The Effect of the Number of Open Vertebral Segments on the Prognosis of Newborns with Midline Closure Defect: A Single Surgeon, Single Center Experience

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ABSTRACT

AIM: To investigate the effect of the number of open vertebral segments on the prognosis of newborns with midline closure defects (MCD), and the optimal timing for ventriculoperitoneal shunt (VPS) placement in those with MCD accompanied by hydrocephalus.

MATERIAL and METHODS: A total of 63 patients (35 girls and 28 boys) were admitted to the neonatal intensive care unit between April 2016 and January 2019. The patients' MCDs were examined in terms of type, localization, number of open vertebral segments, accompanying hydrocephalus (HC), surgical technique, and complications.

RESULTS: The mean follow-up period was 12 months (6-24 months). Ten cases of meningocele (M) (15.9%), 41 cases of myelomeningocele (MM) (65%), and 12 cases of encephalocele (E) (19.1%) were identified. A VPS was inserted in 44 (69.8%) patients (E, 8; MM, 34; and M, 2), performed in 33 patients during the same admission, while 11 were shunted after discharge during the follow-up period. Thirty-four of the 41 cases of MM and all cases of M and E were primarily closed, while the remaining MMs required skin flaps. The M and MM cases were categorized according to the number of open vertebral segments and examined in terms of neurological deficit, length of hospital stay, and complications.

CONCLUSION: In all pediatric cases, case-by-case evaluation, attention to hypothermia and meticulous hemostasis, protection of functional neural tissue, closing the defect as soon as possible, and treating accompanying HC during the same session, were considered. Additionally, the neural tissue density correlated with the number of open vertebral segments and it was considered prognostically more valuable.

KEYWORDS: Newborn, Midline closure defect, Hydrocephalus, Surgical treatment

ABBREVIATIONS: MCD: Midline Closure Defect, **M:** Meningocele, **MM:** Myelomeningocele, **E:** Encephalocele, **VPS:** Ventriculoperitoneal shunt, **HC:** Hydrocephalus, **ETV:** Endoscopic third ventriculostomy

■ INTRODUCTION

Midline closure defects (MCDs) are congenital malformations that still exist despite modern medical technologies. They cause heavy social and economic problems to the society (9,37). MCDs appear in the first weeks of embryogenesis due to the closure defects occurring in the brain, spinal cord, and spine (1,25,37). An encephalocele (E) is formed as a result of the neural tube not closing in the early period, and a failure of closure in the later period of embryogenesis leads to a meningocele (M) or a myelomeningocele (MM) (4). In E, neural tissues usually herniate into the sac due to occipital bone defects (40). MM is the most common form of MCD, with an incidence of 1/1000, and is seen in 4.4-4.6 of 10.000 live births in the USA (38). M is a cystic lesion, and involves the cerebrospinal fluid (CSF) and the dura covered by a membrane, with no neural tissue in the

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sac (9,14). E is a subtype of MM located in the cranium (11,40). The prognosis of these malformations, which are often seen as sac structures, varies according to the size and location of the sac, and accompanying anomalies (1,36). The choice of treatment is surgery. Skin closure, repair of dural defects, and preservation of neurological function are the main goals of surgery, aiming to close the skin defect with restoration of the neural plate and the dura, respectively, after careful preoperative planning for maximum protection of neural functions with care taken for hemostasis and hypothermia. In our study, we aimed to discuss the effect of the number of open vertebral segments on prognosis, and also the ideal timing of ventriculoperitoneal shunt (VPS) placement for accompanying hydrocephalus (HC) in newborns with MCD, in light of the current literature.

■ MATERIAL and METHODS

This study was conducted in accordance with Istanbul Medipol University Ethics Committee (E-10840098-772.02-2658).

Sixty-three neonatal patients with a gestational age of over 36 weeks, birth weight of more than 2500 g, and no apparent accompanying disease were included in the study. All surgeries were performed by the same surgeon at the same center. The cases were evaluated retrospectively, and the MCDs were examined in terms of type, localization, concomitant anomaly, surgical technique, and complications. Newborns with M (Figure 1A-E), MM (Figure 2A-F), and E (Figure 3A-F) were included in the study and followed up for at least 6 months (range, 6-24 months). Patients with severe anomalies related to other organ systems were excluded.

