UK centres are not following the Royal College of Pathologists' recommendations for storage of Guthrie cards: a national policy is needed

Stored neonatal blood spots are a valuable source of DNA for retrospective diagnosis.1 A recent working party of the Royal College of Pathologists recommended storage of neonatal screening test (Guthrie) cards for at least 20 years provided that no deterioration of the sample has occurred.2 Our recent attempts to trace such cards convince us that a UK national policy and central funding for storing Guthrie cards is necessary.

Mitochondrial encephalopathy with stroke-like episodes (MELAS) is frequently associated with a mitochondrial DNA point mutation A3243G.3 Segregation and proliferation of this mutation in interpregnancy tissue (ECON) is not well understood. Levels of the 3243 mutant in blood are usually lower than in muscle4 and cross sectional data suggest that the level of mutant DNA may fall with increasing age.5 There is concern that cases of MELAS may be missed if diagnosed using the polymerase chain reaction (PCR) on blood. Longitudinal studies are necessary to clarify this issue. We have conducted a European collaborative study using Guthrie cards to compare levels of the 3243 mutant mtDNA in blood at birth and during diagnosis, under the auspices of the European Neuromuscular Centre.

We identified patients with MELAS born in the UK after 1970 and, with the informed consent of the patients or parents or both as appropriate, sought their Guthrie cards. A European collaborative study using Guthrie cards to compare levels of the 3243 mutant mtDNA in blood at birth and during diagnosis, under the auspices of the European Neuromuscular Centre.

Cyclopia and sirenemia in a liveborn infant

Recently, Chen et al published the case of a stillborn infant who presented with cebrophyly, holoprosencephaly, spina bifida, and sirenemia. We would like to describe a liveborn infant with cyclopia and sirenemia, identified in the Spanish Collaborative Study of Congenital Malformations (ECEMC). This case is similar to the one published by Chen et al, although with a more severe form of clinical holoprosencephaly with cyclopia, absent nose with presence of a proboscis, and without any evidence of spina bifida.

In 1992, we participated in an epidemiological study in an international collaboration, providing data from the ECEMC to the study group. A Polish collagenesis of muscle tissue were describing here in detail was published in the paper by Källén et al just to illustrate the title of that paper (The cyclops and the mermaid) but the case, which was included in the epidemiological analysis, was not described at all. In 1994, in a Letter to the Editor, we commented that we had observed a case with cyclopia and sirenemia that may be a clinical representation of a probable case observed in Ravenna, but the case was not described.

The infant was the product of the second pregnancy of a 29 year old mother and a non-consanguineous 33 year old father, both healthy. There was no family history of congenital malformations. The first pregnancy ended, a year earlier, in a normal male infant. In 1978, the proband was born spontaneously at 39 weeks of a second uncomplicated pregnancy, apart from a respiratory tract infection during the first 15 days of gestation. The mother denied any exposure to known teratogens, including alcohol and tobacco. She also denied having had problems in conceiving. At birth, the infant's weight was 1600 g (<3rd centile). The infant died at 15 minutes and had macrocephaly, absent nose with presence of a proboscis, cyclopia, sirenemia, and a clinical right forearm deficiency. No external genitalia or anus were visible. The umbilical cord contained only an artery and a vein. It was not possible to perform any radiological study, karyotype, or necropsy.

The prevalence of any type of holoprosencephaly in the series of 1245 863 births monitored by the ECEMC between 1980 and 1996 is 0.83 per 10 000 births, while the prevalence of cyclopia and sirenemia is 0.10 and 0.08 per 10 000 births, respectively. In an epidemiological study on the association of holoprosencephaly and caudal dysgenesis, it was shown that both types of malformations tend to be preferentially associated. That is, both are associated in the same child with a frequency that is significantly higher than would be expected just by chance. However, the combination of the two most extreme forms of alteration of the cephalic and caudal part of the embryo, cyclopia, and sirenemia, is very infrequent. In fact, our case was identified among a total of 1245 863 births, which appears that this is the first one published with cyclopia and sirenemia, bringing three to the total published cases with different degrees of holoprosencephaly and sirenemia.7 Cyclopia and sirenemia are gross alterations of early blastogenesis. Thus, as Opitz postulated8 and we reported,9 the combination of the two conditions, which is lethal, is a polytopic response of the alteration of the primary field, mostly affecting the midline. We have also observed that mothers of infants with blastogenic defects have a higher proportion of previous abortions that may mask the recurrence risk. However, we consider that in cases of holoprosencephaly (with different degrees of severity) and sirenemia, in the absence of teratogenic exposures and maternal diabetes, the recurrence risk at birth should be very low.

We think that it is important to present this case in detail since, at present, it is the only one that has the two most severe forms of alteration of the cephalic and caudal part of the embryo (cyclopia and sirenemia), and also because it was identified among a series of consecutive births, which allows the estimation of the birth prevalence of this entity.

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