42

Lethal Pallister-Killian syndrome and Fryns syndrome: diagnostic considerations. K.B. Clarkson, K. Coming, A. Toburen. Greenwood Genetic Center, Columbia Office, Columbia, S.C.

Clinical similarities between Pallister-Killian and Fryns syndrome have been previously noted. A newborn with diaphragmatic hernia, diffuse corneal opacities, dysmorphic facies, and hypoplastic nails was believed to have Fryns syndrome. Chromosome analysis of peripheral lymphocytes showed 46, XY in 20 cells counted (525 band level). Despite maximal support, the baby remained unresponsive to therapy. Given the poor prognosis, it was agreed that respiratory support be discontinued. Autopsy confirmed a large left diaphragmatic defect/pulmonary hypoplasia, bilateral ureteral dilation, and intraventricular hemorrhage. Mild shortening of the upper limbs and cleft of the soft palate were also noted. Testicular tissue chromosome analysis showed isochromosome 12p in all 20 cells examined. There appears to be a subset of patients with Pallister-Killian who present in utero or neonatally with lethal manifestations. The most common cause of death in these individuals has been a large diaphragmatic hernia with resultant pulmonary hypoplasia. Although reports vary, the frequency of diaphragmatic hernia in lethal Pallister-Killian syndrome may be as high as 50%. We suspect that Pallister-Killian, lethal type, is underdiagnosed. Most routine cultured lymphocyte chromosome analyses will not demonstrate isochromosome 12p, leaving Fryns syndrome as the most likely diagnosis. Our case further substantiates the need for solid tissue chromosome examination in individuals with diaphragmatic hernia and other congenital anomalies.

43

Rubinstein-Taybi syndrome with hepatoblastoma. J.A. Claus, M.S., B.G. Kousseff, M.D., J.R. Ranells, M.D.,and G.A. Jervis. University of South Florida Regional Genetics Program, Tampa, FL.

We report a two-year old male patient, with Rubinstein-Taybi syndrome, phenylketonuria and hepatoblastoma. The patient, GP, was the first child of a 35-year old gravida 2 para 0-0-1-0 mother. The mother has mitral valve prolapse and left conductive hearing loss secondary to abnormal ossicles. Prenatal triple marker screen indicated an increased risk for Down syndrome. Amniocentesis was declined. Fetal sonograms suspected a Dandy-Walker variant with no hydrocephalus and severe IUGR. Delivery was at thirty-two weeks gestation by emergency Cesarean section for pre-term labor and vaginal bleeding secondary to subchorionic hematoma. Apgar scores were 6/8; birth weight was 1282 g (75th centile; corrected for gestation), birth length was 38 cm (5th centile;), and OFC was 27 centimeters (5th centile; corrected). The umbilical cord had three vessels and was thick. A large PDA was diagnosed. He required a ventilator and phototherapy. EKG was abnormal with right axis deviation. Genetics consult revealed a prominent nose, pencil-like eyebrows, low-set ears, hypoplastic nipples, undescended testes, broad first digits and angulated thumbs. Hypotonia was noted. The impression was Rubinstein-Taybi syndrome. Indomethacin reduced the PDA. Newborn metabolic screening at 6 days of age showed a phenylalanine level of 8 mg/dl. Follow up level was 62.2 mg/dl at 15 days of age. He was diagnosed with classic PKU. Neopterin, biopterin and dihydropteridine reductase levels were normal. Karyotype was 46,XY. Ophthalmalogic evaluation was normal. Cranial sonograms showed no posterior fossa abnormality. MRI scan showed increased signal on the periventricular and subcortical white matter. The finding was considered nonspecific and possibly consistent with prematurity. Renal sonogram showed slightly small kidneys with mild left hydronephrosis. At two years of age GP presented with chronic constipation and feeding difficulties as well as low grade fevers and an enlarged liver. A surgical biopsy showed hepatoblastoma. Although a variety of rare tumors have been reported in individuals with Rubinstein-Taybi syndrome, this is the first report of hepatoblastoma in this condition.

44

The Scapuloiliac Dysostosis (Kosenow Syndrome) Spectrum –Two Additional Cases. Alison M. Elliott[1], David L. Rimoin[1], David R. Witt[2] and Ralph S. Lachman[1]. [1]Cedars-Sinai Medical Center, Los Angeles, CA, [2]Kaiser Permanente, San Jose, CA.

Scapuloiliac dysostosis (also known as Kosenow syndrome, Pelvis-Shoulder Dysplasia) (MIM 169550) is a rare skeletal dysplasia which usually demonstrates extreme hypoplasia of the scapulae and ilia. The clavicles are also often affected (hypoplastic or elongated). Other radiological findings which have been reported include: lordosis of the lumbosacral spine, rounded appearance of the vertebral bodies (in infancy), rib anomalies and overconstriction of the femora. Dysmorphic features can include eye and ear abnormalities. We present two unrelated patients with Scapuloiliac Dysostosis, each of whom has additional abnormalities not previously reported in the literature. Patient #1 was an adult female with primary amenhorrea, features of Turner syndrome and a normal female karyotype. She also had partial hearing loss and hydronephrosis. In addition to her hypoplastic scapulae and ilia, she had lumbar lordosis and severe spinal dysraphism in the (lower lumbar) sacral region. The femoral heads were small with severe coxa vara. Patient #2 was a stillborn male with multiple skeletal abnormalities and malformations. Clinically, he had microphthalmia, short palpebral fissures, ambiguous genitalia and clubbed feet. Chromosomes were normal male. Radiologically, apart from the hypoplastic scapulae and ilia, he had a bell-shaped chest with thin ribs. There were radial head dislocations of the elbows, bilaterally. The proximal femoral area did not articulate with any ossified structure and the fibulae were absent. Kosenow syndrome seems to represent a spectrum of disorders including patients with only pelvic involvement to patients with multiple malformations in addition to the hypoplastic scapulae and ilia. This entity appears to exhibit genetic heterogeneity, as both autosomal dominant and recessive inheritance have been suggested.

45

Withdrawn