The patients' spinal magnetic resonance imaging (MRI) scans were evaluated and they were divided into two groups according to the number of open vertebral segments. Group

1 included patients with one or two open vertebral segment anomalies (Figure 4A-G) and Group 2 included those with three or more open vertebral segment anomalies (Figure 5A-I). When all the spinal MRIs of the newborns were examined, some of the sacs were very large, despite being accompanied by small defects, making surgical treatment more reasonable. Therefore, as previously stated, newborns were grouped according to the number of open posterior vertebral segments.

Physical and neurological examinations, including height, weight, and head circumference of the newborns, were evaluated. Blood urea and creatinine levels, and urogenital ultrasonography (USG) were performed to detect urological abnormalities. Complete blood count, routine erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) values were evaluated for infection. The MRIs were examined to evaluate the sac content and the presence of additional spinal anomalies in all patients. Patients with low birth weight and germinal matrix bleeding were excluded from the study. All surgeries were performed under general anesthesia with an intravenous antibiotic injection 30 minutes before surgery. The antibiotic was continued for 72 hours after the surgery. Spinal and cranial MRI or computed tomography (CT) scans were evaluated, and the sac size, number of defective segments, accompanying HC, and additional anomalies were analyzed. In addition, in newborns with accompanying HC with an Evan's rate of over 50%, two medium-pressure VPSs (*Novus*TM*, Integra®, NJ, USA*) were placed during the same session after repairing MCD. Duration of hospitalization, antibiotic treatment, and morbidity were evaluated according to patient characteristics. Prognosis and complications were recorded during the follow-up.

Statistical Analyses

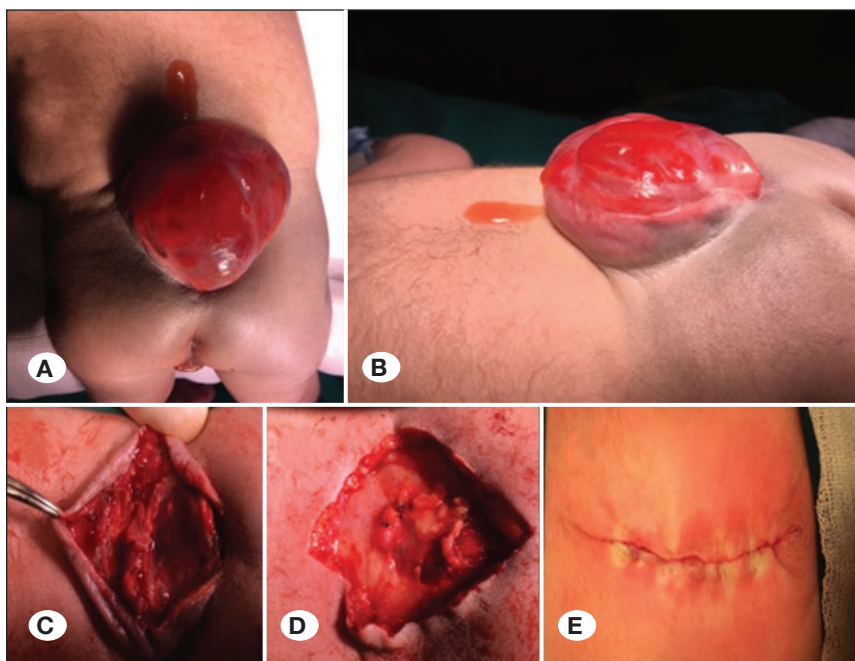Raw data were analyzed using a demographic statistical

Figure 1A-E: Lumbar meningocele. Preoperative **(A, B)**, intraoperative **(C, D)** and posteoperative images.

method. Mann-Whitney U, chi-square, and Fisher's exact tests were used. The confidence interval was 0.95, and statistical significance was set at p<0.05. PSPP (a free software application for analysis of sampled data, intended as a free alternative for IBM SPSS Statistics) and Microsoft Excel were used.

