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Fragile X mutation screening among unselected pregnant women seen for genetic counseling: Findings of a pilot study. B. Finucane[1], V. Speare[2], B. Allitto[3], J. Adelberg[4], S. Schmidt[5], E. Simon[1], and N. Blagowidow[2]. [1]Elwyn, Inc., Elwyn, PA, [2]Crozer-Chester Medical Center, Chester, PA, [3]Genzyme Genetics, Framingham, MA, [4]Howard University, Washington, D.C., and [5]Beaver College, Glenside, PA.

The number of couples at risk for having a child with fragile X syndrome is twice that of cystic fibrosis, based on a fragile X premutation carrier rate of 1 in 259 women. Its prevalence and the availability of highly accurate laboratory testing have raised the possibility of population screening for fragile X mutations. We offered fragile X carrier testing to over 300 pregnant women seen for prenatal genetic counseling, a majority of whom had been referred for advanced maternal age and abnormal triple screen results. Women were informed about the testing through an explanatory pamphlet and face-to-face discussion with a genetic counselor. Testing was offered free of charge except in cases where such testing would have been indicated based on a personal or family history of mental retardation, in which case insurance was billed. A majority of women agreed to testing. The prevalence of women with pre- and full mutations in our cohort was consistent with previous estimates, although a larger than anticipated number of women had results in the premutation "gray zone" between 40 and 50 CGG repeats. Acceptance rates were significantly lower among women referred for discussion of abnormal triple screen results. This subset of women was much less likely than the rest of the cohort to accept fragile X carrier testing, even when they opted for invasive prenatal diagnostic procedures for chromosome abnormalities.

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Hirschsprung's disease in a patient with translocation resulting in a partial trisomy of the long arm of chromosome 1. E.M. Garcia Soto[12], B.K. Goodman[12], G. Thomas[12], C. Theda[123]. [1]Kennedy Krieger Institute, [2]Johns Hopkins University School of Medicine, Baltimore, MD and [3]Frederick Memorial Hospital, Frederick, MD.

Review of the literature reveals a relatively well defined phenotype associated with partial trisomies of chromosome 1q. We report a patient with the karyotype 46,XX, der(14) t(1;14) (q32.1;q32.3) who shows several of the features previously described in patients with partial trisomy of the distal part of chromosome 1q: Growth retardation, dysmorphic features including a high forehead, small ears and eyes, large anterior fontanel, pronounced nasal bridge with long nose, triangular mouth, micro-retrognathia, overlapping of the 3rd and 4th toe, clinodactyly of the 5th finger, sacral dimple and hirsutism. An echocardiogram revealed anomalous return of the upper left pulmonary vein and a large secundum atrial septal defect. On head ultrasound a left choroid plexus cyst was noted.

In addition, the newborn manifested acute bowel obstruction on the third day of life due to Hirschsprung's disease (aganglionosis proven on biopsy). While other abnormalities of the gastrointestinal system such as pyloric stenosis and gallbladder abnormalities have been reported in partial trisomy 1q, to our knowledge, there are no previous reports of Hischsprung's disease in these patients.

Hirschsprung's disease is a polygenic disorder. Several loci on different chromosomes (such as chromosomes 5, 10, 20, and especially the endothelin-B receptor gene on chromosome 13q22) have been associated with the condition. No links to either the long arm of chromosome 1 nor chromosome 14q have been reported. While a causative relationship between the partial trisomy 1q and the presence of aganglionosis of the colon can not be established in our patient at this point, the definition of the exact break points, comparison with the clinical phenotypes of patients with slightly different breakpoints and patients with Hirschsprung's disease without chromosomal abnormalities, and review of the genes assigned to the distal parts of the long arms of chromosomes 1 and 14 seem of interest and may provide further understanding of the pathophysiology of this trisomy and the associated gastrointestinal malformation.

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Cerebrovascular accident leading to cortical blindness in a patient with bird-headed dwarfism. M. J. Hajianpour[1], A. Jamali[2], S. H. Sayar[3], A. Talebian[3], A. K. Hajianpour[3]. [1]Section of Med. Genetics, Tehran Univ. of Med. Sci., Tehran, Iran, [2]Private office, Abbas-abad Ave., Tehran, Iran, and [3]Med. Genetics Center, Iranian Blood Transfusion Service, Tehran, Iran.

We present a 12-year-old female with characteristic manifestations of bird-headed dwarfism (BHD). She was born full-term by normal vaginal delivery to a 33-year-old, G6, P5, SAB1 mother. Her parents are first cousins, and her two brothers and three sisters are healthy. Her birth weight, height and head circumference were 2120 gm, 45 cm and 32 cm, respectively. Metabolic and endocrine work-up were normal during infancy. Chromosome analysis was 46,XX. Bone marrow aspiration revealed hypercellularity. The present weight, height and head circumference are 7850 gm, 70 cm and 41.5 cm, respectively. She has a narrow face with beak-like protrusion of the nose, receding mandible, multiple small hyperpigmented skin lesions and scalp hair loss. She developed photophobia at age three years with a normal ophthalmologic examination. At age six years, she developed recurrent attacks of headache and nausea; the brain CT scan was normal. At age ten years, following unilateral paresis of the left leg, hematoma of the right occipital region was diagnosed, leading to infarction at both occipital lobes with cortical blindness and loss of speech several weeks later. Consequently, she was found to have hypertension, hypercholesterolemia, proteinuria, hypocalcemia, hyperphosphatemia and low parathormone levels. Due to critical condition of the patient, brain angiography was not feasible. The clinical manifestations in this patient expands the phenotypic spectrum of BHD.

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Immune deficiency (IgG2 deficiency), minimal centromeric association and facial dysmorphism. M. J. Hajianpour[1], H. Golkari[2], S. H. Sayar[3], A. Farhoodi[2], A. K. Hajianpour[3]. [1]Section of Med. Genetics, Tehran Univ. of Med. Sci., Tehran, Iran, [2]Children Med. Center, Tehran Univ. of Med. Sci., Tehran, Iran, and [3]Med. Genetics Center, Iranian Blood Transfusion Service, Tehran, Iran.

The patient is a 16-year-old male, with a history of recurrent respiratory infections and bronchiectasis requiring lobectomy at age 7 years. His parents are first cousins. He had a brother who died at age 8 years and reportedly had similar condition and diabetes insipidus. He has three healthy sisters. The patient has failure to thrive; his weight, height and head circumference are all below the 3rd percentile for age. He has a triangular facies with wide palpebral fissures, relative hypertelorism (OC 9.5, IC 3, IP 6, PF 3.2 cm), malar hypoplasia, prominent nasal bridge, relatively large nose, long philtrum, thin upper vermilion, prominent lower lip, retromicrognathia and hepatosplenomegaly. The immunologic work-up revealed IgG2 deficiency and defective cellular killing activity. The α_1 -antitrypsin level and sweat test were normal. Chromosome analysis revealed 46,XY karyotype, with 11 cells out of 51 showing centromeric association of two-to-three chromosomes, but not exclusively involving chromosomes 1, 9 and 16, reported in immunodeficiency-centromeric instability-facial anomalies (ICF) syndrome. The facial features in this patient are similar to those seen in ICF syndrome, except for the prominent nasal bridge and malar hypoplasia. The type of immune deficiency in this patient is also somewhat different from those reported in ICF. Therefore, our patient may represent a variant of ICF syndrome, or a separate entity.