A case of isotretinoin embryopathy with bilateral anotia and Taussig-Bing malformation

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SUMMARY: Ceviz N, Özkan B, Eren S, Örs R, Olguntürk R. A case of isotretinoin embryopathy with bilateral anotia and Taussig-Bing malformation. Turk J Pediatr 2000; 42: 239-241.

We report a newborn infant with multiple congenital anomalies (anotia and Taussig-Bing malformation) due to exposure to isotretinoin within the first trimester. In this paper we aim to draw to the fact that caution is needed when prescribing vitamin A-containing drugs to women of childbearing years.

Key words: maternal isotretinoin intake, anotia, Taussig-Bing malformation.

Although it has been reported that the use of low or moderate doses of vitamin A (<10,000 IU) during the first trimester of pregnancy is not teratogenic and provides some protection to the fetus[1], teratogenicity of both the lack of and excess of vitamin A during embryonic development has been proven by many studies[2-4].

In this report, we describe a newborn infant with multiple congenital anomalies who had been exposed to isotretinoin, a retinoid prescribed for severe recalcitrant cystic acne, in the first trimester of pregnancy. The case was reported to draw attention to prescription rules for vitamin A analogues in sexually active fertile women.

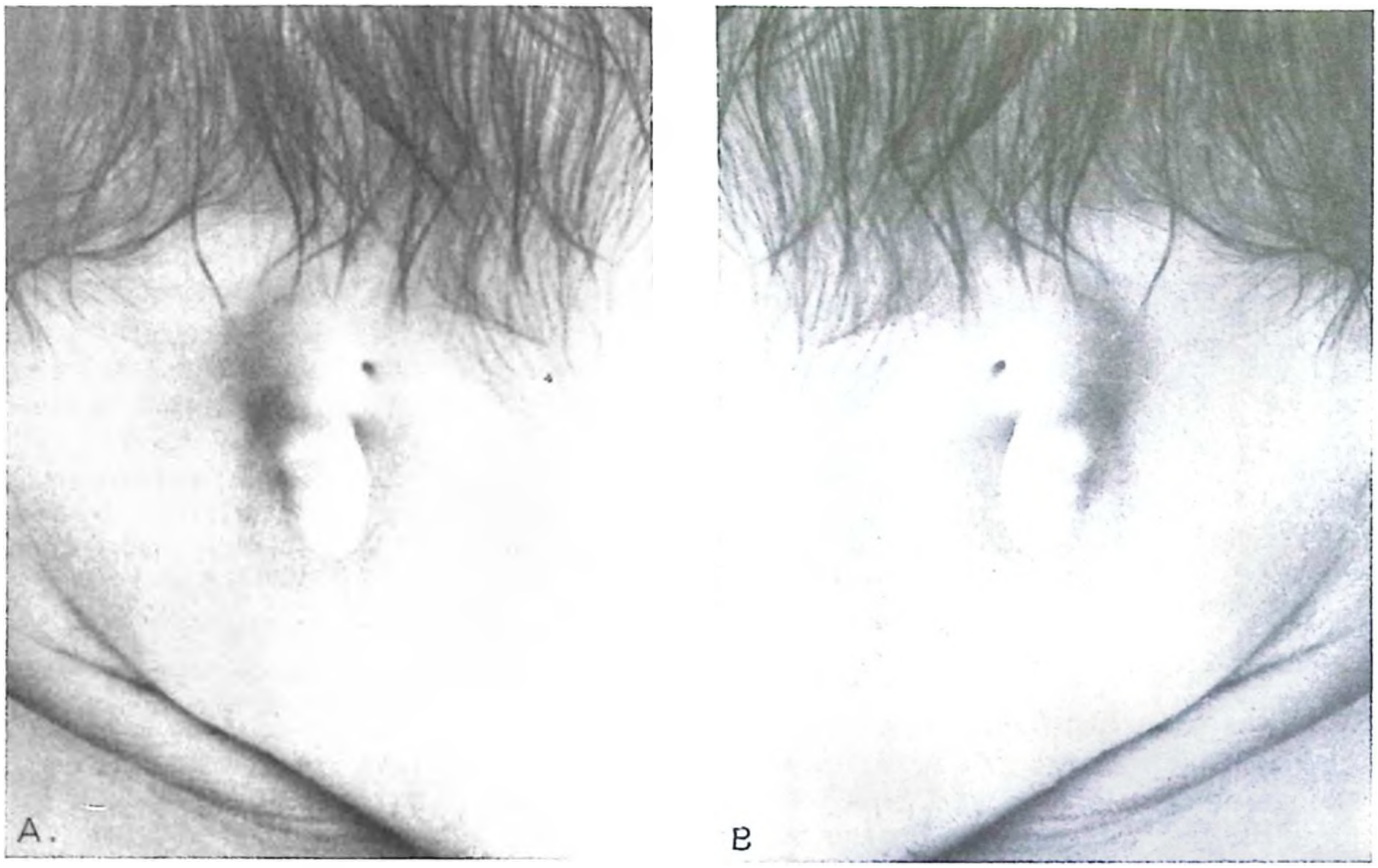
Case Report

A two-day-old term newborn infant was admitted to the Neonatology Outpatient Clinic with the complaints of absence of auricles, tachypnea, and feeding difficulties. The infant was a product of a pregnancy complicated by isotretinoin ingestion during the first two months (40 mg/day). The mother was well educated (engineer-argonomist). The preparation had been prescribed by a dermatologist, unaware of the pregnancy, for treatment of severe recalcitrant cystic acne. After a normal pregnancy, the newborn was born in a state hospital by normal vaginal delivery. The first problem noted was the absence of auricles bilaterally, and on the 2nd day of birth, tachypnea and tachycardia developed.