■ RESULTS

Demographics, anatomical localization of the sac, accompanying HC, and VPS complications in newborns are presented in Table I. Our patients were predominantly newborns with MM (65%, n=41). M and MM were
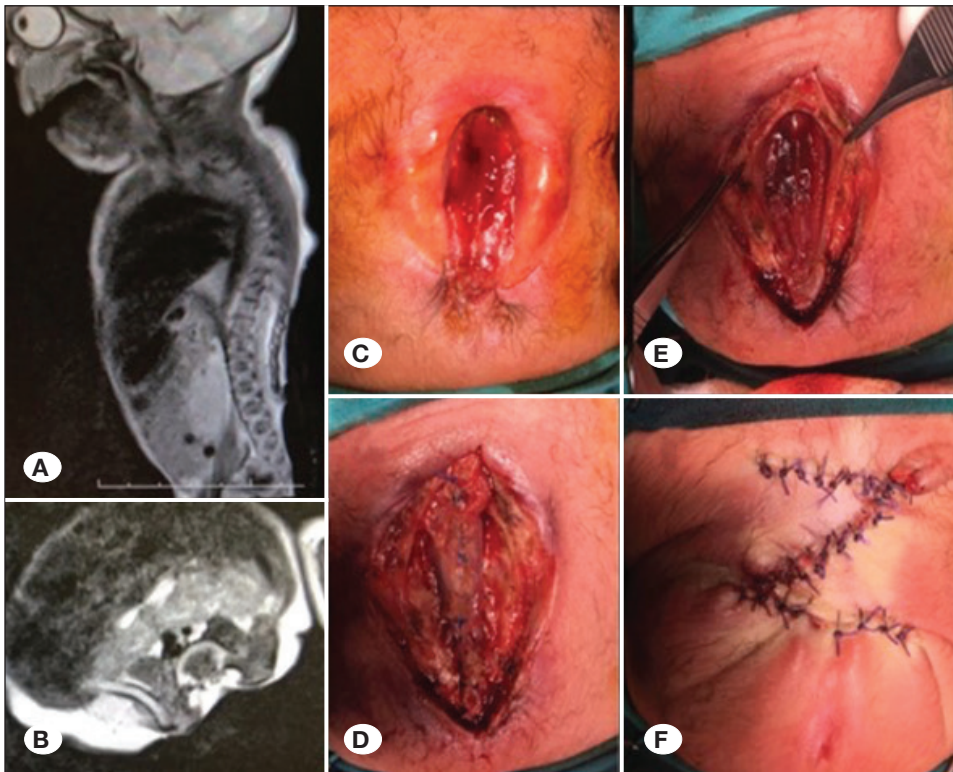

Figure 2: Lumbar myelomeningocele. T2-weighted sagittal **(A)**, and axial **(B)** magnetic resaonance imaging studies. Preoperative **(C)**, intraoperative **(D, E)**, and postoperative **(F)** images.
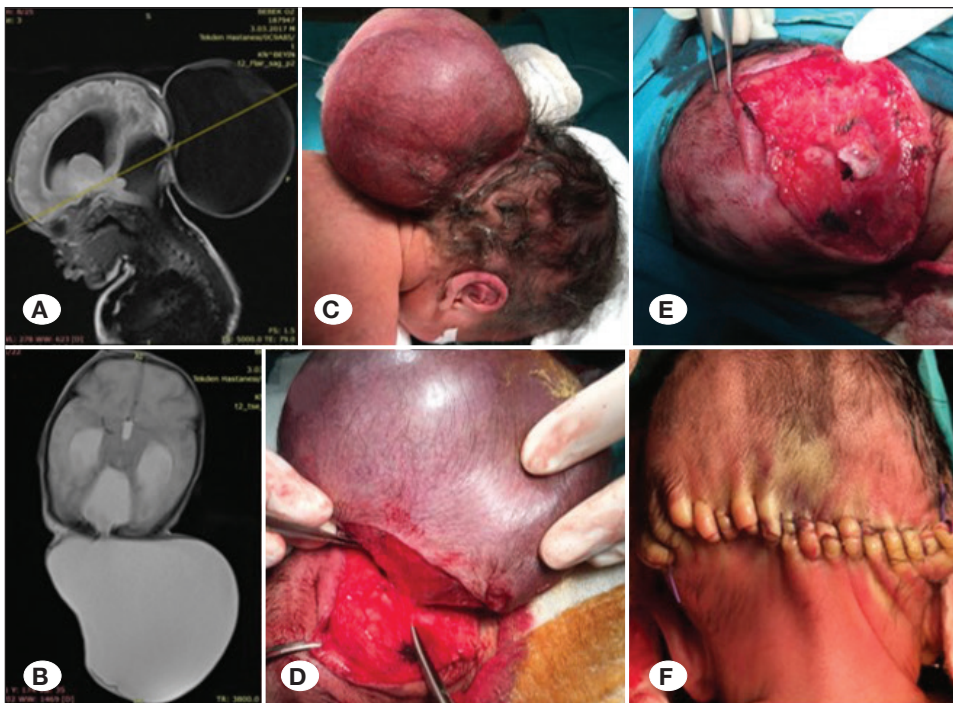

