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Megacystis microcolon intestinal hypoperistalsis syndrome

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Megacystis microcolon intestinal hypoperistalsis syndrome (MMIHS) is a rare and the most severe form of functional intestinal obstruction in the newborn. The major features of this congenital and usually lethal anomaly are abdominal distension, bile-stained vomiting, and absent or decreased bowel peristalsis. Abdominal distension is a consequence of the distended, unobstructed urinary bladder with or without upper urinary tract dilation. Most patients with MMIHS are not able to void spontaneously. This article reviews the pathogenesis of MMIHS as well as the clinical, radiological, surgical and histological findings in all reported cases of this syndrome.

Megacystis microcolon intestinal hypoperistalsis syndrome (MMIHS) is a rare congenital and generally fatal cause of functional intestinal obstruction in the newborn. This syndrome is characterized by abdominal distension caused by a distended non-obstructed urinary bladder, microcolon and decreased or absent intestinal peristalsis.[1] Usually incomplete intestinal rotation and shortened small bowel are associated.

Pathogenesis

The MMIHS was first described in 1976 by Berdon and coworkers and to date, 182 cases have been reported in the literature.[1-87] The etiology of this syndrome remains unclear. Several hypotheses have been proposed to explain the pathogenesis of MMIHS: genetic,[20,28,36,37,42,44,52,61,63,75] neurogenic,[5,8,12,15,20,21,35,39,40,53,63] myogenic,[2,57,80,81] and hormonal origin.[11]

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Histologic studies of the myenteric and submucosal plexuses of the bowel of MMIHS patients have found normal ganglion cells in the majority of the patients, decreased in some, hyperganglionosis and giant ganglia in others.[63] An imbalance between several kinds of intestinal peptides was suggested as one of the possible causes of hypoperistalsis in MMIHS patients.[39,60] Recently, Piotrowska and coworkers[81,87] reported absence of interstitial cell of Cajal (ICCs) in the bowel and urinary bladder of patients with MMIHS. ICCs are pacemaker cells which facilitate active propagation of electrical events and neurotransmission and their absence may result in hypoperistalsis and voiding dysfunction in MMIHS. Puri and coworkers[2] showed, in 1983, vacuolar degenerative changes in the smooth muscle cells (SMCs) with abundant connective tissue between muscle cells in the bowel and bladder of patients with MMIHS and suggested that a degenerative disease of smooth muscle cells could be the cause of this syndrome. Several subsequent reports have confirmed evidence of intestinal myopathy in MMIHS.[57,80,81] Ciftci and coworkers[57] reported a case without vacuolar degeneration but with excessive smooth muscle glycogen storage. They postulated that the pathogenesis involves a defect of glycogen-energy utilization. Other investigators have reported absence or marked

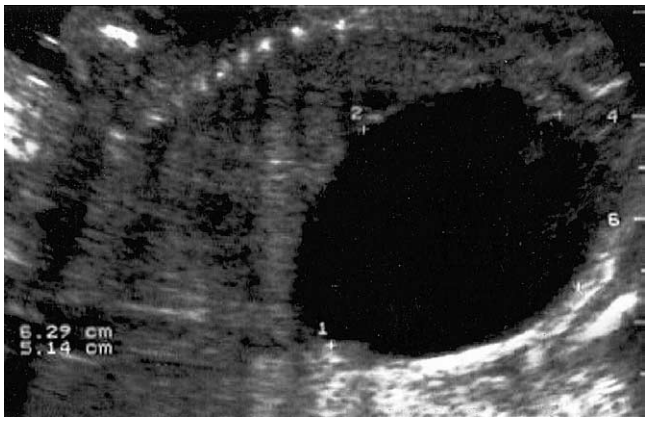

Figure 1 Large fetal bladder seen on a longitudinal view of abdominal ultrasound at 22 weeks gestation. The fetus is in prone position.

reduction in α-smooth muscle actin and other contractile and cytoskeletal proteins in the smooth muscle layers of MMIHS bowel.[80,81] Contractile and cytoskeletal proteins are important structural and functional components of SMCs and play a vital role in the interaction of the filaments in smooth muscle contraction.

