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DO CERTAIN DRUGS CAUSE THE MEGACYSTIS-MICROCOLON-INTESTINAL HYPOPERISTALSIS SYNDROME*

*Hasan Doğruyol MD***

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The megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS) was first described by Berdon et al[1] in 1967. Since then an increasing number of cases with this congenital abnormality has been reported in the literature[2-11]; they all describe this disease as a syndrome of unknown etiology.

Last year, we reported the case of a baby with the megacystis-microcolon-intestinal intestinal hypoperistalsis syndrome who was the product of a mother who had taken clomiphene during pregnancy[12]. I have recently seen another MMIHS case in an offspring of a mother who had taken scopolamine, dipyrone and trimethoprim-with-sulfamethoxazole in the first month of pregnancy. This second instance of the same abnormality associated with drug intake during pregnancy encouraged me to explore the possibility of a relationship between maternal drug ingestion and MMIHS.

Case Report

A baby girl of 40 weeks' gestational age weighing 2,600 g was born on January 17, 1988 to a 23-year-old mother. On April 21, 1987, her mother was prescribed talcid (hydrotalcit 1500 mg × 30 days), Buskaljin^{R} (hyoscine-N-buthyl bromide 30 mg: natrium methyl-amino-phenyl-dimethyl pyrazolon methane sulfonate 750 mg × 30 days) and Sulfatrim^{R} (trimethoprim 180 mg, sulfadiazine 820 mg 15 days) for gastrointestinal discomfort and urinary infection which she had taken regularly during the first month of pregnancy.

Immediately after delivery, the infant's abdomen appeared markedly distended. Bile-stained material was suctioned from the stomach.

Spontaneous micturition occurred but no defecation was observed until fifteen hours after delivery. Auscultation detected silent abdomen. Abdominal ultraso-

* From the Department of Pediatric Surgery, Uludağ University Faculty of Medicine, Bursa.

** Associate Professor of Surgery, Uludağ University Faculty of Medicine.

nography revealed peritoneal fluid and hyperechoic areas due to distension of the bowels. Roentgenograms showed intestinal obstruction, and barium enema examination failed to demonstrate beyond the rectum.

At the twentieth hour an exploratory laparotomy was performed which revealed all the classical findings of megacystis-microcolon-intestinal hypoperistalsis syndrome (Figs. 1, 2). This was terminated in surgery.

Sepsis developed postoperatively, and the patient died on the fifth day after the operation. Her parents did not give permission for an autopsy.

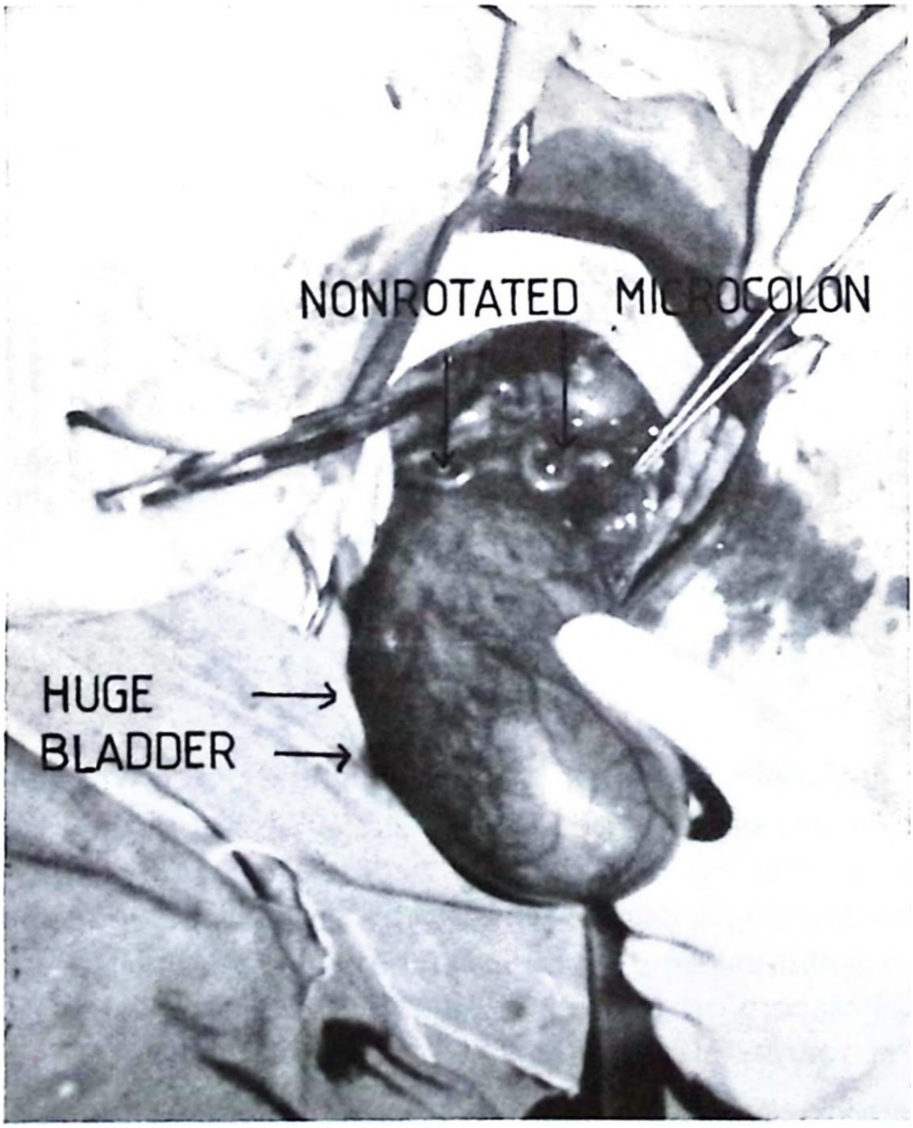

Fig. 1: Operative view of the case revealing a hug bladder and nonrotated microcolon.