Figure 3: Occipital encephalocele. T1-weighted sagittal **(A)**, and T2-weighted axial **(B)** magnetic resonance imaging studies. Preoperative **(C)**, intraoperative **(D, E)**, and postoperative **(F)** images.
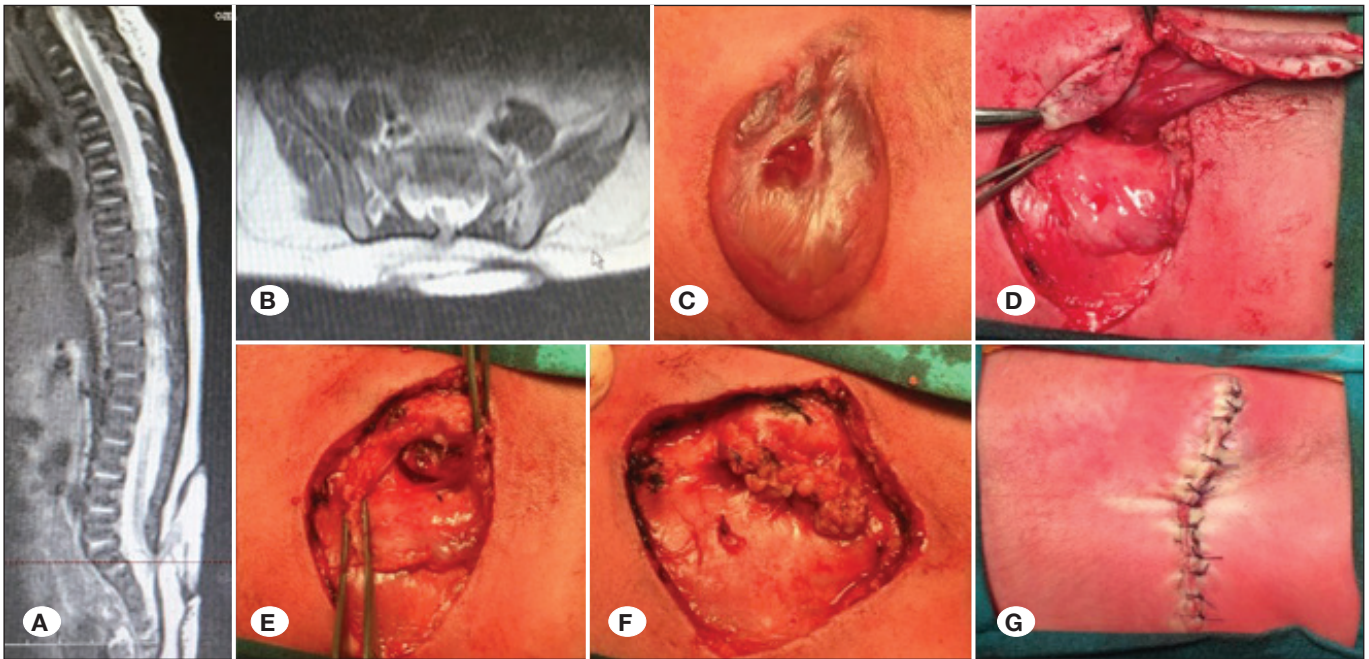
