19.1 Introduction

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 nonobstructed urinary bladder, microcolon and decreased or absent intestinal peristalsis [1]. Usually incomplete intestinal rotation and shortened small bowel are associated.

19.2 Pathogenesis

MMIHS was first described in 1976 by Berdon et al. 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 [11].

Histological studies of the myenteric and submucosal plexuses of the bowel of MMIHS patients have found normal ganglion cells in the majority of patients, decreased in some, and hyperganglionosis and giant ganglia in others [63]. An imbalance between several kinds of intestinal peptides has been suggested as one of the possible causes of hypoperistalsis in MMIHS patients [39, 60]. Recently, Piotrowska et al. [81, 87] reported absence of interstitial cells 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 et al. [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 SMCs could be the cause of this syndrome. Several subsequent reports have confirmed evidence of intestinal myopathy in MMIHS [57, 80, 81]. Ciftci et al. [57] reported a patient 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 the absence or a marked 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 (nAChR) subunits, which show some of the phenotypic features of MMIHS suggests a basis for this condition. Xu et al. [88, 89] produced a MMIHS phenotype in beta 4/alpha3 (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 et al. [74] carried out in situ hybridization and immunocytochemistry studies to determine whether alpha 3 mRNA or alpha 3 subunit protein was expressed in the resected specimens of small bowel from patients with MMIHS. They found lack of α3 nAChR staining in most MMIHS tissues, thus suggesting that the absence of functional α3 subunit containing nAChR may provide a
possible explanation for the underlying pathogenesis of MMIHS.

19.3 Prenatal Diagnosis

There are 54 previous reports describing fetal sonography findings associated with MMIHS. The most frequent finding was enlarged bladder (88%), with hydrenephrosis seen in 31 fetuses (57%) [63, 72, 84]. Normal amniotic fluid volume was revealed in 32 fetuses (59%), increased volume in 18 (33%) and decreased volume in 4 (7%). In three fetuses (5%) [19, 36, 52] abdominal distension caused by a 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 one fetus [46], oligohydramnios changed in polyhydramnios at the end of the third trimester.

Serial obstetric ultrasonography showed that the earliest finding in MMIHS is an enlarged bladder, detectable from 16 weeks of gestational age (Fig. 19.1). A later finding is hydrenephrosis, caused by the functional obstruction of the bladder. Usually polyhydramnios develops late, appearing during the third trimester.

19.4 Clinical Presentation

Of the 182 patients reported in the literature, the sex of 141 patients was mentioned: 98 were female and 43 were male. Four pregnancies were terminated after ultrasonography had detected MMIHS, which was confirmed at autopsy in all cases. The duration of 98 pregnancies was reported: 58 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 or less. Dystocia caused by abdominal distension was reported in eight cases. In four cases cesarean 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 and 500 ml of urine, respectively, from the 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 those of other neonatal intestinal obstructions. Abdominal distension is a constant and early finding; other symptoms include bile-stained vomiting and absent or decreased bowel sounds. A distended, nonobstructed urinary bladder can be relieved by catheterization. Of 182 infants, 61 had bilious vomiting and 23 failed to pass meconium. The majority of patients were not able to void spontaneously.

A total of 19 sets of siblings affected with MMIHS have been reported—18 families had two affected siblings and 1 had three. Four sets of affected siblings were born to consanguineous parents [20, 29, 36, 37]. Consanguinity was also present in the parents of an affected child [52] born to a member of the family reported by Penman and Lilford [36]. In three further reports an older sibling of an affected child died just after birth because of intestinal obstruction [5] or multiple abnormalities [34, 54]; another sibling of an affected child was affected by prune-belly syndrome [16]. The occurrence of MMIHS in 19 sets of affected siblings together with consanguinity in four sets of parents suggest an autosomal recessive pattern of inheritance [29, 36, 52].

19.5 Radiological Findings

Radiological evaluation usually suggests the diagnosis of MMIHS. Plain abdominal films showed either dilated small-bowel loops or a gasless abdomen with evident gastric bubble. An enlarged urinary bladder was present in all patients who had cystography or ultrasonography (Fig. 19.2). Cystography showed vesicoureteral reflux in eight patients [6, 10, 19, 62, 63] and a urachal remnant in one patient [16]. Intravenous urography or ultrasonography detected unilateral or bilateral hydrenephrosis in 84 patients [62, 63]. In one patient ultrasonography detected a dysplastic right kidney [44]. One patient had bilateral duplex kidneys [82]. Among 44 patients who had an upper gastrointestinal series both before and after laparotomy, hypo- or aperistalsis in the stomach, duodenum and small bowel was a constantly detected symptom. In three patients reverse peristalsis from the small bowel into the stomach was also observed [1–11]. In two patients hyperperistalsis was associated with gastroesophageal reflux [7, 28] and in one patient the esophagus was aperistaltic [46]. Barium enema showed microcolon in all 71 patients in whom this study was performed (Fig. 19.3); in 39 patients malrotation was associated.