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Case Report

A window for effective diagnosis: Erythema nodosum in a girl with newly diagnosed ulcerative colitis

通往有效診斷的那扇窗：一名初診斷潰瘍性結腸炎的女孩的結節性紅斑

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An eight-year-old girl presented with tender erythematous nodules over bilateral shins and right forearm for two weeks. She had a recent admission for fever and loose stool with a presumed diagnosis of gastroenteritis. Erythema nodosum associated with infective gastroenteritis was initially suspected. But further history revealed a two-month history of recurrent fever and loose stool with a history of short stature. Investigations showed iron-deficiency anaemia, positive fecal occult blood and negative stool microbiological workup lead to the suspicion of an alternative diagnosis. Skin biopsy showed panniculitis with septal and lobular involvement. Subsequent colonoscopy confirmed the diagnosis of underlying ulcerative colitis.

一名 8 歲女孩，過去兩週在雙側小腿和右前臂出現疼痛的紅色結節。此前她曾因發燒和稀便而入院，當次被推測診斷為腸胃炎。這次開初懷疑是與感染性胃腸炎相關的結節性紅斑，但經病史探索後，發現她有兩個月的反復發熱和稀便史，並身材矮小的病史。檢查顯示有缺鐵性貧血及大便潛血陽性，大便微生物檢查則呈陰性，以上種種不期然令人懷疑有其他鑒別診斷的可能。皮膚活檢顯示脂膜炎伴有隔膜和小葉受累。隨後的結腸鏡檢查診斷出潛在的潰瘍性結腸炎。

Keywords: Erythema nodosum, panniculitis, ulcerative colitis

關鍵詞：結節性紅斑、脂膜炎、潰瘍性結腸炎

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Case report

An eight-year-old girl from Sri Lanka was admitted to the paediatric ward via the emergency department with painful nodules over her bilateral shins and right forearm (Figure 1) for two weeks. She was first seen at the paediatrics clinic nine months prior to this admission for short stature with her height 2 cm below the 3rd percentile and her body weight at the 3rd percentile. She had repeated episodes of fever and

loose stool for two months prior to this admission. Stool for bacterial culture, entero-virus panel, ova and cysts were negative. She was given amoxicillin-clavulanic acid by a private doctor for her fever and loose stool, otherwise she did not take any other medication.

Clinical examination showed multiple tender erythematous nodules without epidermal change over bilateral shins and right extensor forearm (Figure 1). She was afebrile. Chest, cardiovascular, and abdominal examinations were unremarkable. There was no organomegaly.

Laboratory results showed anaemia with Hb 8.5 g/dL, elevated total white cell count at $17.9x10^9$/L with neutrophilia $11.3x10^9$/L and thrombocythemia $969x10^9$/L. She had hypoalbuminemia with albumin 32 g/L. Electrolytes, liver and renal function tests were unremarkable. Erythrocyte sedimentation rate (ESR) was high at 115 mm/hr and C-reactive protein (CRP) was elevated at 15.4 mg/dL. She had iron deficiency with serum iron level at 2.2 umol/L, total iron binding capacity (TIBC) 41 umol/L and transferrin saturation (TRF) of 5%. Autoimmune panel including anti-nuclear antibody (ANA), anti-extractable nuclear antigen (anti-ENA) were unremarkable. Anti-streptolysin-O titre was not elevated. Fecal occult was positive on 3 separate days.

An incisional biopsy performed over patient's left leg showed an unremarkable epidermis and minimal perivascular inflammation (Figure 2). Subcutaneous tissue showed areas of fat necrosis associated with histiocytic infiltration and foamy macrophages in the fat lobules and the septum. Focal lipomembranous changes were seen.