Figure 4: Group 1. T2-weighted sagittal **(A)**, and axial **(B)** magnetic resaonance imaging studies. Preoperative **(C)**, intraoperative **(D, E, F)**, and postoperative **(G)** images.
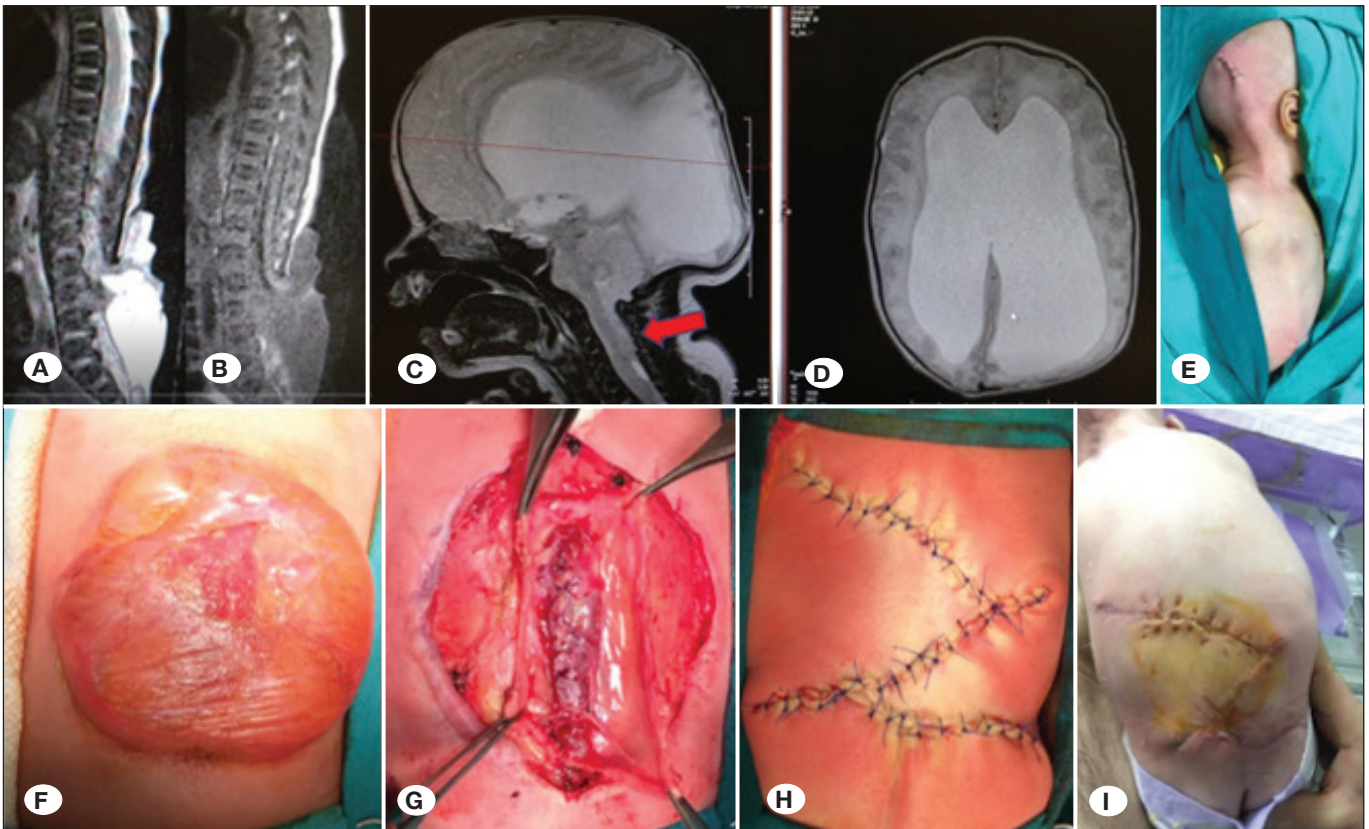

