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Short report

Polyvalvular heart disease with joint hypermobility, characteristic facies, and particular skin abnormalities: New cases of "polyvalvular heart disease syndrome" or new association?

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ABSTRACT

Polyvalvular heart disease has been reported in a handful of "private" syndromes that have been recently suggested to represent a single dominantly inherited condition, the polyvalvular heart disease syndrome.

We report five cases in two unrelated families (one sporadic case in the first family and three siblings and their father in the second family) with the same association of polyvalvular heart disease, distinctive facial appearance, and, except the father in family 2, major joint hypermobility. Interestingly, in three of our patients (2 siblings and the sporadic case), electron microscopy revealed characteristic ultrastructural skin abnormalities with abnormal amorphous or microfibrillar deposits under the capillary basal membrane in the papillary dermis, suggestive of a connective tissue disorder, but different from Marfan syndrome or Ehlers-Danlos syndrome. Moreover, in family 2, three others sibs died in early infancy of their heart defect.

Our two families and the other published cases might illustrate intrafamilial and interfamilial variability within a single condition. However, our two families disclose major joint hypermobility, normal stature, and ultrastructural skin abnormalities that were not described in the previous reports. These discrepancies let us to consider them as affected by a distinct disorder of the connective tissue.

1. Introduction

Valvular heart disease has been reported in several syndromes. Pulmonary valve stenosis in Noonan syndrome and supravalvular aortic stenosis in Williams-Beuren syndrome are associated with recognizable dysmorphic patterns [1]. Mitral valve prolapse (MVP) can be inherited as an isolated abnormality or as part of a syndrome affecting connective tissues, such as Marfan syndrome [14] or Ehlers-Danlos syndrome (EDS) [4]. Polyvalvular heart disease has been reported in a handful of "private" syndromes [5,7,9,18] that have been recently suggested to represent a single dominantly inherited condition, the polyvalvular heart disease syndrome [7].

We report here five cases in two unrelated families (one sporadic case in the first family and three siblings and their father in the second family) with the same association of polyvalvular heart disease, distinctive facial appearance, major joint hypermobility, and specific ultrastructural skin abnormalities on electron microscopy.

2. Materials and methods

2.1. Patients

Two unrelated families were investigated.

The index case of family 1 (S1), a 4-year-old girl, was the single child of healthy non-consanguineous parents of French origin (Fig. 1).

The parents of family 2 were from Romania and apparently unrelated. They had had three daughters (all affected, with one

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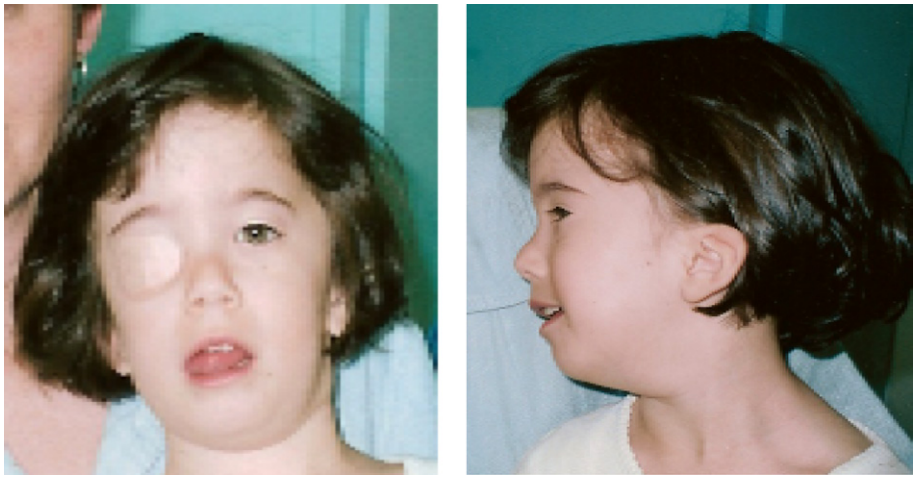

Fig. 1. Facial appearance of sporadic case S1; note the dolichocephaly, the broad forehead with frontal hair upsweep, the ptosis, the long philtrum with thin vermillion of the upper lip, and the micrognathia.

death) and four sons (three affected, with two deaths). The family pedigree of family members is shown in Fig. 2a.