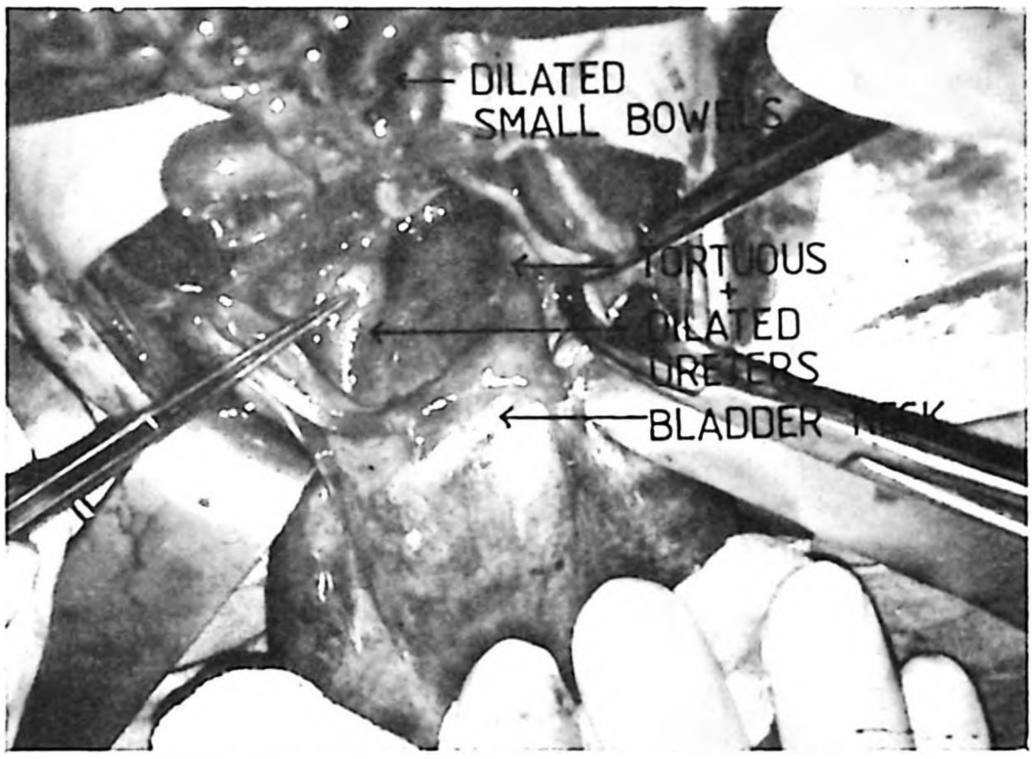

Fig. 2: A close-up view of the same area: tortuous, dilated ureters and dilated small bowels are seen.

Discussion

In previously reported cases of MMIHS great importance was given to the antenatal ultrasound appearance and histopathological examination of the bowel and urinary bladder[1,3,5,9] but as of yet there has been no mention of a relationship existing between maternal drug ingestion and MMIHS.

In our first case, the mother of the baby was given clomiphene citrate (50 mg × 5 days) for two cycles and became pregnant at the end of the second cycle. Clomiphene has been widely accepted as a drug having a possible teratogenic effect, and some congenital abnormalities have been reported in both clomiphene-induced pregnancies and the babies who had been exposed to the drug during pregnancy[13,14]. We therefore present this case as another instance of congenital anomalies associated with maternal clomiphene treatment[12]. However, a causal relationship between MMIHS and maternal clomiphene ingestion has not yet been established.

There are several reports in the literature describing congenital defects in the offspring of mothers who had taken trimethoprim-sulfadiazine[15], and scopolamine derivatives[16] during pregnancy. Dipyrone, a methane sulfonate derivative of amiopyrine has disappeared from the therapeutic scene in most countries because of its potentially fetal toxicities[17]. Pharmaceutical companies recommend that these drugs should not be used during pregnancy. It must be stressed, however, that without performing any experimental studies, it is very difficult, and even impossible, to prove whether these drugs cause malformations. However,

the second instance of the same abnormality associated with maternal drug ingestion led to the formulation of the hypothesis: "Do certain drugs cause the megacystis-microcolon-intestinal hypoperistalsis syndrome?".

Summary

A case of megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS) in the offspring of a mother who had ingested scopolamine, trimethoprim-sulfadiazine and dipyrone during pregnancy is presented. In order to determine whether a relationship exists between maternal drug ingestion and MMIHS, the need for further experimental studies is stressed.

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