Figure 5: Group 2. T2-weighted **(A)**, and T1-weighted **(B)** lumbar, sagittal magnetic resonance (MR) imaging studies. T2-weighted sagittal **(C)** (red arrow shows tonsillar herniation), and axial **(D)** MR images. **E)** Postoperative image after ventriculoperitoneal shunt surgery. Preoperative **(F)**, intraoperative **(G)** and postoperative images **(H, I)**.

predominantly localized in the lumbar region (64.7%, n=33). HC was detected in 82.9% (n=34) of MM cases; this rate was 65.9% (n=27) at birth. Likewise, VPS was placed in 66.6% (n=8) of E cases; this rate was 41.6% (n=5) at birth. Additionally, VPS surgery was performed in 2 (20%) of the 10 M cases; this rate was 10% (n=1) at birth. In total, we performed VPS surgery in 44 patients (69.8%), and shunt complications occurred mostly in patients with MM (29.3%, n=12). The most common complications were wound dehiscence (36%, n=16) and proximal end obstruction of the VPS (15.9%, n=7).

With respect to open vertebral segments, the number of cases, neurological conditions of newborns, duration of hospitalization, and complications are shown in Table II. There were 30 patients (58.8%) in Group 1 and 21 patients (41.2%) in Group 2. When the neurological signs of the newborns were examined, the neurological deficit rate in Group 1 was 53.3% (n=16) and 76.2% (n=16) in Group 2. Wound dehiscence and CSF leakage were found to be increased in Group 2, which naturally increased the length of hospital stay and antibiotic administration period, and significantly reduced complication rates in Group 1 (p=0.0001, p=0.001, and p=0.012, respectively).

Table I: Characteristics of Cases

	Meningocele		Myelomeningocele		Encephalocele		p	Total	
Number of cases (n)	10		41		12			63	
Gender (female / male)	6 / 4		17 / 24		5 / 7		0.41	28 / 35	
Sac location	C - 1 T - 2 L - 7 LS - 0		C - 2 T - 6 L - 26 LS - 7		-		0.52	C - 3 T - 8 L - 33 LS - 7	
[a]**Hydrocephalus (at birth)**	1		27		5		**0.005**	33	
[b]**Hydrocephalus (at follow-up)**	1		7		3		0.65	11	
Hydrocephalus (total)	2		34		8		**0.001**	44	
Primary sutured cases	10		34		12		0.12	56	
Complications (VP shunt)	a	b	a	b	a	b		a	b
- Proximal obstruction	0	0	4	1	1	1		5	2
- Distal obstruction	0	0	2	0	2	0		4	0
- Valve failure	0	0	0	1	0	0		0	1
- Infection	1	0	3	1	1	0		5	1
- Wound dehiscence	0	1	7	5	1	2		8	8

C: Cervical, T: Thoracal, L: Lumbal, LS: Lumbosacral, a: Hydrocephalus at birth, b: Hydrocephalus at follow-up.

Table II: Characteristics of Cases according to Open Anomaly Vertebral Segment Prevalence

	Group 1	Group 2	p
Number of cases (n)	30	21	0.21
Neurological condition			
- Paraplegia	6	10	**0.036**
- Paraparesis	7	5	0.97
- Monoparesis	3	1	0.49
Hospitalization (days)	7 ± 3	15 ± 4	**0.0001**
Antibiotic administration (days)	4 ± 2	7 ± 3	**0.001**
Complications	8	13	**0.012**
- CSF leak	0	2	0.16
- Wound infection	1	6	**0.015**
- Wound dehiscence	7	5	0.97

◼ DISCUSSION

Closure of MCD and associated HC management are two of the most basic, but never simple, features of pediatric neurosurgery. MMs have been reported to be five times more common than M and are more common in girls than in boys (18,19,24). In our study, the incidence of MM was four times higher than that of M, and MM was more common in girls (male: 44.4%, n=28; female: 55.5%, n=35). In our MM cases, the F/M ratio was 1.4/1, while it was 1.2/1 in Musluman et al.'s series (36).