Patient S1 and three children of family 2 (two girls 10 and 12 years old, and one 7-year-old boy (II-2, II-3, and II-5 respectively)) were referred to the Pediatric Endocrinology and Genetic Unit of the University Hospital of Toulouse to evaluate dysmorphic features and major joint hypermobility. Father of family 2 had a mild phenotype and was added to the patients' description. In family 2, three other sibs died in early infancy of their heart defect but, as they were not evaluated in our hospital, further data were not available.

Informed consents were obtained from the patients and parents. Clinical evaluation, radiological investigation (skeletal survey,

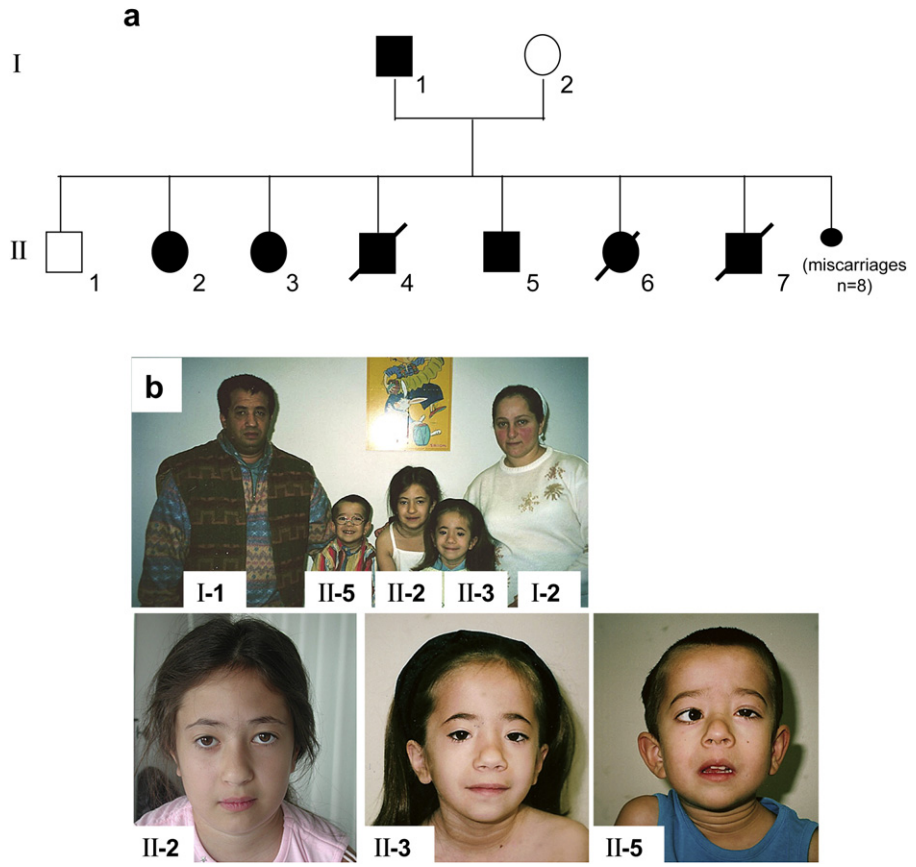

Fig. 2. a) Family pedigree and cardiac malformations: I-1 moderate aortic regurgitation, II-2 and II-3 mitral valve prolapse with moderate mitral regurgitation and moderate aortic regurgitation, II-4 atrial and ventricular septal defects and pulmonary stenosis, II-5 moderate mitral regurgitation without mitral valve prolapse, II-6 atrial septal defect, II-7 ventricular septal defect and pulmonary stenosis. Affected patients are represented in black. b) Facial appearance of family members I-1, I-2, II-2, II-3 and II-5. Note for patients I-1, II-2, II-3, and II-5 the mild facial asymmetry, the short palpebral fissures, the ptosis, the blunted nose, the thin vermillion of the upper lip, and the low-set ears.