A preventable problem: Isotretinoin embryopathy

Dear Editor,

Isotretinoin is a synthetic vitamin A derivative which is used for treatment of nodulocystic and severe acne. It is a teratogenic factor which can lead to intrauterine death and congenital anomalies in humans and the clinical picture it causes is named isotretinoin embryopathy (1). A three months-old infant who was born from a mother who used isotretinoin during her first month of pregnancy without realising that she was pregnant is presented in this article to emphasize that this drug should definitely not be started in women who plan a pregnancy.

A three month-old male presented to our clinic with a prediagnosis of multiple anomalies because of congenital cleft palate and low-set and malformed ears. When maternal history of the baby who was born from the first pregnancy of a 19-year-old mother with a birth weight of 2400 g was deepened in terms of the infant’s malformations, it was learned that the mother used isotretinoin at a dose of 0.5 mg/kg/day until the fourth week when she realized that she was pregnant because of widespread acnes on her face.

The mother discontinued the drug on the fourth week, when she realized that she was pregnant.

Physical examination revealed the following findings: height 54 cm (3-10\textsuperscript{th} percentile), body weight 3800 g (10-25\textsuperscript{th} percentile) and head circumference 38 cm (25-50\textsuperscript{th} percentile). Ptosis was present in the left eyelid (Picture 1). Low-set malformed auricle, micrognatia (Picture 2) and cleft palate (Picture 3) were observed. A 2/6 systolic murmur was heard in the mesocardiac area.

Laboratory examinations revealed that complete blood count, biochemical tests and urinalysis were within normal limits. Patent foramen ovale was found on echocardiographic examination. Hydrocephaly, Dandy Walker malformation and cerebellar vermis hypoplasia (Picture 4) were found on cranial magnetic resonance (MR) imaging. The patient is still being followed up and treated in our clinic.

Isotretinoin embryopathy which is caused by isotretinoin is manifested by auricle anomalies, cleft palate, micrognatia, cardiac defects, aortic arcus malformations and central nervous system anomalies (1,2). Our patient had findings compatible with

---

Address for Correspondence: Habip Almiş MD, İnönü University, Medical Faculty, Department of Pediatrics, Malatya, Turkey
E-mail: drhabipalmis@yahoo.com Received: 02.14.2012 Accepted: 02.26.2012

Turkish Archives of Pediatrics, published by Galenos Publishing
isotretinoin embryopathy including auricle anomalies, ptosis, cleft palate, micrognatia, patent foramen ovale, hydrocephaly, Dandy Walker malformation and cerebellar vermis hypoplasia.

In a study performed by Lammer et al. (1) in 1985, 21 cases exposed to isotretinoin were examined and craniofacial anomaly was found in 17 subjects, cardiac anomaly was found in 12 subjects, central nervous system anomalies were found in 18 subjects and thymus development anomalies were found in 7 subjects. In vivo and in vitro studies have shown that isotretinoin affects the development of cranial neural crest cells (3).

Pregnancy test should definitely be performed in women in whom isotretinoin treatment will be started and if the test is negative, treatment should be only started after obtaining informed consent. The treatment should be limited to one month and the drug should be discontinued at the end of one month. However, it was reported that it could lead to ear anomalies despite discontinuation of the drug one month before pregnancy (4-6). A dose of 0.5-1.5 mg/kg/day isotretinoin has been reported to be enough for teratogenicity (7). Our patient was exposed to 0.5 mg/kg/day isotretinoin. In a case reported from our country, “anotia” and Taussing-Bing malformation were described (8). When the history and physical examination findings of the anomalies of our patient are considered, it is clear that it is caused by isotretinoin.

Conclusively, we believe that the best approach would be not to start drugs including isotretinoin which have teratogenic effect in pregnant women or in women with child-bearing potential.

Habip Almiş, Yunus Emre Kum, Yeşim Önal, Cengiz Yakıcı
İnönü University, Medical Faculty, Department of Pediatrics, Malatya, Turkey

References