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is in agreement with the consensus sequence for N-linked glycosylation Asn-Xaa-Thr/Ser.

Several lines of evidence indicate that this extra N-glycosylation site, created by the mutation, is utilized. A population of profibrillin-1 molecules migrating more slowly on SDS-PAGE than the control’s sample was observed in the patient’s sample. Immunohistochemical and ultrastructural analyses revealed that the microfibril formation was severely affected in the patient’s fibroblast culture. In the presence of tunicamycin, an inhibitor of N-glycosylation, the patient’s cell culture was capable of producing a better-organized microfibril network. The creation of a neonatal cDNA construct consisting of exons 24–37 of the FBN1 gene was also proven to be a powerful tool in the analyses of the consequences of this mutation. The polypeptide translated from the minigene construct carrying the analogous II048T mutation migrated more slowly on SDS-PAGE than the corresponding wild type polypeptide. Treatment with either tunicamycin, endoglycosidase H or N-glycosidase F abolished the migration difference indicating that the difference was originally related to the over-N-glycosylation of the mutant polypeptide.

We conclude that excessive N-glycosylation due to a newly formed N-glycosylation site represents an interesting novel pathogenic mechanism for Marfan syndrome and should stimulate further studies.

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hernia in the right thorax. She had the typical marfanoid habitus; mitral valve insufficiency (MI); mitral- and tricuspid valve prolapse and aortic diameter > P95.

Bilateral blepharophimosis of the eyelids was an unusual finding. After lateral canthotomy normal eyes were seen. The hernia was operated on. At the age of two months a second admission was necessary because of severe dyspnea, possibly due to severe MI. However, no signs of pulmonary hypertension at chest catheeterization, no high pCO2 level and no pulmonary engorgement on X-ray were found. On echo/Doppler cardiology a large left atrium with severe MI was seen. Afterload reduction did not change the clinical condition and at last mitral valve replacement by a St. Jude prosthesis was performed. At the time of surgery diffuse pulmonary emphysema was noted. A short period after surgery the patient’s condition improved, but after a respiratory syncytiatal viral infection she died at the age of four months. Post mortem investigations confirmed severe heart disease and pulmonary emphysema.

Conclusions: be aware of fatal pulmonary emphysema in the neonatal Marfan syndrome.

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MICROFIBRILLAR PROTEINS: THE LONG AND THE SHORT OF IT

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Microfibrils having a diameter of 10–12 nm are widely distributed in many tissues of the body, often but not always in association with elastin. Characterization of the microfibrils remains incomplete, but recent findings have suggested that the proteins composing the microfibrils can be grouped into two classes: (1) large ones > 150 kDa and (2) small ones < 50 kDa. The large class contains two closely related gene families, the fibrillins (FBNs) and latent TGF-β-binding proteins (LTBPs), which share structural domains, including epidermal growth factor and 8-cysteine motifs. Presently, two distinct FBNs and three LTBPs are known. Phylogenetic analysis suggests that these two gene families have evolved from a common ancestor gene. The small class of proteins is more heterogeneous and as a group they have been designated microfibril-associated proteins (MFAPs). Sequence analysis has not revealed any homology among them. MFAP1 is a 439 amino acid, highly acidic protein whose human gene is located near the FBN1 locus, 15q15-q21. MFAP2, previously designated MAGP, is a 183 amino acid protein with a wide tissue distribution, whose human gene locus is 1p36.1-p35. MFAP3 is a 362 amino acid protein whose human gene is near the FBN2 locus, 5q21-q31. It is not known whether the linkage of these two MFAPs near FBN loci has any functional significance or is merely coincidental. Several other glycoproteins including emilin and a 36 kDa protein have been localized to the microfibrils. While it is likely that the FBNs provide the basic scaffolding of the microfibrils, the function of the other proteins is unclear. They may stabilize the microfibril structure, interact with other matrix components as has been demonstrated for MFAP2 and elastin and thereby act as nucleation sites in fiber formation, or serve as cytokine storage depots as has been suggested for the LTBPs.

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