

## Case Report

# Subcutaneous granuloma annulare presented as multiple nodules of the lower leg

## 皮下環狀肉芽腫表現為腳部多發性結節

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This is a case report of a 20-month-old boy who presented with multiple asymptomatic nodules on the left pretibial area. He had no history of diabetes or other systemic diseases. Family history was unremarkable. Skin biopsy showed palisading granuloma in deep dermis and subcutis consistent with subcutaneous granuloma annulare. Response to intralesional steroid treatment was satisfactory.

此病例之患者是一個 20 個月大男嬰，表現為左脛前區無徵兆結節。病人身體良好，無糖尿病或其他系統性疾病。無家族史。皮膚活組織檢查見真皮深層及皮下有欄柵狀肉芽腫，與皮下環狀肉芽腫吻合。皮損激素注射療效理想。

**Keywords:** Palisading granuloma, subcutaneous granuloma annulare

關鍵詞：欄柵狀肉芽腫，皮下環狀肉芽腫

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## Introduction

Subcutaneous granuloma annulare (SGA) often presents as a deep-seated soft-tissue mass in paediatric-age population. There has been

controversy on the association of this granuloma annulare variant with diabetes mellitus or other systemic diseases. The following case report is a young boy with SGA.

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## Case report

A 20-month-old Pakistan boy presented with a growing lump on the left shin in May 2003. According to the father, it started as a pea-sized skin lesion and had been growing for one month. It was non-itchy and painless. There had been no history of discharge, spontaneous bleeding or preceding trauma. He did not suffer from any systemic illnesses including fever or joint pain. He was the second child of the family. The other two

siblings did not suffer from any similar skin problem. His past health was good. He was born in Hong Kong and his vaccination was up to date.

On examination, there was an annular lesion on the left pretibial area (Figure 1). The lesion was 5 cm x 3 cm in size. The skin surface was mildly erythematous without scaling. On palpation, the lesion consisted of multiple underlying dermal or subcutaneous nodules. The nodules were firm and non-tender. Differential diagnoses of annular lesion were granuloma annulare, sarcoidosis, tuberculoid leprosy, subacute lupus erythematosus and annular lichen planus. In children, the skin nodule could also be due to rheumatoid nodule or subcutaneous nodule of rheumatic fever.

Blood tests including renal and liver tests, fasting sugar, anti-nuclear antibody were all normal. Skin biopsy reviewed an unremarkable epidermis. Both the lower dermis and subcutis showed multiple fairly well defined necrobiosis, surrounded by palisaded histiocytes. The necrobiosis contained considerable amount of mucin. Mild perivascular lymphohistiocytic infiltration was also present in the dermis. No vasculitis was seen. The histologic features were consistent with subcutaneous granuloma annulare (Figures 2 & 3).

Intralesional corticosteroid was given once in July 2003. Although the left nodules were regressing over two-month period, another similar lesion became apparent on the right pretibial area. The new lesion was smaller, non-itchy and painless (Figure 4).

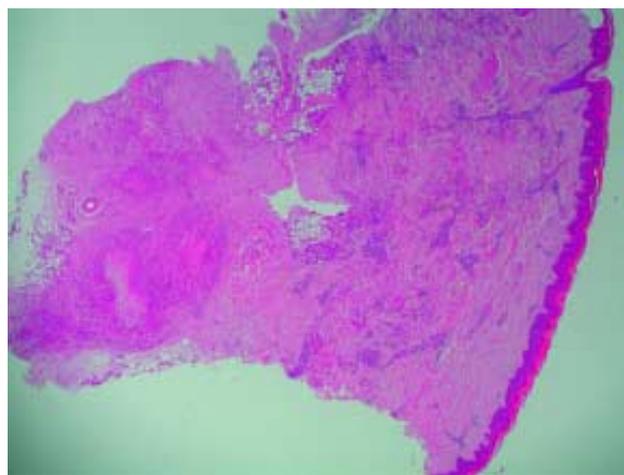
## Discussion

Granuloma annulare (GA) is a self-limiting inflammatory skin condition occurring in both adults and children. Subtypes of granuloma annulare are localised GA, generalised GA, SGA, perforating GA, patch GA, arcuate dermal erythema and actinic granuloma.<sup>1</sup>

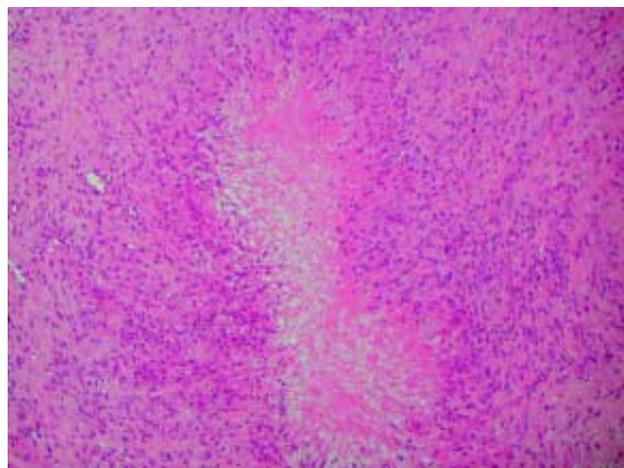
SGA is one subtype that occurs almost exclusively in paediatric-age population. In the literature, this condition is also called deep GA, pseudo-



**Figure 1.** Annular lesion on left pretibial skin.



**Figure 2.** H&E, original magnification X 4. Multiple necrobiotic granulomas are found in the subcutaneous tissue.



**Figure 3.** H&E, original magnification X 20. The necrobiotic granuloma is composed of a centre of necrobiosis with abundant mucin, and a peripheral rim of palisaded histiocytes.



