



Case report

Chronic granulomatous inflammation caused by latent tuberculosis presented as a subcutaneous mass: A case report with review of literature

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ABSTRACT

Chronic granulomatous inflammation is a global disease caused by infection, auto-immune disease, toxic, or idiopathic factors. Pathological finding shows formation of distinct granulomas composed of aggregates of epithelioid macrophages, with a peripheral cuff of lymphocyte and plasma cells. Chronic granulomatous inflammation can occur in many different areas of the body, including the skin. Here, we report a case of a 64 years old woman who developed subcutaneous chronic granulomatous inflammation in the upper thigh, caused by latent tuberculosis. We also review granulomatous lesion in various countries with different incidence rate of tuberculosis and vascular feature, evaluating its effect when clinicians encounter.

Introduction

Chronic granulomatous inflammation is a global disease caused by infection, auto-immune disease, toxic, or idiopathic factors. Infectious cause include *Mycobacterium tuberculosis*, Non-tuberculous mycobacteria, *Aspergillus* spp, etc., while non-infectious cause include autoimmune disease such as sarcoidosis or toxic such as chronic beryllium disease [1,2]. Pathological finding of chronic granulomatous inflammation shows formation of distinct granulomas composed of aggregates of epithelioid macrophages, with a peripheral cuff of lymphocyte and plasma cells [1]. Granulomatous inflammation can be histologically divided into two categories, caseating and non-caseating. Caseating granulomas are characterized by the presence of dead or necrotic tissue that has a caseous necrosis, where histological features are not preserved. Non-caseating granulomas do not contain necrotic tissue and are composed of activated immune cells such as macrophages and T-lymphocytes [3]. Chronic granulomatous inflammation can occur in various parts of the body such as the lung, liver, gastrointestinal tract, or skin [2, 4,5]. The purpose of this article is to report a case of subcutaneous chronic granulomatous inflammation with high vascularity caused by latent tuberculosis.

Case report

A 64 years old woman visited our clinic with a chief complaint of a

lump on the right anterior thigh. The patient had no underlying disease or specific medical history, nor any symptoms of infection. A physical examination was conducted, revealing a hard protruding mass approximately 2 centimeter of width and length, which was palpable. There was no change of skin surface or color. Ultrasonography was performed, showing an isoechoic mass in subcutaneous level [Fig. 1].

An excisional plan was made based on a clinical diagnosis of lipoma or fibroma. Surgical removal was done a week after the first visit under local anesthesia. After the incision, a vessel with a diameter of approximately 0.1 cm was found in the subcutaneous area without surrounding tissue; thus, ligation was performed. It was later found that this vessel was connected to the mass. After the ligation, careful dissection was carried. However, the patient's mass had high vascularity thus multiple surgical ligation was needed. Ultrasound showed the mass lying above the rectus femoris, thus excision was made just above the fascia with the margin secured. The excised mass consisted of multiple pea-sized hard nodules with a dark yellow color. Against one's expectation, the histopathologic examination showed chronic granulomatous inflammation with a caseous type [Fig. 2]. The patient had no history of tuberculosis or other infectious disease, with no distinct chest x-ray finding. Interferon gamma release assay (IGRA) was followed to rule out any chance of tuberculosis, and the result was positive. The patient underwent treatment of latent tuberculosis, 3 months of isoniazid and rifampin.

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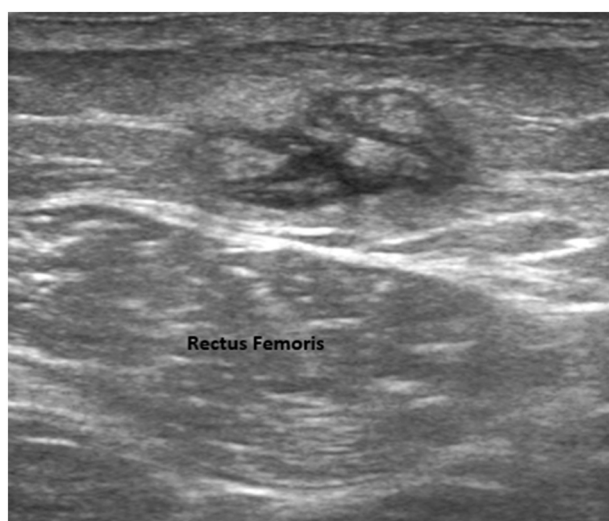


Fig. 1. Ultrasonography of isoechoic mass in subcutaneous level sized $1.76 \times 2.02 \times 0.8$ cm, formed by small multiple nodules and hypoechoic fluid. Rectus Femoris muscle is depicted underneath the mass.

