44

Breast C.A.R.E. Breaks: An Innovative Cancer Genetics Education Model For Health Care Professionals

H. Hampel, P. Gregory and J. Graham. The Arthur G. James Cancer Hospital & Research Institute, Ohio State University, Columbus, OH.

We have developed a model educational program that provides health care professionals with a basic background in cancer genetics, a clear step-by-step approach to assessing a patient's genetic susceptibility to breast cancer and referral information. Breast C.A.R.E. (Cancer Assessment and Risk Evaluation) Breaks are innovative in-service workshops for nurses and primary care physicians provided within their work setting. These training courses include a convenient risk assessment pocket guide and a companion reference workbook. This CEU/CME course was piloted with oncology nurses at the James Cancer Hospital, currently 125 nurses have participated.

Health care professionals are taught how to elicit a cancer family history, recognize individuals with an increased breast cancer risk, evaluate the risk and refer the patient for genetic counseling, when appropriate. The Breast C.A.R.E. Pocket Guide is a user-friendly, compilation of risk algorithms in an easy-to-use flow chart format.

Pre- and post-course evaluations provide information about the impact this course has on clinical practice. Prior to the course, 40% of nurses assumed that hereditary breast cancer can only be maternally inherited; 77% overestimated the percentage of breast cancer that is hereditary; 36% were not comfortable providing patients with information about hereditary breast cancer while nearly 50% were comfortable referring the patient to a specialist. Before the course only 12% felt comfortable to assess patients' hereditary cancer risk; however, 43% were comfortable after their training. Interestingly, 65% noted that more of their patients are asking about hereditary cancers. These results underscore the importance of providing cancer genetics education to health care professionals.

This project was supported by a grant from the Columbus Affiliate of the Susan G. Komen Breast Cancer Foundation.

45

Oro-facio-digital syndrome or Joubert syndrome?

K. Haug[1], S. Khan[2], R. König. [1]Institute of Human Genetics and [2]Childrens Hospital, University of Frankfurt/Main, Germany.

We here present two sibs with overlapping features of oro-facio-digital syndromes (OFD) and Joubert syndrome. The index patient is the 4th child of healthy nonconsanguineous turkish parents. At birth the female patient showed large hydrocephalus, hypertelorism, deep-set eyes, nystagmus, broad mouth, thick oral frenulae, cleft palate, hamartomas of the tongue, postaxial polydactyly of the fingers, normal toes, hypotonia and severe retardation. Cranial MR revealed extreme dilatation of the ventricles and Dandy Walker malformation. The child had no psychomotor development, was unable to swallow and manifested severe seisures. The patient died at the age of 2 months from recurrent apnoes. The brother of the index patient was born after an unsupervised pregnancy at term. He had prominent forehead, broad, deep nasal bridge, cleft palate, multiple hamartomas of the tongue, irregular alveolar ridge, retrogenia, large, bilateral postaxial polydactyly of the fingers and toes, broad halluces. He had an abnormal breathing pattern with phases of tachypnoe and apnoe. Cranial MR revealed hypoplasia of the cerebellar vermis, Dandy-Walker malformation and hypomyelination of the corpus callosum. Renal ultrasound demonstrated multiple small cysts. At the age of 4 months the child was severely retarded and had recurrent seizures. He could not fix and had a mild nystagmus. The oral-facial-digital (OFD) syndromes are a heterogeneous group of disorders characterized by facial, oral and digital anomalies. Other features, like cerebral or cerebellar anomalies are often present, which make it difficult to ascertain whether these cases indicate variable expressivity or represent other entities. Beside these features our patients showed the typical breathing pattern and ocular anomalies of Joubert syndrome suggesting that there may be a continuum between OFD syndromes and Joubert syndrome. We discuss this hypothesis in regard of the data in the literature.

46

Familial posterior urethral valves as a cause for prune-belly.

R. J. Hopkin[1], M Walker[1], J. Stanek.[2] [1]Children's Hospital Research Foundation, Cincinnati OH, [2] University of Cincinnati College of Medicine.

