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 constrictions, 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 all 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 pigmentary disorders, but several other unrelated cutaneous abnormalities were

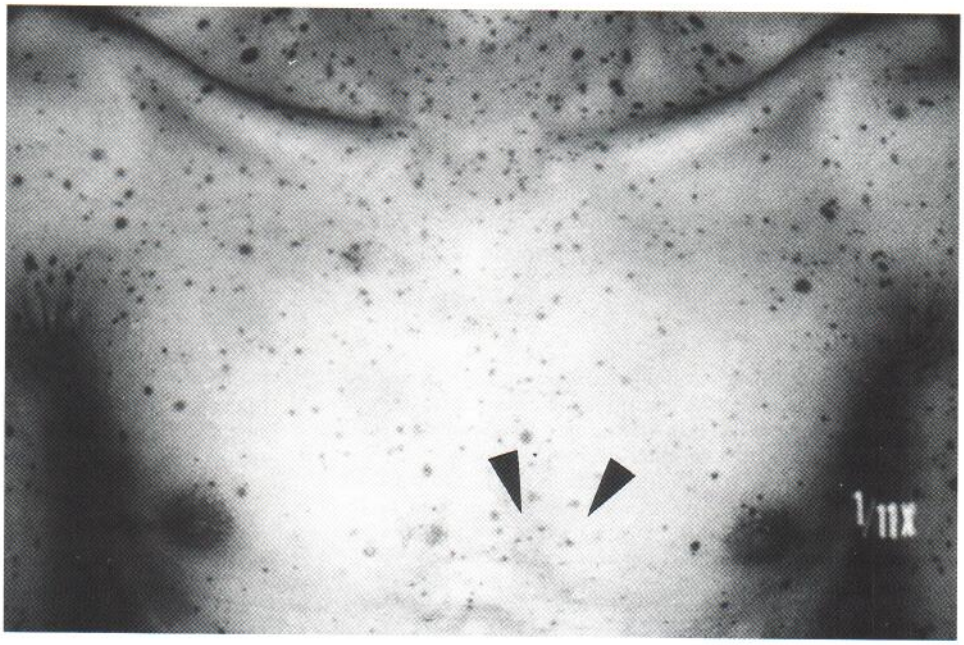

Fig. 1. Skin-colored nodules intermingled with multiple lentigines on the anterior chest (*arrowheads*).

also included. One of the characteristic features in our case was a hyperelastic skin change. Hyperelasticity of the skin has been reported in 4 Japanese cases including our case (4), in contrast to only one case noted in Voron's report. Thus, this skin change seems to be a rather characteristic feature for Japanese cases of the LEOPARD syndrome. Moreover, such a finding seems to be consistent with the hypothesis that the basic genetic defect in this syndrome is of neuroectodermal origin, with secondary pleotropic changes in the tissues derived from the mesoderm (5). Further ultrastructural and biochemical studies of the skin are required to exclude a possible relation with Ehlers-Danlos syndrome.

Melanocytic nevus, noted in our case, was not specifically described in the review, but from our finding in the present patient some of the pigmented macules seem to be composed of them rather than lentigo simplex.

Interestingly, we also found the coexistence of steatocystoma multiplex in our patient. Steatocystoma multiplex is a rather uncommon nevoid malformation of the sebaceous follicles (6), which is inherited as an autosomal dominant trait in many cases. Cyst formation, which usually begins in early adult life or in adolescence, is thought to be under the influence of androgenic hormones (6), like sebaceous glands. To our knowledge, there has been no other case report of the LEOPARD syndrome complicated by steatocystoma multiplex. However, since the lesions in our patient consisted of tiny skin-colored papules on the chest, they might be overlooked at a cursory inspection.

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