoidosis. Serum angiotensin converting enzyme (ACE) has been used to monitor disease activity, response to treatment and to predict risk of recurrence. Elevated ACE level is found approximately 40-80% in sarcoidosis[16]. Kveim-Siltzbach skin test performed by intradermal injection of reagent prepared from sarcoid lymphoid tissue is now uncommon and no longer approved by FDA[14]. Other investigation such as CBC, BUN, creatinine, liver function test, serum calcium, biochemical and metabolic blood tests, urine analysis, chest X-ray, pulmonary function test, electrocardiography and ophthalmologic examination should be evaluated[17].

In general, asymptomatic sarcoidosis is not necessary to be treated. Spontaneous resolution can occur[18]. Side effects of corticosteroid in asymptomatic patients usually outweigh the benefit of treatment. However, asymptomatic ocular sarcoidosis, asymptomatic disorders of calcium dysregulation, asymptomatic nephrolithiasis and renal insufficiency from sarcoidosis should be treated because these conditions may lead to permanent organ impairment. For multiple organs involvement, treatment should be based on the indication of organ involvement. The first line systemic drug is corticosteroid. And the second line drugs are corticosteroid sparing agents such as methotrexate, azathioprine, mycophenolate, cyclosporine, antimalarial agent, leflunamide, infliximab and adalimumab[19].

This patient was diagnosed as oral sarcoidosis proven by histopathology and other granulomatous disorders were excluded. There was no improvement of lung lesions after treatment as smear-negative pulmonary tuberculosis with IRZE regimen, EBUS-TBNA and EBUS guided sheath were subsequently done. Histopathology from right upper lung also confirmed pulmonary sarcoidosis. The treatment is systemic corticosteroid (prednisolone 20 mg/day).

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