It has been reported that the lumbar region is the most common location for MM (1,14,25). Faraj et al. reported that 60% of MMs were located in the lumbar region (15). In our study as well, the lumbar region was the most common location for MM (63.4%, n=26).

Neurological, orthopedic, and urological anomalies may be associated with MM. The most common one is HC, occurring at a rate of 80%-90% (41). Therefore, in this section, we particularly focus on the associated HC (excluding other related symptoms, such as urologic and orthopedic anomalies). Eseoglu et al. reported that HC often coexists in patients with MM, and they detected HC in 73.4% of their cases (14). Müslüman et al. reported that 62.3% of cases with MM were accompanied by HC (36). Among our cases, 82.9% (n=34) of MM were accompanied by HC. In MM, HC can occur at the time of birth or later during growth and development because of craniocervical junction anomalies and/or Sylvian aqueduct stenosis (5). Although 27 (65%) of our 41 patients with MM had VPS placement at birth, HC was detected in seven patients in the 1st month of follow-up.

Surgery is the treatment of choice for the management of MM. Intrauterine surgery aims to minimize the prolonged time of contact between the amniotic fluid and the sac, reducing the risk of brainstem herniation and nerve root irritation, thereby decreasing the risk of development of postpartum HC (16,35). Early randomized controlled studies have suggested that MM patients benefit from prenatal surgical treatment (6,16). Moron et al. reported a 70% success rate in Chiari malformations using open fetal surgery, with extremely low surgical failure and perinatal mortality rates, and no maternal mortality or serious maternal morbidity (35). There are also studies reporting the risk of preterm labor, abortion, and premature rupture of membranes in intrauterine fetal surgery (29,35).

Although there are many opinions on the timing of postpartum surgical treatment in the literature, the most common has been to perform surgery in the first 72 hours, under suitable conditions (14,15,21,25,36,43). Early (in the first 72 hours) radical surgical approach (sac repair and VPS placement in the same session in appropriate cases) in newborns with MM reduces morbidity and mortality rates, causes lower infection rates, and reduces the length of stay (14,25,41). Ulsenheimer et al. reported that correction of MM should be performed as soon as possible, preferably in the first 72 hours, and they stated that the 14 patients who had developed infection in their 31 patient-series had developed it due to delayed timing of surgery, and that they reduced the morbidity rate with

appropriate antibiotic therapy (43). Jabaiti et al. divided their patients into two groups as early- and late-operated, in an MM series of 48 cases (23). They reported infection rates of 19.5% (in 2 of 19 patients) in the early repair group and 20.7% (6 of 29 patients) in the late repair group (23).

Another challenging topic is the management of HC in newborns, particularly when it is complicated with MCD and/ or other accompanying anomalies. In a recent meta-analysis study of medical records between and 1998-2014, McCarthy et al. stated that shunt malfunction and infection rates did not differ between delayed and simultaneous HC treatment, although recently, HC treatment has become more delayed. Additionally, they proposed that inpatient HC treatment failure rate was twice as high in patients who received endoscopic third ventriculostomy (ETV) treatment. This supports the argument that the effectiveness of ETV in children under 1 year of age is still controversial (30). Recently, in a case series consisting of 45 newborns (35.7%) and 81 infants (64.3%), Salem-Memou et al. reported that VPS was the first-line treatment in newborns (68.8%), while ETV was the preferred approach in infants (74.1%), with an overall complication rate of 26.1% (57.6% for VPS and 4.1% for ETV) (39). Moreover, in a systematic review, Blount et al. ascertained that there was insufficient data to conclude that ventricular size and morphology affect neurocognitive development (7). We operated on our cases as soon as possible in the first 72 hours (range, 1-9 days). In the presence of accompanying HC, we placed VPS in the same session. Despite performing the surgery as soon as possible and using appropriate prophylactic antibiotics, the infection rate was 13.6% (n=6). In some studies, the mortality rate of patients with MM was reported to be approximately 14% (27,31). Gross et al. reported no mortality in their series (19). This rate was 32% in a series by Mirzai et al. (33). No mortality was observed in the present study.

