Metastatic Crohn’s disease in a Chinese girl

Metastatic Crohn’s disease, in which non-caseating granulomatous infiltration of the skin occurs at sites separated from the gastro-intestinal tract by normal tissue, is the least common dermatologic manifestation of Crohn’s disease. We report a 15-year-old girl with metastatic Crohn’s disease presenting as granulomatous vulvar papules and nodules with typical histopathologic features. To the best of our knowledge, this is the first case of metastatic Crohn’s disease in Chinese children reported in the English medical literature.

Introduction

Crohn’s disease is an ulcerative granulomatous inflammatory disease originally named regional ileitis by Crohn et al1 in 1932. It is a multisystem disease with many skin and mucous membrane manifestations related to the primary granulomatous process and to nutritional deficiencies. In most instances the cutaneous changes follow the intestinal disease, but occasionally mucocutaneous lesions can lead to the diagnosis of Crohn’s disease prior to bowel involvement. Metastatic Crohn’s disease (MCD) is defined as a granulomatous cutaneous reaction separated from affected areas of the gastro-intestinal tract by normal skin.2 We report a 15-year-old girl with MCD who also had a history of intestinal Crohn’s disease.

Case report

A 15-year-old Chinese girl presented to the Yaumatei Dermatology Clinic in August 2005 with a history of warty papules on her labia majora for around 1 year. She had been diagnosed with intestinal Crohn’s disease by the paediatricians and surgeons at Queen Elizabeth Hospital the month before after 2 years of follow-up for recurrent perianal abscesses and fistulae. On physical examination, labial swelling with multiple warty papules was noted, but no evidence of sexual abuse was found. Blood tests revealed a raised erythrocyte sedimentation rate of 92 mm/hr with a blood picture consistent with iron deficiency anaemia. She had previously been diagnosed (in 2004) with recurrent vulvar cellulitis by the surgeons at Queen Elizabeth Hospital and was treated with multiple courses of antibiotics and iron replacement. The swelling usually resolved with antibiotic treatment but recurred when these were discontinued. The surgeons took eight biopsies from the vulva, labia majora, anus, and anovestibular fistula on two separate occasions (September 2004 and February 2005). Specimens taken from the vulva and anus showed acute-on-chronic inflammation with non-caseating granulomas and prominent secondary lymphangiectases (Fig 1). In February 2005, a Ziehl-Neelsen (ZN) stain for acid-fast bacilli (AFB) and a periodic acid-Schiff with diastases digestion (PASD) stain for fungi were negative. A polymerase chain reaction (PCR) for Mycobacterium tuberculosis was performed on the vulvar and anal specimens but was negative. An early morning urine culture was...
negative for *M tuberculosis* and her chest radiograph was normal.

In early 2005, the patient started to develop abdominal pain and recurrent diarrhoea. She was also noted to have delayed puberty with growth retardation and subsequently referred to a paediatrician for further management. Her weight and height were on the third percentile for her age. A computed tomographic scan of her abdomen demonstrated inflammatory changes in the colon and small bowel. A colonoscopy showed inflammatory lesions in the colon without any strictures or cobblestoning. During colonoscopy a biopsy was taken from the descending colon that showed epithelioid granulomas, but a PCR for *M tuberculosis* was negative. Crohn’s disease was diagnosed from the history and the colonoscopic findings in July 2005.

Dermatological examination of the patient’s perineal region in August 2005 revealed swelling of the labia with erythema. There were multiple papules and nodules on the labia varying from 1 mm to 5 mm in diameter (Fig 2). Perianal erosions and exudates were seen but not oral mucosal lesions. Development of secondary sexual characteristics was delayed. Dermatological differential diagnoses included granulomatous disorders (such as MCD, foreign body granuloma, AFB infections, and deep fungal infections), condylomata acuminatum, condylomata lata, lymphangioma circumspectum, angiokeratoma, chronic lymphoedema, and hidradenitis suppurativa.

The patient and her family declined a repeat skin biopsy for histology and culture. A review of the previous skin biopsies showed non-caseating granulomas with multinucleated Langerhans giant cells. The ZN stain for AFB and the PASD stain for fungus were negative, consistent with a diagnosis of MCD.

Treatment with an elemental diet together with iron and folate supplements was begun. She was given metronidazole 200 mg three times daily and sulphasalazine 500 mg four times daily and topical mometasone furoate. A marked reduction in vulvar swelling and gastro-intestinal symptoms was noted and the patient put on 5 kg of weight in 6 months. She reached puberty after treatment and her weight and height increased to the 25th percentile for age.