Physical examination revealed the bilaterally deformed and rudimentary auricles (Fig. 1). The patient had cyanosis in addition to the signs of heart failure (hepatomegaly, tachypnea, tachycardia). Increased precordial activity was apparent. Chest x-ray showed cardiomegaly and increased pulmonary vascular markings. On echocardiodiographic examination (Fig. 2), a) atrial situs was normal, b) a large subpulmonary ventricular septal defect (VSD) and a secundum atrial septal defect (ASD) were present, c) both great arteries originated from the anterior right ventricle, and d) tricuspid insufficiency jet velocity indicated approximately 70 mmHg of right ventricular pressure. Thus, the diagnosis was double outlet right ventricle, subpulmonary VSD (Taussig-Bing malformation), secundum ASD and pulmonary hypertension.

Ultrasonographic evaluation of cranium and abdomen showed no pathology. Cranial computed tomography (Fig. 3) showed atresia of the external ear canal, tympanic membrane, middle ear and antrum. Other structures (cochlea, semicircular canals and middle ear bones) were normal.

Digoxin and furosemide were administered for congestive heart failure. Cardiac catheterization and angiocardiography confirmed the diagnosis of Taussig-Bing malformation and ASD with pulmonary hypertension (systolic, diastolic and mean pulmonary artery pressures were measured as 64,13 and 34 mmHg, respectively). The family did not accept any surgical approach. The patient was discharged, and he died at home.



(a) (b)

Fig. 1. Figure depicts the bilaterally deformed and rudimentary auricles. a) Right, b) Left.

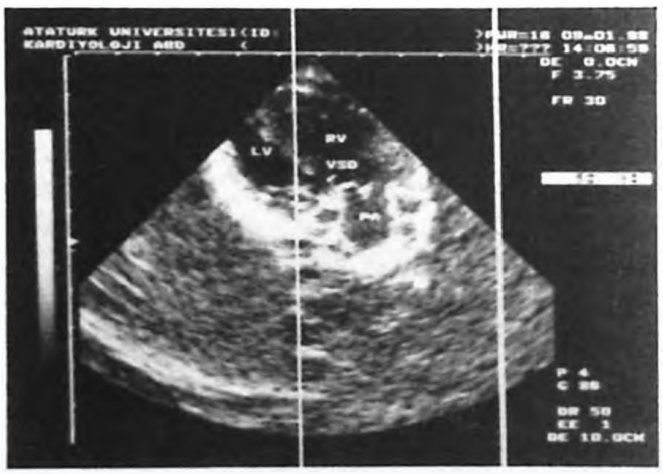


Fig. 2. A two-dimensional echocardiogram (parasternal long axis) shows the double outlet right ventricle and subpulmonary ventricular septal defect (VS). RV: right ventricle, LV: left ventricle, PA: pulmonary artery, AO: aorta.

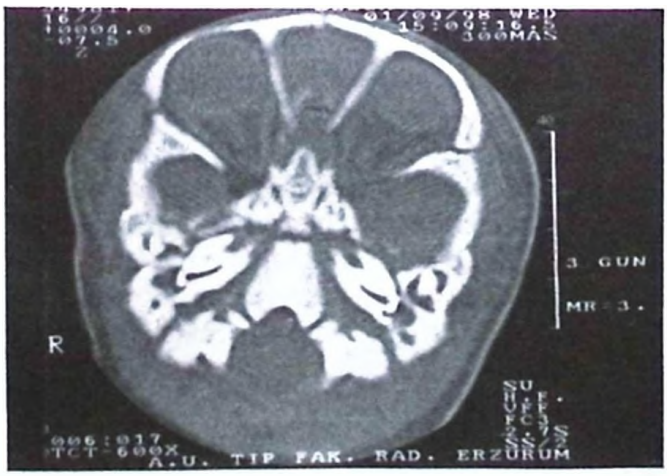


Fig. 3. Computed cranial tomography demonstrates atresia of the external ear canal, tympanic membrane, middle ear and antrum.

Discussion

Vitamin A analogues are known to be teratogenic in laboratory animals[5,6] and their teratogenicity has been reported in clinical case reports[4]. Exposure to isotretinoin has been reported to be associated with an unusually high relative risk for a group of select major malformations[5]. The most often reported malformations are related to craniofacial (microtia/anotia, micrognathia, cleft palate), cardiac (conotruncal heart defects, aortic-arch abnormalities), thymic and central nervous system structures (retinal or optic-nerve abnormalities, central nervous system malformations), suggesting the involvement of the cranial neural crest[6].

Our case had typical manifestations of fetal exposure to vitamin A derivatives (with craniofacial and cardiac defects).

In Turkey, isotretinoin can only be prescribed by dermatologists. Although an informed consent usually is obtained and a detailed explanation is given about the teratogenicity of vitamin A anologues, it is not mandatory to evaluate female patients in terms of possible pregnancy.

Our case with a well-educated mother suggests that the current application can be insufficient and can result in undesired outcomes. In conclusion, we propose that vitamin A analogues not be prescribed without obtaining a negative pregnancy test from fertile women. Also, in countries where adolescent pregnancies are frequent, women taking any teratogenic drug, like isotretinoin, should be actively practicing birth control while on this drug.

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