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A new genetic syndrome among the Old Order Amish of Smicksburg Pennsylvania. G.L. Matika[1], M.A. Del Vecchio[1] and C.A. Bay[1,2]. [1]Children's Hospital of Pittsburgh, Pittsburgh, PA, and [2]University of Pittsburgh, School of Medicine, Pittsburgh, PA.

The Old Order Amish are a religious sect well known for their simple way of life and are of interest to geneticists due to the unique opportunity they provide for the study of genetic diseases. The Old Order Amish have a high rate of consanguinity and therefore have a higher proportion of recessive genetic conditions than non-Amish populations. We have evaluated individuals described as having developmental delays from an Old Order Amish community located in Smicksburg, PA. Approximately 22% of couples in this community are known to be consanguineous. We evaluated one family in which four of the fourteen siblings (two males and two females) had what appeared to be a syndrome previously undescribed among Amish or non-Amish populations. Features seen in all of the siblings included moderate to severe mental retardation, hypotonia, microcephaly, a short philtrum, hypoplastic alae nasi, and a long columella. Three of the siblings had short stature, deep set eyes, prominent lips, pectus excavatum, and hyperextensible joints. Two of the siblings had prominent eyebrows, knee contractures, atrophy of the interossei muscles, disconjugate gaze and hyperreflexia. Other less common findings included delayed sexual maturation, subluxable patellae and cataracts. The individual with cataracts had an ulcerative ocular illness at age 13 years with subsequent cataract formation. Chromosome analysis, and metabolic testing including urine organic and amino acids were completed and were normal. The parents denied consanguinity. Two maternal aunts and an uncle are said to be similarly affected, however they have not consented to an evaluation. Two maternal cousins, brothers to each other and both evaluated by us, also have some overlapping but nonspecific features. The family would not permit photographs at the time of the evaluation.

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Unique skeletal dysplasia with cataracts, ataxia, learning disability and mild facial dysmorphism. D.R. McLeod[1], G. Boag[1], R. Trussell[1], C. Skov[1], C. Adams[1]. [1]Alberta Children's Hospital, Calgary, Alberta Canada.

We present two sisters from a non-consanguineous family with a unique constellation of features. The first child was born after an uncomplicated pregnancy with bilateral cataracts detected in the neonatal period. A metabolic work-up was negative and physical exam was normal. Review at age 3 years showed proportionate short stature, delay in gross motor milestones and minor dysmorphic features. Her karyotype was 46,XX and growth hormone stimulation testing was normal. A skeletal survey at age 9 years showed delayed bone age, unusual calcification within the disc spaces, flattened vertebrae with an ovoid shape, abnormally shaped epiphyses of the hands and feet, and a few wormian bones. When seen at age 10 years, she had significant learning problems and the added feature of ataxia.

Her younger sister presented in the neonatal period with bilateral congenital cataracts and at review at age 8 years had proportionate short stature, ataxia, learning disability and similar mild dysmorphic features and skeletal findings to her sister. A cranial CT scan was normal except for small optic nerves.

Literature and syndrome database review did not provide a diagnosis and their features appear to represent a new autosomal recessive condition.

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AREDYLD syndrome with focal segmental glomerulosclerosis. E McPherson. Magee-Womens Hosp. and Univ. of Pittsburgh, PA.

The syndrome of AcroRenal-Ectodermal Dysplasia-Lipoatrophic Diabetes (AREDYLD) appears to be extremely rare with only 2 cases reported. A third patient, described here, presented in her early 30's with infertility, lipoatrophy of the face, diabetes, hypercholesterolemia, and nephrotic syndrome. Renal biopsy showed focal segmental glomerulosclerosis. She has normal areolae, but no breast tissue. Other ectodermal features are milder than in previous patients (slow-growing hair, but no significant anomalies of the teeth or nails). Despite normal menses and structurally normal internal genitalia, she has been unable to conceive. She has short stature, small acrogeric hands and feet and microcephaly, but her intelligence is above average. She is an only child with no affected relatives. Her karyotype is normal, 46XX.

This patient has symptomatic progressive glomerular disease of adult onset whereas the previous patients had minor structural anomalies of the renal calyces. Although her renal disease is more severe, she is not more seriously affected otherwise since her ectodermal involvement is mild and her diabetes is of later onset.

The phenotype of AREDYLD now appears to include: a variety of renal anomalies ranging from minor malformations to glomerular disease; minor anomalies of the hands and feet; amastia or breast hypoplasia with or without other ectodermal anomalies (such as sparse hair, hypodontia, hypohidrosis or nail dysplasia); lipoatrophy, primarily involving the face and hands; diabetes; and hypercholesterolemia. Three cases have been reported, all in females. Autosomal recessive inheritance has been postulated because the first reported patient was born to consanguineous parents and had a possibly affected deceased sister, but autosomal or sex-linked dominant cannot be excluded.

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Anonychia and absence of distal phalanges in a patient with apparently balanced t(17;21)(q24.2;q11.2). E McPherson, T Prosen, and U Surti. Magee-Womens Hospital and University of Pittsburgh, PA.

Anonychia involving all 20 digits is a rare malformation which can occur alone or as part of several syndromes (Type B brachydactyly, Laband syndrome, deafness-onchodystrophy, facio-audio-synphalangism, anonychia-ectrodactyly, etc.). The distal phalanges are often absent or hypoplastic. Both autosomal dominant and autosomal recessive anonychia/onchodystrophy have been reported. None of the genes for syndromic or non-syndromic anonychia have been mapped.

We report an infant with 20 digit anonychia, absence of terminal phalanges, and minor facial anomalies (mild micrognathia, small mouth, slightly beaked nose with broad nasal bridge). She was the product of a pregnancy complicated only by advanced maternal age and elevated maternal serum HCG. Amniocentesis showed her karyotype to be 46XX t(17;21)(q24.2;q11.2). This was an apparently balanced de novo translocation. Parental chromosomes were normal. Prenatal ultrasound and fetal echocardiography were interpreted as normal and the patient was born at term with a weight of 3496g, length of 47cm and OFC 35.5 cm. Examination in the newborn period showed absence of all nails and distal phalanges (confirmed on X-ray) with the above-mentioned minor facial anomalies. There were no features to suggest any of the known anonychia syndromes. Repeat karyotype confirmed the apparently balanced translocation. On follow-up at 3 months of age, her general health, growth and psychomotor development were normal.

The occurrence of anonychia in a patient with an apparently balanced translocation could be due to a subtle microdeletion or duplication, altered function of a gene or genes near the breakpoints, or could be coincidental. The normal growth and development of the patient as well as the absence of previous reports of anonychia in patients with duplications or deletions involving 17q or 21q make subtle chromosomal imbalance less likely. Disruption of a gene near the breakpoint could have a dominant effect or perhaps unmask a recessive gene on the other allele. Chromosome studies in other patients with anonychia could lead to mapping of a gene for nail development.