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Clinical Report

Choanal Atresia: The Result of Maternal Thyrotoxicosis or Fetal Carbimazole?

Julian Barwell,[1]* Grenville F. Fox,[2] Jonathan Round,[2] and Jonathan Berg[3]

[1]*Department of Clinical Genetics, Guy's and St. Thomas's Hospital Trust, Guy's Hospital, London, UK*
[2]*Department of Neonatology, Guy's and St. Thomas's Hospital Trust, Guy's Hospital, London, UK*
[3]*Division of Medical and Molecular Genetics, GKT School of Medicine, King's College London, Guy's Hospital, London, UK*

We present the fourth published case of a child affected with choanal atresia following maternal treatment with carbimazole. The mother was receiving her highest dose of carbimazole at the crucial period for development of the choanae, between days 35 and 38. © 2002 Wiley-Liss, Inc.

KEY WORDS: choanal atresia; carbimazole; teratogens; Graves disease; thyrotoxicosis

INTRODUCTION

The effects of carbimazole and other antithyroid medication in pregnancy have been studied previously. Defects of the scalp are the most common malformation associated with carbimazole exposure [Greenberg, 1987]. Mujtaba and Burrow [1975] reported the outcome in 21 pregnant women who had been treated for thyrotoxicosis. Five children had congenital abnormalities, including a scalp defect, imperforate anus, an interrupted aorta, and hypospadias. Momotani et al. [1984] studied 643 infants born to mothers with Graves disease in Japan. They observed only six infants with congenital defects, including cleft lip, polydactyly, imperforate anus, anencephaly, ear anomalies, and encephalocele. Only two of these infants had mothers who had been treated with methimazole (the active metabolite of carbimazole), and none of them had choanal atresia. It was therefore believed that maternal treatment with carbimazole constituted a very low risk to the fetus, and that the benefits of such treatment outweighed any possible teratogenic effects.

Three cases of a child affected with choanal atresia following maternal treatment with carbimazole/methimazole have previously been described. Greenberg [1987] described a girl with short stature, choanal atresia, and mixed sensorineural/conductive hearing loss. She had alopecia over the parietal region, upslanting palpebral fissures, and no nipples. Her mother had been on long-term methimazole treatment. Wilson et al. [1998] described a boy with bilateral choanal atresia and developmental delay. He had hypoplastic nipples, a broad forehead, midline anterior cowlick, short upslanting palpebral fissures, a small nose and mouth, and a short philtrum. A third case of bilateral choanal atresia and tracheoesophageal fistula was described by Clementi et al. [1999]. Other features included scalp defects, minor facial anomalies, and psychomotor delay. In this paper, we describe a fourth example of a child with choanal atresia in association with maternal treatment with carbimazole.

CLINICAL REPORT

This male infant was born at 36 weeks gestation: his birth weight was on the 50th centile, and his head circumference was on the 25th centile. At birth he was noted to have difficulties with feeding and breathing through his nose. A computed tomography (CT) scan demonstrated a mixed membranous/bony choanal atresia, but no other abnormality, and the brain structure was normal. The atresia was confirmed by direct vision with endoscopy. On examination, he was not obviously dysmorphic. The nipples and palpebral fissures were normal, and there was no evidence of cutis aplasia. A diagnosis of CHARGE syndrome was excluded by investigations which showed that his eyes, kidneys, ears, and brainstem-evoked responses were all normal. The atresia was relieved by boring, with placement of nasal stents for six weeks post-operatively. Recovery was uneventful.

*Correspondence to: Dr. Julian Barwell, Department of Clinical Genetics, Guy's and St. Thomas's Hospital Trust, 7th Floor New Guy's House, Guy's Hospital, London SE1 9RT, UK.
E-mail: Julian.Barwell@gstt.sthames.nhs.uk

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There was no other relevant family history. The proband's two-year-old sister was well and unaffected. His mother was 28 years old, and did not drink or smoke. She was diagnosed with Graves disease after feeling continually hot, and was started on a low dose of carbimazole. A month later, while on this treatment, she became pregnant. During the first trimester, tremor and sweating proved quite difficult to control, and the dose of carbimazole was increased to 60 mg/day. In the second month of pregnancy, her thyroid function results were: free T4 54.9 pmol/L (normal range 9.1–23.8), free T3 36.3 pmol/L (normal range 2.5–5.3), and TSH < 0.05 (normal range 0.49–4.67). The dose of carbimazole was reduced to a maintenance level during the second trimester. As the pregnancy progressed, her thyroid function normalized. The baby's postnatal thyroid function was normal.

DISCUSSION

This is the fourth reported case of maternal carbimazole in association with choanal atresia. However, it is not entirely clear from the literature whether or not the mothers of the previous cases were clinically and biochemically euthyroid during early pregnancy. The choanal atresia may be related in part to thyrotoxicosis. In our case, the mother was quite obviously thyrotoxic, with both symptoms and very abnormal thyroid function tests. However, we have been unable to find any previous evidence of an association between choanal atresia and maternal thyrotoxicosis alone. Maternal hyperthermia is known to be a teratogen, leading to defects when a threshold 'dose' of heat is reached—e.g., a rise in body temperature of at least 2.0°–2.5°C, sustained for 24 hours [Chambers et al., 1998]. These defects are mostly found in the central nervous system, e.g., open neural tube defects [Chambers et al., 1998]. Other abnormalities include a raised frequency of atrioseptal defects and hypoplastic left heart [Tikkanen and Heinonen, 1991], as well as microcephaly, microphthalmia, and neurogenic contractures [Edwards, 1998]. It is feasible that maternal hyperthermia alone could be a factor in the development of choanal atresia, but again, we have been unable to find any evidence of this in the literature.

In our patient, the highest dose of carbimazole was administered during the first trimester. Interestingly, the choanae are formed between days 35 and 38 of gestation, when the bucconasal membrane ruptures as the epithelia lining the oral and nasal cavities come into contact with each other. We feel that our case adds weight to the argument that carbimazole treatment in early pregnancy may cause choanal atresia. However, maternal health must be taken into consideration when treating thyrotoxicosis. Clearly, without treatment, maternal thyrotoxicosis and hyperthermia may cause a significant degree of morbidity and mortality in both mother and child. Further research is required to establish the safest form of treatment for thyrotoxicosis in pregnancy.

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