LEOPARD Syndrome Associated with Steatocystoma Multiplex and Hyperelastic Skin

Report of a Japanese Case

Sir,

The LEOPARD syndrome, also known as multiple lentigines syndrome, is characterized by multiple lentigines which are associated with a wide range of developmental defects (1–3). It is autosomal dominantly inherited with high penetrance and variable expressivity. The acronym LEOPARD stands for lentigines, ECG abnormalities (conduction defects), ocular hypertelorism, pulmonary stenosis, abnormalities of the genitalia, retardation of growth, and deafness (1). Voron et al. (2) proposed specific criteria for diagnosis, emphasizing several other cutaneous abnormalities including café au lait spots and dermatoglyphic abnormalities.

We present here a Japanese patient with the LEOPARD syndrome who showed unique combinations of several other rare cutaneous changes, so far unreported, such as steatocystoma multiplex and hyperelastic skin.

A 27-year-old man, who had had generalized pigmented macules from birth, was referred to our clinic. The pigmented macules had increased in number in his childhood. He had also noticed several small skin-colored nodules on his anterior chest 10 years earlier. Physical examination revealed that most of the macules were flat, but some of them showed a slight elevation. The lesions, which were 2 to 3 mm in size and brown to brown-black in color, were concentrated mainly on his face, neck, and chest but were widely scattered almost all over the body, including the axilla and genitalia. Visible mucosal membranes, however, were spared. In addition to such pigmented macules, 2 to 3 mm sized, skin-colored papules were distributed on the anterior chest (Fig. 1). Other findings included ocular hypertelorism, mature cataract and exotropia on his left eye, scoliosis, hypermobile joint, hyperelastic skin, fusion of C2–C3 vertebrae, left complete double pelvis and ureter, and right partial sensorineural deafness. An electrocardiogram showed paroxysmal atrial contractions, left axis deviation, and incomplete right bundle branch block. No endocrinological abnormalities, including MSH and urinary 17-ketosteroids, were found. There was no history of similar conditions in his family.

Skin biopsy specimens obtained from a flat pigmented macule, a slightly elevated one, and a skin-colored nodule on his anterior chest showed histologic features compatible with lentigo simplex, intradermal type of melanocytic nevus, and steatocystoma multiplex, respectively.

Based on his review of 80 cases in the literature, Voron et al. (2) grouped the features noted in this syndrome into nine categories, i.e., lentigines, other cutaneous abnormalities, cardiac abnormalities, genitourinary abnormalities, aberrant endocrine findings, neurologic defects, cephalofacial dysmorphism, short stature, skeletal abnormalities, and family history consistent with an autosomal dominant mode of inheritance. Furthermore, they proposed the following minimum criteria for diagnosis: 1) if the patient has multiple lentigines, the features of at least two other above-mentioned categories must be present; 2) if lentigines are absent, a diagnosis may be made if more than three other categories are present, and a family history of the syndrome, as defined in (1). Our case definitely fulfilled the criteria for the LEOPARD syndrome by the demonstration of multiple lentigines and six other manifestations.

Among 80 cases, Voron et al. (2) noted that 22 had various cutaneous abnormalities. Most of them are pigmented disorders, but several other unrelated cutaneous abnormalities were

![Fig. 1. Skin-colored nodules intermingled with multiple lentigines on the anterior chest (arrowheads).](image-url)
Cyclosporin A in Metastatic Crohn’s Disease

Sir,

Skin lesions are frequently described in Crohn’s disease (CD), and their incidence ranges from 22 to 45% (1). Cutaneous manifestations of CD can precede or follow the diagnosis of the bowel disease and can sometimes appear at the same time as the gastrointestinal involvement. Among the cutaneous lesions described in the literature, some, such as perianal fissures and fistulas, vesicopustular eruptions, clubbing and cutaneous manifestations secondary to malabsorption, are related to the severity of the gastrointestinal disease. Others, including metastatic Crohn’s disease (MCD), do not seem to be related to the degree of intestinal inflammation (2). We report here a case of MCD of the vulva successfully treated with cyclosporin A (CyA).

CASE REPORT

A 20-year-old female patient was referred to our department on account of the presence of ulcerative vulvar lesions resistant to treatment. Previous treatment included both systemic and local antibiotics, topical corticosteroids, antiseptics and curettage of the lesions.

The history revealed the patient to have been suffering from CD since the age of 11. Recurrences of the disease had been treated with cycles of sulfasalazine, corticosteroids and metronidazole; and in 1989 a colectomy with ileostomy leaving a closed rectum was necessary. After the operation the patient developed a perianal dermatitis but her general condition was good until April 1993, when the first lesions appeared on the genitilia. At first the patient noted erythema and oedema of the labia majora and minora. In the following months the clinical picture progressively worsened and cutaneous abscesses appeared which then spontaneously turned into ulcers. There was no active inflammation of the rectum. The patient was sent to us by the surgeons who were planning to carry out a valvectomy. When the patient came under our observation she was not undergoing any therapy. The clinical examination revealed widespread erythema and oedema on the labia majora and minora, extending to the perineal and perianal areas, as well as numerous ulcerative lesions (Fig. 1). The patient complained of acute pain. The histologic examination confirmed the diagnosis of MCD, revealing the presence of mildly acanthotic epidermis with neutrophilic exocytosis prevalently on the uppermost layers and perivascular and interstitial inflammatory cell infiltrate consisting of lymphocytes, plasma cells, histiocytes, epithelioid cells and multinucleated giant cells. Stains for fungi, acid fast bacilli and spirochetes were negative.

In December 1993 we began treatment with CyA at the dosage of 4 mg/kg/day after first checking for the absence of clinical, laboratory or anamnestic contraindications. This dosage was maintained for a month, after which the vulvar ulcers appeared to be considerably improved. The dosage was then reduced by 1 mg/kg/day each month for 2 months until the complete resolution of clinical manifestations. A further month of therapy at the dosage of 2 mg/kg/day maintained the clinical remission. CyA treatment was stopped in April 1994 and the patient was still free of relapses in October 1994.

DISCUSSION

MCD refers to cutaneous or mucous granulomatous lesions separated from the affected gut by normal intact mucosal or skin (3). It is a rare inflammatory condition presenting different