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Say-Meyer syndrome: A new case with magnetic resonance imaging of the brain, cardiac abnormality and X-linked dominant inheritance pattern. G.S. Gottesman[1], J.A. Silhavy[1], G.K. Singh[1] and D.S. Martin[2]. Departments of [1]Pediatrics and [2]Radiology, Saint Louis University School of Medicine and Cardinal Glennon Children's Hospital, St. Louis, Missouri.

We report a new case of Say-Meyer syndrome, a rare X-linked disorder characterized by metopic suture synostosis, a high-arched palate, short stature and delayed development. Proband was a nine-month-old boy admitted to our hospital for evaluation of failure to thrive and global developmental delay. Genetics evaluation revealed: marked growth failure; microcephaly; a closed anterior fontanelle; hypotelorism; esotropia; long eyelashes; a high, narrow palate; distal hypospadias. Neurologic examination demonstrated diffuse hypotonia, diminished deep tendon reflexes, and excessive head lag. A search of the London Dysmorphology and POSSUM databases suggested Say-Meyer syndrome as the unifying diagnosis.

This infant's medical history was complicated by prematurity at 32 weeks gestation, postnatal supplemental oxygen requirement and abnormal heart sounds. Cardiac evaluation identified Ebstein anomaly of the tricuspid valve as the etiology of his cardiac problems requiring ongoing medical surveillance.

Magnetic resonance imaging (MRI) of the brain revealed a decreased volume of white matter with associated atrophy. The brain stem was small. The corpus callosum was thin and the genu and rostrum were not visualized. Increased signal intensity in the periventricular regions suggested periventricular leukomalacia. The ventricles were enlarged. Skull radiographs showed a decreased interorbital distance and a sclerotic metopic suture.

X-linked recessive inheritance has been described. The infant's mother attended special education classes. She had marked hypotelorism, a long face, a high-arched palate, and a thin body habitus.

This case of Say-Meyer syndrome includes the first report of brain MRI findings and a previously unreported cardiac defect. Clinical features noted in the mother of this infant that suggest that Say-Meyer syndrome may be an X-linked dominant disorder with variable penetrance rather than an X-linked recessive disorder.

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Minimal Phenotypic Findings of Down Syndrome in a Patient with True Trisomy 21. M. J. Hajianpour[1], A. K. Hajianpour[2], H. Sayar[3], F. Manoochehri[3], C. Mackie Ogilvie[4]. [1]Gene Trek, South Gate, CA, [2]Alfigen-The Genetics Institute, Pasadena, CA, [3]Iranian Blood Transfusion Service, Tehran, Iran, [4]Guy's Hospital, London, UK.

We present a 23-year-old Iranian male, who was born full-term by normal vaginal delivery to a 27-year-old, G1, P0 mother. His birth weight was 2.5 kg. The birth height and head circumference are not available. The gestational and neonatal periods were uneventful. Developmental milestones were delayed. He could sit without support at age two years, walked at age 4 years, and talked in sentences at age 7 years. Despite apparent developmental delay, no diagnostic work-ups were performed. Reportedly, he attended regular school up to the 7th grade. He has not been able to hold a job steadily. He came to our attention while a pedigree was prepared for his sister who came to our clinic for a routine pre-marital genetic counseling, and he was then evaluated due to his history of "learning disability."

On physical examination, his weight was 58 kg, his height was 150 cm, and his head circumference was 54.5 cm. He is communicative. He can read and write well. His IQ is 65-70. He has a stooped posture, and minor dysmorphic features, such as mild epicanthic folds, slightly downslanting palpebral fissures (not upslanting), prominent nose with slightly elongated nasal septum, narrow palate, and fine motor incoordination. The rest of the physical examination including the heart auscultation and dermatoglyphics were normal. No dysmorphic genetic syndrome was suspected. A chromosome analysis was performed because of the history of developmental delay, which revealed 47,XY,+21. Repeat chromosome analysis and FISH using the whole chromosome 21 paint and distal Q21 probe showed straightforward trisomy 21, i.e., all three chromosomes 21 painted over entire length, and no regions of chromosomes 21 were translocated elsewhere in the genome. Patients with the features of Down syndrome and relatively good performance are likely to have mosaicism, which is not always easy to demonstrate. Therefore, the possibility of mosaicism in this patient exist. An attempt for fibroblasts culture from a skin biopsy sample was unsuccessful. He has recently married. Reportedly, he has difficulties in his sexual performance.