**Figure 4.** Newly developed right shin lesion.

rheumatoid nodule or subcutaneous palisading granuloma. The classic clinical picture of SGA is a soft-tissue mass that is firm, non-tender and immobile. It can present as a single nodule. Nevertheless multiple nodules occur in one third to two third of the cases. The sites of predilection are the extremities and scalp in which occiput is the most common site. It often occurs in the first five to six years of life. Boys are twice as common as girls to have this type of GA.

The aetiology and pathogenesis of GA are basically unknown. It has been postulated that the disease is an aberrant T-cell response leading to an inflammatory reaction.<sup>2,3</sup> Various conditions have been associated. These included trauma, insect bites, infections, vasculitis and bone marrow transplantation. Understandably, trauma is not uncommon in such exposed sites of young children. Infections such as borrelia, herpes zoster and streptococcus have been implicated. GA as a whole has been associated with a number of systemic diseases such as diabetes mellitus, sarcoidosis, AIDS and autoimmune diseases.<sup>4</sup> However, the subcutaneous variant of GA does not have a definite association with any systemic diseases. As early as 1959, Draheim et al followed up 54 children cases of SGA.<sup>5</sup> None of the cases

developed connective tissue disease after a follow-up period from one to fourteen years.

This finding was consistent with a more recent study by Grogg et al.<sup>6</sup> These investigators retrospectively collected clinicopathologic data from 34 cases of SGA. After an average follow up of 60 months, no patient developed signs or symptoms of rheumatologic disease. However, two of the cases (5.9%) were associated with insulin dependent diabetes mellitus (IDDM). The proportion of IDDM in this series was roughly 36 times higher than the diabetes mellitus (DM) prevalence in US paediatric population. Therefore the authors argued that DM might be associated with SGA. The study also confirmed a few clinical characteristics of SGA. Firstly, pain or tenderness was not a common feature. It occurred only in 12%. Secondly, most SGA occurred in single site. Those cases with more than one site accounted for only 26.5%. Thirdly, recurrence at the same site or remote site is common. Approximately 53% of the cases were found to have recurrence.

The options of investigation are skin biopsy, blood tests and imaging studies. Skin biopsy is by far the most useful investigation to confirm SGA. It shows "palisading granuloma" or "necrobiotic granuloma". The characteristic histopathology is a central area of homogenous necrotic collagen surrounded by palisading histiocytes and lymphocytes. In the subcutaneous variant, the necrobiosis is distributed in the deep dermis, subcutis and rarely deep soft-tissues. Compared to the superficial variant, SGA is more likely to have larger area of necrobiosis and more eosinophils. However, in reality, deep and superficial lesions may coexist. Palisading granuloma can occur in other skin conditions, such as rheumatoid nodule, necrobiosis lipoidica and rheumatic fever nodule. Due to the histologic resemblance to rheumatoid nodule, SGA is also named as "pseudorheumatoid nodule". Distinguishing these histologic differential diagnoses can be extremely difficult.

The main role of blood test is to rule out associated diseases. As mentioned previously, it is exceedingly uncommon for SGA to be associated with systemic diseases. Any abnormal blood test result will prompt a clinical re-evaluation. Normal result is expected in blood tests. These tests include white cell count, ESR, acute phase reactant, immunoglobulin screening and autoantibody screening. Rheumatoid factor should be considered if the nodule is juxta-articular.

SGA tends to have an excellent clinical outcome. Due to high probability of spontaneous recovery, expectant observation is often recommended. Surgical excision is often not warranted unless the lesion is painful or occurs at a site that interferes with function. On the other hand, recurrence is common. It has been shown that the recurrence rate varied from 40% to 66%.<sup>7-9</sup> Other medical treatments have been proposed, including topical or intralesional steroid, potassium iodide, dapsone, nicotinamide, chlorambucil and isotretinoin. However none of them had good evidence of efficacy.<sup>10</sup>

This case demonstrated the typical clinical features of subcutaneous granuloma annulare. The patient's age and the sites of the lesion were typical of SGA. While the initial lesion did have improvement after intralesional steroid, the exact benefit of this therapy to SGA was not ascertained because SGA could have spontaneous regression. The recurrent course of the disease on another

site, again, was not surprising. Although Grogg et al<sup>6</sup> believed that SGA might be associated with diabetes mellitus, this association was not observed in our patient.

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