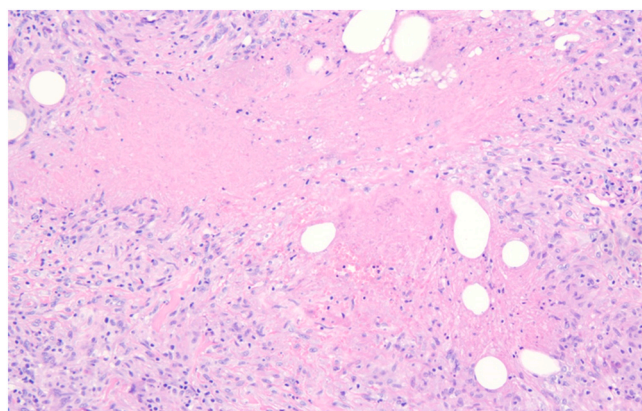


Fig. 2. Pathological finding of the excised mass revealed caseating chronic granulomatous inflammation. Centrally, caseous necrosis is seen as an amorphous pink material, which is surrounded by epithelioid cell granulomas and lymphocytes.

Discussion

World Health Organization reports that approximately a quarter of the global population has been infected by tuberculosis, and more than 10 million people continue to fall ill from it each year [6]. Incidence rate of tuberculosis vary by country, with developing countries comprising most of the prevalence. In Portugal, which has relatively low incidence rate of 16 per 100,000 people [6], conducted a retrospective study of total 48,253 skin biopsies at a tertiary center [7]. Among these, 411 patients were diagnosed with granulomatous skin lesions, of which only 80 cases (19.5 %) were attributed to an infectious cause. Of these, 19 cases (4.6 %) were due to cutaneous tuberculosis, followed by 8 cases (1.9 %) of fungal infection and 7 cases (1.7 %) of leprosy. Majority (80.3 %) were noninfectious granuloma (N = 330), including granuloma annulare (N = 98; 23.8 %), sarcoidosis (N = 47; 11.4 %), and etc. In contrast, India, which has the highest number of tuberculosis cases in the world and an incidence rate of 195 per 100,000 people [6], conducted a similar retrospective study involving a total of 1280 skin biopsies at a tertiary center [8]. A total of 186 patients (14.42 %) were diagnosed with granulomatous skin lesions, of which 161 (86.56 %) were of infectious origin. Cutaneous tuberculosis accounted for 46 cases

(24.73 %), while leprosy was the most common, with 107 cases (57.52 %). Another study conducted in India [9] investigated total of 275 granulomatous lesion biopsies from different tissues. The most common cause was tuberculosis in 130 (47.26 %), followed by leprosy in 35 (12.72 %), and fungal infections in 24 (8.72 %). The majority of the granulomas were found in skin and subcutaneous tissues with 68 (24.72 %) cases, followed by lymph node in 59 (21.46 %), bones and joints in 50 (18.18 %), and respiratory system in 26 (9.46 %). Out of 130 cases of tuberculosis, lymph nodes were involved in 53 (40.76 %), followed by bones and synovial tissue in 35 (26.92 %), cutaneous in 4 (3.08 %), intestinal in 14 (10.76 %), larynx in 11 (8.46 %), and sinus tract in 4 (3.08 %). In China, another country with relatively high incidence rate of tuberculosis 52 per 100,000 people [6], conducted a retrospective study of 256 cutaneous and subcutaneous infectious granulomas [10], found that *Mycobacterium leprae* (N = 68; 26.56 %) was the most frequent cause followed by *Sporothrix schenckii* (N = 61; 23.83 %), *Mycobacterium tuberculosis* (N = 40; 15.63 %), and etc. The distal extremities were the most commonly affected sites (N = 82; 32.03 %), followed by the face (N = 70; 27.34 %) and the upper limbs (N = 57; 22.27 %). In South Korea, total of 373 patients with confirmed tuberculous lymphadenitis were reviewed, and the most commonly involved lymph nodes were cervical lymph node (N = 175; 46.9 %) followed by supraclavicular (N = 84, 22.5 %) [11]. These studies reveal that the nature of granulomatous skin lesion rely very much on the country or regional infection situation, affecting mostly lymph nodes, skin or joints. Thus epidemiological background knowledge may help diagnosing when combined with pathological findings. Furthermore several studies report that hypoxic necrotizing core of tuberculous granuloma are extensively vascularized, with increased serum level of vascular endothelial growth factor (VEGF) in tuberculosis infection [12–14]. Also a chemokine receptor (CXCR4b) is found to promote granuloma formation by sustaining a mycobacteria-induced angiogenesis in an animal study [15].

Thus when encountering a hard subcutaneous mass [10,16] with high vascularity, infectious granuloma should be considered in countries where tuberculosis, leprosy, or fungal infections are prevalent. In countries with less infectious disease, when pathological finding shows caseating chronic granulomatous inflammation, tuberculosis should be considered as the first choice. If a patient with a simple subcutaneous mass have a history of tuberculosis, chronic granulomatous inflammation must be considered and vascular ligation should be prepared prior to surgery. Further studies of vascularity and angiogenetic nature of granuloma may contribute to treatment of granulomatous diseases.

CRedit authorship contribution statement

Jung-Han Kim: Writing – review & editing, Supervision. **Hee Gyun Yang:** Writing – review & editing, Writing – original draft, Investigation, Formal analysis. **Jungho Kim:** Methodology.

Consent

Informed written consent was obtained from the patient for publication of this report.

Ethical approval

IRB review exemption has been confirmed by Public Institutional Bioethics Committee designated by the MOHW.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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