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A Case of Cutis Laxa with Normal Parents but Affected Sibling

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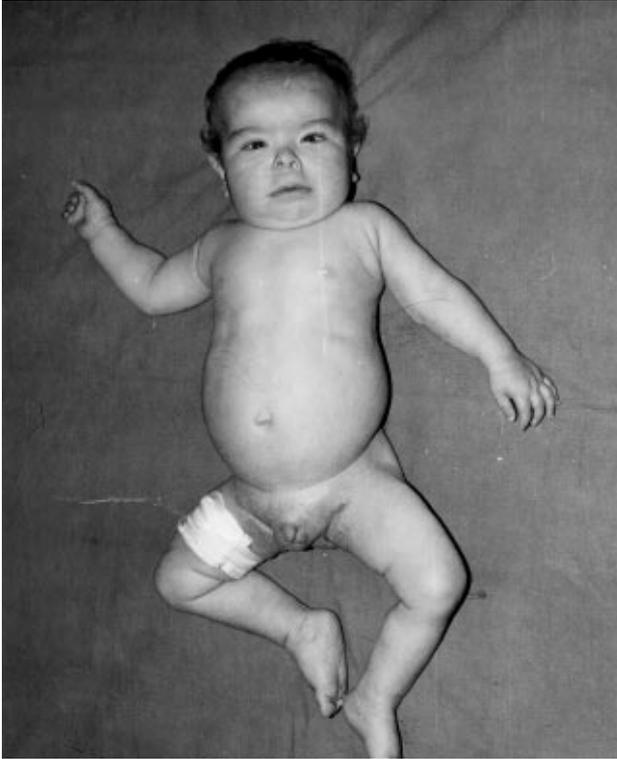


Figure 1. General appearance of the patient with umbilical hernia.

Congenital cutis laxa is a deforming disease that affects the skin as well as the gastrointestinal and cardiopulmonary systems. Autosomal recessive, dominant, and X-linked forms have been described (1). Patients with severe cutis laxa have characteristic facial features including a aged appearance with sagging jowls, a hooked nose with everted nostrils, a short columella, a

long upper lip, and everted lower eye lids. The skin is also lax elsewhere in the body and may resemble an ill-fitting suit. Hyperelasticity and hypermobility of the joints are not present as they are in the Ehlers-Danlos syndrome (2).

The dominant form is generally benign. In infancy, it may be associated with intrauterine growth retardation, ligamentous laxity, and delayed closure of fontanelles. Pulmonary emphysema and mild cardiovascular manifestations may also occur. In contrast, the more common recessive form has severe complications, such as multiple hernias, rectal prolapse, diaphragmatic atony, diverticula of the gastrointestinal and genitourinary tracts, cor pulmonale, emphysema, pneumothoraces, peripheral pulmonary artery stenosis, and aortic dilatation (2).

A one year old male patient was hospitalized for fever, cough, and noisy breathing. He had frequent respiratory infections since 3 months of age. He was the first child of first degree cousins. He had two sisters one of whom had a similar problem. There was no history of cutis laxa in the previous generations. Unfortunately, cutis laxa was diagnosed elsewhere in his older sister and she was not available for examination.

On physical examination, he had coarse rales bilaterally. He had a loose skin, and inguinal, and umbilical hernia (Figure 1 and 2). The echocardiography showed mild pulmonary stenosis. There were no gastrointestinal diverticula on the contrast radiographs.

The pathogenesis of cutis laxa is not well known. Abnormalities that have been described include excessive destruction of elastin, decreased elastase inhibitor levels,



Figure 2. Facial fetures of the patient demonstrating aged appearance, everted nostrils, long upper lip, and lax skin.

and decreased elastin messenger RNA levels in fibroblasts. Our patient had a relatively benign course and none of the internal complications could be demonstrated. Therefore, he seemed to have the dominant form of the disease. The fact that the parents were not affected could be explained by the occurrence of autosomal dominant diseases such as

achondroplasia as a result of spontaneous mutation in the offspring of healthy parents. However, germline mosaicism may offer a better explanation for two siblings with the same dominant disease and healthy parents. This mechanism involves a somatic mutation that has occurred in a germline cell or precursor of the parent that persists in all the clonal descendants of that cell and eventually reaches a proportion of the gametes (3). Alternatively, the lack of cutis laxa phenotype in the parents could be due to variable penetrance and/or expressivity of the defective gene.

If it were due to a new mutation, the recurrence risk in a subsequent child would be equivalent to the population risk which is negligible. However, the possibility of a new mutation was unlikely because of two affected siblings. If it were due to germline mosaicism, the recurrence risk would be low, but not negligible, estimated at 1 to 7 percent range. Although variable penetrance/expressivity was unlikely because of lack of disease in the previous generations, this possibility could not be totally excluded. This would impose the greatest risk with 50 percent chance of transmitting the gene but unpredictable expressivity. Therefore, the parents were

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