The triad of abdominal muscle deficiency, urinary tract dilation, and cryptorchidism defines prune-belly (PB). The etiology is unknown and undoubtedly heterogeneous. Severe obstructive uropathy (OU) has been suggested as the common factor leading to PB. Posterior urethral valves (PUV) are the most common cause of OU in males, but do not occur in females. The precise embryonic origin of PUV is not known, but may be remnants of the urogenital membrane, residual mesonephric tissues, or exaggerated expression of normal structures. PUV are usually sporadic with rare familial recurrence. Transcription controlling genes such as the HOX genes have been cited as potentially contributing to PB in at least some cases. Some of the HOX genes are known to be important in urogenital morphogenesis. We have recently encountered a family with 3 males in 2 generations with PUV and PB. Oligohydramnios was diagnosed in the proband at 20 weeks gestation by ultrasonography. Additional findings included a massively distended bladder and bilateral clubfeet. Chromosome studies were normal, 46,XY. Autopsy revealed PUV, absence of the abdominal musculature, severe hydronephrosis, and pulmonary hypoplasia. Family history was significant for a stillborn maternal uncle with PUV and PB, and a maternal first cousin age 3 years who has PB and renal insufficiency secondary to PUV. To our knowledge, this is the first report of familial PB affecting individuals in 2 generations. However, if one includes milder manifestations of OU without PB at least 2 families with an affected father and son have been reported, suggesting possible autosomal dominant inheritance in at least some families. We found no reports of multi-generational X-linked recessive inheritance of OU or PB; however, several cases of familial recurrence involving siblings or cousins have been reported. The recurrence of PB in this family may represent autosomal dominant inheritance with sex-limited expression or X-linked inheritance of PUV. Future studies involving families such as this will allow identification of the genetic causes of PUV and related disorders.

47

Prenatal diagnosis of a skeletal deformation resulting from leiomyomata uteri.

S. Hudson, J.L.Roberts, E. Clarin and V.M. Anderson. State University of New York: Health Science Center at Brooklyn, NY.

Introduction: Leiomyomata uteri are associated with preterm labor and fetal loss, but we generally do not consider that they might cause fetal deformations. As a result, preconceptional myomectomy is not recommended as it may further impair fertility through intraperitoneal adhesion formation.
Case Report: We report on a patient who presented with profuse vaginal bleeding at nineteen weeks gestation. Sonogram demonstrated placenta previa and several myomas; the largest two measuring seven and five cm. The right femur was bent at a 90^0 angle while the remainder of the skeletal survey was normal. Severe oligohydramnios was present, limiting internal organ visualization of the fetus. In light of the heavy bleeding and oligohydramnios, the patient was informed of the poor prognosis for this pregnancy, and its risks to her, however she opted not to interrupt it. The patient continued to bleed intermittently, and then, four weeks later she bled profusely necessitating emergency hysterotomy to evacuate the uterus. A non-viable, 450gram male infant was delivered and the patient was transfused four units of packed red blood cells. The patient did not initially consent to autopsy, and cell culture for karyotype was not obtained. Autopsy confirmed the presence of an acutely deformed femur, and an X-ray showed normal bone mineralization. A horseshoe kidney was the only internal malformation identified.
Discussion: Deformations of the head, limbs, and thorax have been associated with uterine malformations such as bicornuate uterus, with a frequency of 30%. Reports of deformations caused by leiomyomata uteri are sparse, and this is the first prenatal report of such an event. The asymmetry of the skeletal abnormality makes it unlikely that this is syndromic, even with the horseshoe kidney, as this is usually isolated. It is possible that the oligohydramnios contributed to the constrained, deforming fetal environment. Events of this sort should be considered when counseling patients as to the risks that leiomyomata uteri may entail in pregnancy.
Reference: Miller, ME, Dunn, PM, Smith, DW. Uterine malformation and fetal deformation. *J Pediatr 1979; 94:378*