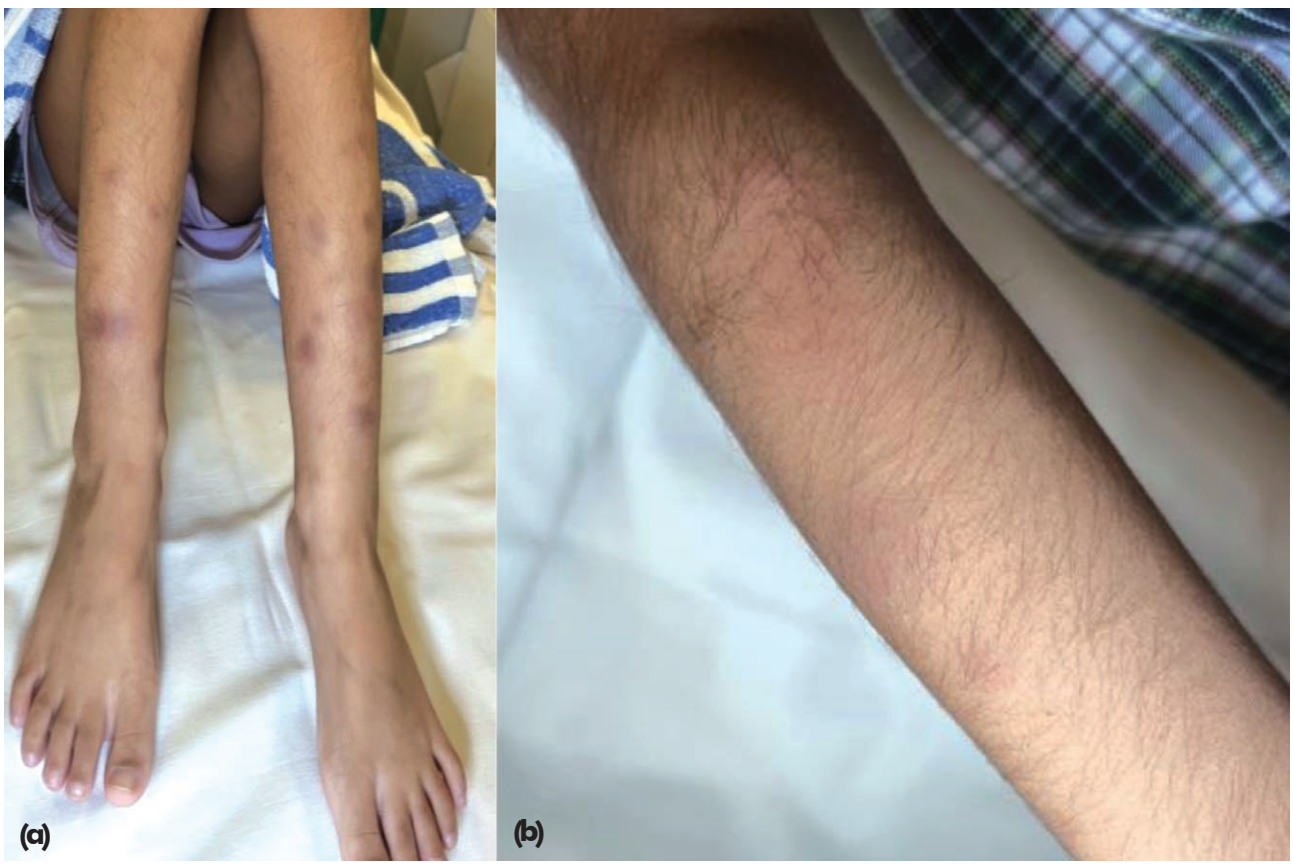

Figure 1. (a) Multiple tender erythematous nodules over bilateral shins and (b) right forearm with no epidermal changes.

No multinucleated giant cells or caseating necrosis was identified. There was no evidence of vasculitis. No acid-fast bacillus (AFB) or fungus was seen with Ziehl-Neelsen, Wade-Fite stains and Periodic acid-Schiff stain respectively. Direct immunofluorescence was negative.

Oesophago-gastro-duodenoscopy was normal. Colonoscopy demonstrated oedema and inflammation throughout the entire colon with multiple ulcers seen from recto-sigmoid up to the caecum. Colonic biopsies for AFB with mycobacterial culture and *Mycobacterium tuberculosis* polymerase chain reaction (TB-PCR) were negative and there was no evidence of malignancy.

The patient was diagnosed with ulcerative colitis associated with secondary erythema nodosum (EN). Prednisolone 20 mg daily was initiated with resolution of all tender nodules after 1 week of treatment. Fever and loose stool subsided. Her ESR and CRP levels normalised. Azathioprine 25 mg daily was introduced as a steroid-sparing agent at her subsequent out-patient follow up with no recurrence of EN.

