Fetal Anomalies in Rheumatoid Arthritis Patient Exposed to Low Dose Methotrexate

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MJAFI 2009; 65 : 80-81

Key Words : Methotrexate; Fetal anomalies

Introduction

Low dose weekly methotrexate (MTX) is widely used in the treatment of rheumatoid arthritis and is now increasingly used in other rheumatic conditions, including systemic lupus erythematosus and juvenile arthritis. Because of its antimetabolic and cytotoxic actions, questions of its safety in those of childbearing age are likely to become increasingly important. We present a case of first trimester exposure to low dose methotrexate in rheumatoid arthritis patient where fetus developed multiple anomalies.

Case Report

A 29 years old Gravida 2, Para 1 lady reported with history of nine weeks of amenorrhea. She was married for five years and had full term normal delivery three years back. She was a known case of rheumatoid arthritis and was on low dose methotrexate since last 14 months. She had no other significant medical or surgical history. Her previous menstrual cycles were regular. On examination, her general condition was good. Systemic examination did not reveal any abnormalities. There were no joint deformities. Routine investigations including ultrasonography were normal. She was counseled that there is a chance of abnormality in fetus, she however opted for continuation of pregnancy. Methotrexate was stopped. Patient was not using any NSAIDs (nonsteroidal anti-inflammatory drugs). Repeat ultrasonography at 17 week showed multiple anomalies and patient opted for termination of pregnancy. Female abortus of 375 gm showed anencephaly (Fig. 1), spina bifida (Fig. 2), low set ears, long webbed fingers and dextroposition of heart. Fetal karyotype could not be done.

Discussion

Rheumatoid arthritis is a chronic inflammatory/autoimmune disease more common in female. Onset is frequently during childbearing age (20-40 years). Current drug therapy for rheumatoid arthritis consists

of combination of NSAIDs and disease modifying anti rheumatic drugs (DMARDs) like methotrexate [1]. Methotrexate is a methyl derivative of aminopterin and was first described in 1947 [2]. Methotrexate demonstrates significant teratogenicity [3]. The effects are unpredictable, making counseling difficult in individual cases. The pattern of anomalies associated with first trimester exposure includes microcephaly, cleft palate, neural tube defects, delayed fetal growth, abnormal cranial ossification, ocular hypertelorism, small low set ears, severe micrognathia and limb abnormalities (aminopterin syndrome) [4]. Hence methotrexate is generally contraindicated during pregnancy. The critical dose for the 'aminopterin syndrome' is probably above 10 mg of methotrexate per week and the critical period is probably between six to eight weeks of gestation [5]. Nguyen et al [6], described new born with multiple anomalies that were exposed to a significantly lower dose of methotrexate before six weeks' gestation. Our patient had taken 7.5 mg/week of methotrexate till nine weeks of gestation. Women wishing to continue with a pregnancy following exposure to methotrexate in the first trimester can be informed that there is a chance of abnormality in the fetus on the basis of data from cases of methotrexate exposure [6].

In cases of methotrexate exposure, the drug should be stopped and women wishing to continue pregnancy after counseling should be offered treatment with folinic acid for at least five months in order to minimize methotrexate effects on fetus. Women should be warned that there may be small increased risk of spontaneous abortion early in pregnancy and advised against taking methotrexate if they are considering conception. Those who chose to stop methotrexate and proceed to pregnancy should be advised against conception within six months of taking methotrexate [4]. In the event of

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Fig. 1 : Anencephaly with long webbed fingers

conception within this time, full counseling and close fetal monitoring should be offered. Methotrexate treatment is unlikely to have a major effect on short or long term fertility, but a washout period of six months cessation of treatment prior to conception is advisable to prevent the small chance of chromosomal abnormalities in offspring. There are only few documented cases where first trimester exposure of low dose methotrexate caused multiple fetal anomalies [4]. A negative report could have proved this congenital malformation in the baby is not due to a karyotyping abnormality. In the absence of a karyotype report, Methotrexate as an offending drug is only a possibility in this case.

Conflicts of Interest

None identified

Fig. 2 : Spina bifida

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