

Association of Clomiphene with Iniencephaly

Neural tube defects (NTD) are reported with the use of ovulation-inducing agents like clomiphene(1,2). We report a case of iniencephaly in a baby born to a mother receiving clomiphene.

This 23-year-old primigravida had history of having taken Clomiphene for 2 consecutive cycles starting on day 5 of her menstrual cycle (50 mg for five days). After the 2nd cycle of clomiphene, she became pregnant. There was no history of taking any other drug for infertility or folate tablets periconceptionally. An ultrasound at 20 weeks showed neural tube defect. At 22 weeks of gestation, she delivered a 300 grams abortus spontaneously. It was an Iniencephalus female fetus who had fusion of the occiput to the cervical spine and retroflexion of the head with an exaggerated lumbar lordosis. The fetus also had an umbilical hernia, clubfoot, micrognathia, and cleft palate. The thoracic and cervical spine were abnormal with spinal dysraphism. The lumbar and sacral vertebrae were normal. The head was hyperextended, mandible hypoplastic, cranial bones incomplete and ribs deformed and crowded.

Iniencephaly is a rare type of neural tube defect involving the occiput and inion combined with rachischisis of the cervical and thoracic spine with retroflexion of the head(3). It is caused by arrest of the embryo in physiological retroflexion in the third week of gestation or failure of normal forward bending in the fourth week. Cardiac, renal, cardiovascular, bony, gastrointestinal anomalies have been described with iniencephaly. Animal studies have shown that administration of vinblastine, streptonigrin

and triparanol have been associated with iniencephaly.

Clomiphene has been reported to be associated with NTD(1,2,4). However, a cause and effect relationship is yet to be established. Speroff, *et al.*(5) found that significant plasma concentrations can be detected up to one month after single dose of 50 mg, therefore presence of clomiphene at the time of ovulation and during the luteal phase could have unwanted effects. It may be speculated that persistent levels of clomiphene could damage the embryo or ovum. On the other hand clomiphene is given to women with infertility problems and the incidence of congenital disorders is more in them. It is possible that the oocyte in some infertile women is inherently defective and induction of ovulation simply allows the defective ovum to get fertilized. Case control studies will be needed to elucidate this.

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