Cyclopia

To the Editor

Regarding the case report "Cyclopia" by Yilmaz and Klinic,[1] I would like to add some information known about the etiology of cyclopia and holoprosencephaly in general. Cyclopia is a defect that derails the normal development of the brain and face. Cyclopia and milder forms of the same developmental disorder, technically known as holoprosencephaly, result from a failure of the embryonic forebrain to subdivide properly. The clinical picture of holoprosencephaly can be viewed as a spectrum of facial anomalies, including cyclopia, ethmocephaly and cebocephaly, since they share similar cerebral malformations. The mildest end of the spectrum is considered hypotelorism with single central incisor.[2]

As many as 50% of the cases are attributable to a chromosome abnormality, the most common one are trisomy 13 (earlier described in the literature as trisomy D), monosomy 18, ring 18, and so forth.[3] Monogenic syndromes such as Meckel syndrome have been reported as having holoprosencephaly and, apparent monogenic inheritance, either autosomal recessive or dominant, have been reported. Holoprosencephaly-like symptoms including cyclopia develop in mouse embryos that lack a normal Sonic hedgehog (Shh) gene.[4] Sonic hedgehog gene and other genes affecting the Shh signal can cause holoprosencephaly, but many cases have not been traced to specific genetic lesions, opening a possible role for environmental factors.

Defective genes can disrupt the embryonic forebrain and stop its partition in people and animals, so can certain toxins, some of them found in wild plants. Toxins that interfere with cholesterol metabolism can cause similar abnormalities as has been shown in lambs with high incidence of cyclopia due to the plant *veratrum californicum* or corn lily, which the ewes had eaten; these compounds resemble cholesterol structurally. This toxins make the cells unable to respond to a critical developmental signal, perhaps because they interfere with the normal traffic of cholesterol within cells.[5] The idea that a disruption in cholesterol transport may prevent embryonic cells to pay attention to the signal, comes from showing that cholesterol also plays a role in activating the signal in the first place.[5]

Carlos Trujillo
Genetics Unit
Dr. Erfan & Bagedo General Hospital
PO Box 6519
Jeddah 21452
Kingdom of Saudi Arabia

Reply from the Author

Author decline to reply

References

1. Yilmaz F, Klinic N. Cyclopia. ***Saudi Med J*** 2003; 24: 298-300.
2. Toriello H. Holoprosencephaly. In: Buysee ML. Birth defects encyclopedia. Massachusetts (USA): Blackwell Scientific Publications; 1990. p. 876-877.
3. Trujillo C. Chromosome 18, ring 18. In: Buysee ML. Birth defects encyclopedia. Massachusetts (USA): Blackwell Scientific Publications; 1990. p. 384-385.
4. Verlinsky Y, Rechitsky S, Verlinsky O, Seckin O, Sharapova T, Masciangelo C et al. Preimplantation diagnosis for sonic hedgegog mutation causing familial holoprosencephaly. ***N Engl J Med*** 2003; 348: 1449-1454.
5. Strauss E. Developmental Biology: One-eyed animals implicate cholesterol in development. ***Science*** 1998; 280: 1528-1529.