Recent work with transgenic mice lacking certain nicotinic acetylcholine receptor (ηAChR) subunits, which show some of the phenotypic features of MMIHS suggests a basis for this condition. Xu and coworkers[88,89] produced MMIHS phenotype in $\beta 4/\alpha 3$ (two of the seven neuronal nicotinic acetylcholine receptor subunits) knockout mice. The $\alpha 3$ and $\beta 4$ subunits have been localized to human chromosome 15. Recently, Richardson and coworkers[74] performed in situ hybridization and immunocytochemistry studies to examine if $\alpha 3$ mRNA or $\alpha 3$ subunit protein were expressed in the resected specimens of small bowel from patients with MMIHS. They found lack of $\alpha 3$ ηAChR staining in most MMIHS tissues, thus suggesting that the absence of functional $\alpha 3$ subunit containing ηAChR may provide a possible explanation for the underlying pathogenesis of MMIHS.

Prenatal diagnosis

Fifty-four previous reports have described fetal ultrasound findings associated with MMIHS. The most frequent finding was enlarged bladder (88%) (Figure 1), with hydronephrosis seen in 31 patients (57%).[63,72,84] Normal amniotic fluid volume was revealed in 32 cases (59%), increased volume in 18 (33%) and decreased volume in 4 (7%). In 3 cases (5%)[19,36,52] abdominal distention caused by dilated stomach was detected. Three cases of oligohydramnios during the second and early third trimesters were reported,[13,23,46] probably related to the functional bladder obstruction. In 1 case,[46] oligohydramnios changed into polyhydramnios at the end of the third trimester.

Serial obstetrical ultrasonography showed that the earliest finding in MMIHS is enlarged bladder, detectable from 16 weeks of gestational age. A later finding is hydronephrosis, caused by the functional obstruction of the bladder. Usually polyhydramnios develops late, appearing during the third trimester.

Clinical presentation

Of the 182 cases reported in the literature, sex of the patient was mentioned in 149 patients. Ninety-eight were females and 43 were males. In 4 cases, pregnancy was terminated after ultrasonography detected MMIHS, which was confirmed at autopsy in all cases. The duration of pregnancy was reported in 98 cases. Fifty-eight patients (59%) were born at term, 25 (25.5%) at 36 to 39 weeks of gestation, 12 (12%) at 32 to 35 weeks and 3 (3%) at 31 weeks and less. Dystocia delivery caused by abdominal distention was reported in 8 cases. In four cases Caesarean section was required[14,33,36,45] and in four cases the bladder was so distended that the baby could only be delivered vaginally after removal of 250, 500, 650, 500 mL of urine, respectively, from fetal bladder by paracentesis.[2,39,43,56] The mean birth weight was normal (3 kg) for gestational age.

The clinical symptoms of MMIHS are similar to other neonatal intestinal obstructions. Characterized by abdominal distention, bile-stained vomiting and absent or decreased bowel sounds, abdominal distention was a constant and early finding. A consequence of the distended, nonob-

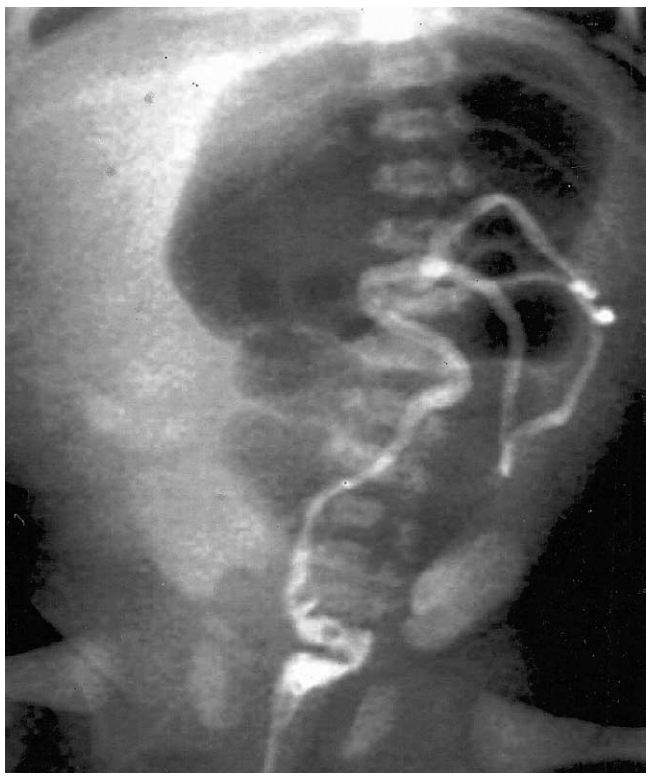

Figure 2 Voiding cystourethrogram showing a massively enlarged bladder in an MMIHS patient.