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Retinitis pigmentosa, growth hormone deficiency and acromelic skeletal dysplasia in two male siblings: possible familial RHYNS syndrome. P. Hedera, J.L.Gorski, University of Michigan, Ann Arbor, MI.

The combination of retinitis pigmentosa (RP), hypopituitarism, and acromelic skeletal dysplasia has been rarely observed. Here we report two brothers with RP, growth hormone deficiency and skeletal dysplasia. The proband was diagnosed with RP at age 9 years after short history of blurred vision; his electroretinogram (ERG) was markedly abnormal. Endocrinologic evaluation because of short stature 5 years later was consistent with growth hormone deficiency; gonadotropin deficiency was also confirmed. At 14 years his examination showed the height below the 5th percentile, mild facial asymmetry without ptosis, and acromelic shortening of distal extremities. The proband's brother was diagnosed with growth hormone deficiency at age 3 years and retinitis pigmentosa at 7 years; ERG was abnormal. He had a history of severe ptosis and mild hearing loss. Examination at age 10 years showed bilateral ptosis, facial asymmetry with right sided maxillary hypoplasia, prognathia and acromelic shortening. Both brothers had normal renal ultrasound. A routine chromosomal analysis was normal. The family history was non-contributory without known consanguinity; both parents were reportedly normal.

The concurrence of RP, hypopituitarism and skeletal dysplasia is very rare. Two unrelated boys with similar features plus renal impairment were reported previously, and a potential syndrome RHYNS was suggested (Retinitis pigmentosa, Hypopituitarism, Nephronophtisis and Skeletal dysplasia). We propose that the clinical picture of these brothers is consistent with RHYNS and that they represent the first instance of a familial occurrence of this syndrome. RP, hypopituitarism and acromelic skeletal dysplasia are cardinal features of RHYNS syndrome and were present in all four reported cases. Nepronophtisis may be absent, at least at the beginning of the disease. The presence of RHYNS in two siblings supports an autosomal recessive mode of inheritance. However, since all 4 known cases are males, this condition may be inherited as an X-linked disorder. Even though we did not detect a microdeletion, this clinical variability may be due to contiguous genes syndrome.

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Testing for the Jewish BRCA founder mutations in archived tissue. Hixon HEC, Scheuner MT. Cedars-Sinai Medical Center, Los Angeles, CA

Testing archived tissue for specific BRCA mutations is feasible and thus can be used to attempt to clarify genetic susceptibility to breast and ovarian cancer. This report will review our experience with 3 Ashkenazi Jewish women at increased risk for breast and ovarian cancer based on family history, and whose affected relatives were deceased. Case #1: JB is a 65 year old woman whose daughter died of ovarian cancer at age 42. Case #2: GG is a 43 year old woman whose sister had bilateral breast cancer at age 41 and 46, and whose mother had ovarian cancer at age 50 and breast cancer at age 55. Case #3: DW is a 47 year old woman whose mother, maternal aunt and maternal grandmother each died of ovarian cancer. Each of our patients underwent genetic counseling followed by testing of the three Jewish BRCA founder mutations, and all had normal results. Given their results, they were counseled that the probability they had an inherited susceptibility to breast and ovarian cancer was decreased but could not be excluded. In order to clarify their genetic susceptibility, archived tumor tissue from deceased family members who had breast or ovarian cancer was obtained with consent of the next-of-kin. DNA was isolated from JB's daughter's 2 year old ovarian tumor, from GG's sister's 3 year old breast tumor and from DW's mother's 11 year old ovarian tumor. In each case, the BRCA1 185delAG mutation was identified, consistent with a germline mutation. Therefore, our patients were counseled that it was highly unlikely that they had inherited the cancer susceptibility in their families, which resulted in our recommendations that participation in enhanced preventive strategies, such as prophylactic surgery or chemoprevention, was no longer indicated and there was no contraindication to postmenopausal hormone replacement therapy. In addition, the test results greatly relieved our patients' anxiety for themselves and their offspring. In conclusion, these results demonstrate the value of testing for the Jewish BRCA founder mutations in archived tissue for the purpose of clarifying genetic susceptibility to breast and ovarian cancer in Ashkenazi Jewish individuals. Thus, this strategy should be considered in Ashkenazi Jewish families with breast and/or ovarian cancer when affected relatives are deceased.