

ABSENCE OF A HAND (ACHEIRIA) IN A CHILD WHOSE FATHER WAS TREATED WITH CYCLOPHOSPHAMIDE FOR BEHÇET'S DISEASE

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Key Words: absence of a hand (acheiria), Behçet's disease, cyclophosphamide treatment

It is probable that alkylating agents administered during the first trimester of pregnancy have a significant teratogenic effect because of their polyfunctional suppression of growth of the baby. It is well known that alkylating agents act as teratogens in animals¹⁻³, but it is very rare in humans⁴⁻⁶. There is only one case in the literature: Greenberg and Tanaka⁷ have reported cyclophosphamide to be a probable cause of fetal abnormalities. In their case the patient, whose mother had Hodgkin's disease and was treated with cyclophosphamide during pregnancy, had several congenital skeletal abnormalities. There have been no cases reported in the medical literature indicating congenital abnormalities due to a father's being treated with cyclophosphamide.

In this paper we would like to report acheiria (absence of the right hand) in a child whose father had received cyclophosphamide for a long period of time.

Case Report

A 6-month-old female child was admitted to Hacettepe Children's Hospital with the chief complaint of absence of the right hand. The pregnancy and delivery had been normal. The mother was 25 and the father 36 years old. The family history revealed that the father had been suffering from Behçet's disease for the preceding 12 years. There was fourth degree consanguinity between the parents, who had been married for 8 years. There were no similar cases of skeletal abnormalities in the family, and the two female siblings (aged 3 and 4 years) were normal. The father had been taking 150 mg cyclophosphamide and 50 mg dexamethasone daily for the preceding 3 years.

Physical examination revealed absence of the right hand. The forearm was present, but there was no palm and only four small fibrous buds of fingers were observed (Figure 1). All other systems were found to be normal.

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Figure 1

Note absence of the right hand.

An X-ray of the right hand revealed the absence of fingers and the other bones of the hand (Figure 2). Chromosomal analysis of the peripheral blood leukocyte cultures was normal in both number and structure.



Figure 2

X-ray of the right forearm showing absence of the bones of the right hand

Discussion

Cyclophosphamide has been extensively used in various diseases as an immunosuppressive agent. Recently, cyclophosphamide has been used as an effective agent in the control and prevention of relapse in Behçet's disease⁸⁻⁹. It is interesting to note that in this case it was the father who was being treated with the mutagenic agent. It is well known that cyclophosphamide affects the rapidly dividing sperm and leads to azoospermia¹⁰⁻¹². In some of these cases, fertility returns after treatment has been discontinued¹³. Five normal children of fathers who have recovered from azoospermia have been reported in the literature. Since affected sperm could only transmit defects by a genetic mutation, there could be no direct effect of the drug on the developing embryo.

However, acheiria usually occurs sporadically. In this case it would be difficult to attribute this abnormality definitely to a mutation. Furthermore Freire-Maia¹⁴ reported recessive inheritance in a family with acheiropodia. In our case there was fourth degree consanguinity between the parents, which could be as likely a cause of a genetic defect as drug mutagenesis.

Until now, there has not been any report in the literature of congenital malformations due to a father's being treated with cyclophosphamide¹³, but the present case made us wonder whether treatment with cyclophosphamide, which produces transient azoospermia, might cause congenital anomalies. Although this postulated relationship must still remain conjectural, we hope that our report will prompt the publication of other existing observations.

Summary

In this article a 6-month-old female patient with absence of the right hand (acheiria) is reported. Interestingly her father had been treated for the preceding three years with cyclophosphamide for Behçet's disease. The purpose of this report is to draw attention to the possibility that cyclophosphamide could be a mutagenic agent in cases where the father had received the drug for a long period of time.

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