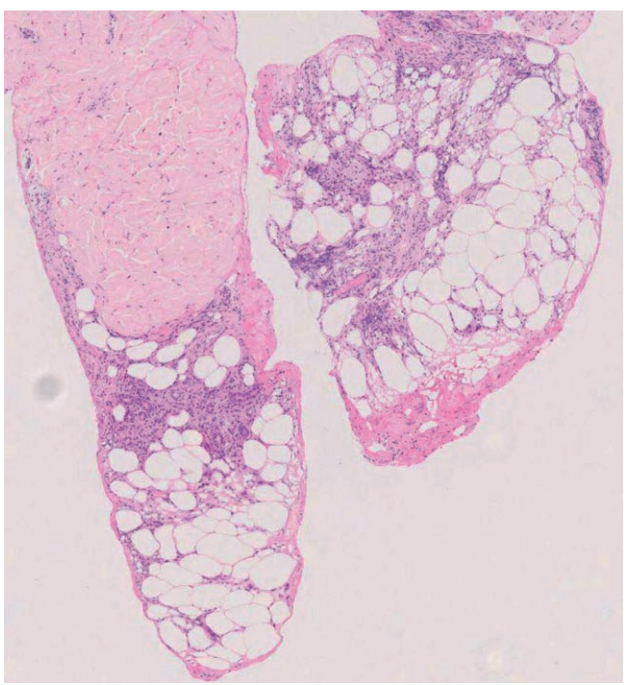

Figure 2. Subcutaneous tissue showed areas of fat necrosis associated with histiocytic infiltration and foamy macrophages in the fat lobules and the septum.

Discussion

Inflammatory bowel disease (IBD), which includes Crohn's disease and ulcerative colitis, is a chronic idiopathic disorder causing inflammation of the gastro-intestinal tract. IBD was traditionally regarded as a disease of westernised nations. The age-adjusted incidence for IBD in Hong Kong was 3.12 per 100 000 person-years in 2014.[1] The incidence of IBD has been rising in newly industrialised countries. The estimated incidence in Southern Asia ranged from 0.09 to 3.91 per 100 000 person-years and 0.69 to 6.02 per 100 000 person-years for Crohn's disease and ulcerative colitis respectively. This compares to 6.3 to 23.8 per 100 000 person-years and 8.8 to 23.14 per 100 000 person-years for Crohn's disease and ulcerative colitis respectively in North America. Sri Lanka was one of the countries in Southern Asia with the lowest incidence and prevalence for IBD.[2]

The most common mucocutaneous lesions associated with IBD are EN, pyoderma gangrenosum and aphthous stomatitis.[3] A prospective cohort study involving 352 children and adults with IBD reported EN occurred in 7.4% of patients with EN being more prevalent in Crohn's disease (13%) than ulcerative colitis (4%).[4] A cross-sectional study involving 73 children with IBD, 40 of them having Crohn's disease while 33 having ulcerative colitis (UC); and EN was reported in 2 out of 33 UC patients (6.1%).[5] Other cutaneous presentation of Crohn's disease includes orofacial granulomatosis which can be a distinguishing sign of Crohn's disease from ulcerative colitis.[6] Bowel symptoms usually develop within a few months from the onset of cutaneous presentation, but delays of up to years have been reported.[7]

EN is the most common form of panniculitis. EN histologically represents the prototype of septal panniculitis but this should not be taken to imply that histopathologic changes are entirely confined to subcutaneous septa.[8] A retrospective study on the clinicopathological characteristics of EN showed the presence of focal peripheral lobular panniculitis favoured secondary EN (OR 1.93, 95% CI [1.01, 3.65], p=0.045).[9] The histopathology in our case showed panniculitis in both septa and fat lobules.

Our patient was from a country with low incidence and prevalence of IBD. EN is common in our local hospital dermatology practice but IBD may not be one of the most common association due to the relatively low incidence and prevalence in Asia compared to the west. EN is more commonly associated with infective causes such as streptococcal infection and bacterial gastrointestinal infection. In this case, the initial impression was panniculitis associated with infective gastroenteritis. However, a detailed history of repeated fever and loose stools with short stature; the degree of iron-deficiency anaemia, reactive thrombocythemia, grossly elevated acute phase reactants (ESR & CRP) and the negative stool microbiological workup raised suspicion for an alternative diagnosis. Positive fecal occult blood due to bacterial dysentery was less likely with prolonged symptoms and negative stool microbiological workup. This should prompt further endoscopic workup for possible IBD with secondary EN. Her history of short stature may be explained by her previously undiagnosed long standing ulcerative colitis.

Although the cause of EN in most cases is idiopathic, a thorough search for any underlying assocated disease is vital as illustrated in our case. Our patient responded well with systemic steroid and azathioprine as a steroid-sparing agent. Prompt treatment for her underlying IBD may hopefully lead to catch-up growth for this patient.

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