similar clinical features, but type 2 can be associated with mild intellectual disability. Type 3 (CAV1 mutation) is very rare, type 4 is the muscular type with pyloric stenosis, flat and striated muscle involvement, and serious arrhythmia. The index case has been followed until the age of 5.5 years, he had a pyloric stenosis operation and elevated CK as different from our three BSCL type 1 patients (5.5, 7.5, and 12-year-old). Interestingly, a Turkish child with BSCL and achalasia was reported with the same PTRF mutation. All of our patients had hypertriglyceridemia, hepatomegaly, and normal neuromotor development. Acanthosis nigricans, HCMP, enlarged hands and feet, and insulin resistance were present in 2 patients with AGPAT2 mutation.

A male infant, who had pyloric stenosis operation, was referred to our department because of developmental hip dysplasia, HCMP, and hepatomegaly. He had reduced adipose tissue, muscular hypertrophy, elevated CK values (1000 IU/L) and normal EMG results. The diagnosis was BSCL.

The identification of homozygous PTRF mutation verified the diagnosis of BSCL type 4.

Because insulin resistance has been described even in the infantile period, BSCL must come to mind in cases with pyloric stenosis and high CK values.

(FC-13)

Progeroid Syndrome Patients with ZMPSTE24 Deficiency Could Benefit When Treated with Rapamycin and Dimethylsulfoxide

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Patients with progeroid syndromes such as mandibuloacral dysplasia, type B (MADB) and restrictive dermopathy (RD) harbor mutations in zinc metalloproteinase (ZMPSTE24), an enzyme essential for posttranslational proteolysis of prelamin A to form mature lamin A. Dermal fibroblasts from these patients show increased nuclear dysmorphology and reduced proliferation; however, the efficacy of various pharmacological agents in reversing these cellular phenotypes remains unknown.

In this study, fibroblasts from MADB patients exhibited marked nuclear abnormalities and reduced proliferation that improved upon treatment with rapamycin and dimethylsulfoxide but not with other agents, including farnesyl transferase inhibitors.

Surprisingly, fibroblasts from an RD patient with a homozygous null mutation in ZMPSTE24, resulting in exclusive accumulation of prelamin A with no lamin A on immunoblotting of cellular lysate, exhibited few nuclear abnormalities and near-normal cellular proliferation. An unbiased proteomic analysis of the cellular lysate from RD fibroblasts revealed a lack of processing of vimentin, a cytoskeletal protein. Interestingly, the assembly of vimentin microfibrils in MADB fibroblasts improved with rapamycin and dimethylsulfoxide.

We conclude that rapamycin and dimethylsulfoxide are beneficial for improving nuclear morphology and cell proliferation of MADB fibroblasts. Data from RD fibroblasts also suggest that prelamin A accumulation by itself might not be detrimental and requires additional alterations at the cellular level to manifest the phenotype.