**Discussion**

Crohn’s disease is an inflammatory bowel disease first described by Crohn et al1 in 1932. Crohn’s disease often begins between the second and fourth decades of life, but one third of the cases of intestinal Crohn’s disease develop before the age of 20 years.3 Its cause remains unknown, but immune mechanisms, enzymatic alterations, genetic factors, and bacterial antigens have all been suggested in its pathogenesis. The age-adjusted incidence of Crohn’s disease in Hong Kong Chinese is 1.0 per 100 000,4 compared with 5.8 per 100 000 in the United States.5

Cutaneous manifestations of inflammatory bowel disease such as Crohn’s disease and ulcerative colitis are relatively common, varying from about 10% at the time of diagnosis to more than 20% during the course of the disease.5 Skin lesions can be classified into three principal classes: granulomatous, reactive, and those secondary to nutritional deficiency.

Granulomatous cutaneous lesions are seen in Crohn’s disease only and have the same histological features as the bowel disease including contiguous perianal skin lesions, oral granulomatous ulcers, and MCD. Contiguous perianal skin lesions such as ulcers with lymphoedema, vegetating
lesions, fissures, fistulae, abscesses, and sinus tracts are the most common skin lesions occurring in about one third of patients and are caused by direct extension of intestinal Crohn’s disease.

First described by Parks et al in 1965, MCD is a rare complication of Crohn’s disease in which granulomatous lesions involving the skin are separated from the gastrointestinal lesions by normal tissue. Although MCD is well recognised in adults, it is extremely rare in children. It may develop simultaneously or precede gastro-intestinal involvement; most cases of MCD are seen before the diagnosis of gastro-intestinal Crohn’s disease is made. Cutaneous MCD lesions may be polymorphous and are generally ulcers, erythematous nodules or plaques. They can be divided into two forms: genital and non-genital. Genital MCD is the most common presentation in children.

Reactive lesions secondary to Crohn’s disease and ulcerative colitis include aphthous stomatitis, pyoderma gangrenosum, erethyma nodosum, erythema multiforme, finger clubbing, palmar erythema, rosacea-like eruption, pyoderma faciale, cutaneous vasculitis, epidermolysis bullosa acquisita, Sweet’s syndrome, secondary amyloidosis, vitiligo, and palmoplantar pustulosis.

A wide range of infectious, neoplastic, and inflammatory dermatoses can affect the anogenital region, making a correct diagnosis and management difficult. Differential diagnoses including sexually transmitted disease, neoplasia, drug reactions, and inflammatory dermatoses should be considered. The clinical differential diagnosis in our case should include infections such as syphilis, lymphogranuloma venereum, granuloma inguinale, mycobacterial infections, actinomycosis, deep fungal infections, schistosomiasis, and cellulitis. Other inflammatory dermatoses that causes ulceration and infiltration such as cutaneous sarcoidosis, Behget’s syndrome, chronic lymphoedema resulting from obstruction, hidradenitis suppurativa, foreign body reactions, and factitial injection of foreign substances should also be considered. Among the necessary investigations are skin biopsy with special stains (eg PASD and AFB), polarising microscopy of tissues, tissue cultures, chest radiograph, and a tuberculin skin test.

Although most cutaneous Crohn’s disease lesions can be cured eventually, they tend to become chronic. The most effective treatment for cutaneous Crohn’s disease is oral metronidazole. Other treatments include topical and intralesional corticosteroids, systemic steroids, sulphasalazine, cytotoxic agents such as azathioprine or 6-mercaptopurine, and surgery. Repeated curettage of ulcers with concomitant oral zinc sulphate administration has produced good results in some patients. Surgical removal of the diseased bowel does not necessarily improve cutaneous Crohn’s disease.

Conclusions

Metastatic Crohn’s disease exhibits polymorphic clinical features that resemble many other dermatoses. Any unusual cutaneous lesions in patients with Crohn’s disease should be biopsied. It is essential to exclude common sexually transmitted infections such as genital warts and secondary syphilis in the genital form of MCD. The dermatologists and physicians should be aware of such a condition as it may precede gastro-intestinal involvement. To the best of our knowledge, this is the first reported case of MCD in Chinese children in the English medical literature.

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References