We believe that although a prognostic correlation with the diameter of the sac and the neural content present in the sac has been reported, the neck of the sac is also an important prognostic factor, depending on the number of vertebrae involved, just like the importance of the neck of an aneurysm while planning the treatment of a cerebral aneurysm. In the literature, we did not encounter any study examining the effect of the number of open vertebral segments on the prognosis of M and MM. However, there are some studies concerning the effect of sac diameter and sac localization on prognosis (14,36). In their series of 64 cases, Eseoglu et al. reported that sac localization had no effect on prognosis. However, the diameter of the sac and the presence of neural tissue within the sac are important prognostic factors (14). Müslüman et al. reported that babies with a sac smaller than 25 cm^2 could be operated on without the need for a flap, resulting in a lower risk of infection, shorter hospitalization period, and better prognosis (36). Additionally, with respect to fetoscopic sac repair, Corroenne et al. concluded that prenatal repair of patients with large NTD (over 170 mm^2 at referral for the evaluation of a prenatal NTD repair) presented a lower proportion of hindbrain herniation reversal 6 weeks after surgery, a higher risk of dehiscence, and a higher need for postnatal repair (12). In our study, patients with smaller

sacs were classified as Group 1, which had a significantly better prognosis than Group 2, similar to other studies in the literature. We also found that as the number of involved vertebrae increased, the neural tissue content that migrated into the sac also increased. All of our M cases were classified as Group 1. Our MM cases were more commonly found in Group 2; therefore, pathological findings on neurological examination were more frequent in Group 2 than in Group 1 (paraplegia, p=0.036). We found that the number of open vertebrae was strongly correlated with prognosis and that the duration of hospitalization was significantly lower in Group 1 than in Group 2 (p<0.0001).

Encephalocele is a MCD that develops due to closure defects of the calvarial bones at various stages and locations, frequently in the occipital bone (27,32). The meningocele sac contains only CSF, and the additional presence of cerebral or cerebellar tissue present makes it an encephalocele (32). It can be found with HC as well (11,27,32). In a series of encephalocele patients, Shokunbi, Chapman, Lorber, and Mealey reported associated HC rates of 16%, 50%, 65%, and 36%, respectively (11,27,32,40). HC was present in 66% of our encephalocele cases.

Split cord malformations may accompany MMs; however, they are often underdiagnosed, and patients may be discharged without appropriate treatment (18,38). Iskandar et al. reported that in their MM series, 6% of patients had accompanying split cord malformation (22). None of the patients in our study had split cord malformations. However, we detected type II Chiari malformation in 17 cases (26.9%) and type II Chiari malformation accompanied by holocord syringohydromyelia in one patient with MM.

Neurological deterioration, wound infection, CSF leakage, shunt infection, and acquired Chiari malformations are the main complications of MM surgery (1). Anegbe et al. reported that infection of the neural placode, HC, location of the lesions above the lumbar region, and surgical repair were statistically significant risk factors for intracranial infection among myelomeningocele patients (3). The incidence of shunt complications has been found to be 22.6%-66% in the first year after surgery for MCD and VPS (2,10,13,17,20,26). ETV was proposed for avoiding shunt-related complications. Although ETV was associated with a statistically significantly lower risk of procedure-related infection compared to shunts, the mortality, CSF leak, and reoperation rates were similar between ETV and shunt groups for pediatric HC in a systematic literature review including a search of PubMed (Medline) and Cochrane until October 2018 (42). Furthermore, Zhao et al. proposed ETV for patients younger than 3 years with obstructive or communicating HC in the event of shunt malfunction with a 40.5% (15/37) overall ETV failure rate (44). Alatas et al. evaluated 52 patients with myelomeningocele. Thirty-one patients required placement of VPS, and seven patients (22.6%) underwent shunt revision within the first year of life (2). Caldarelli et al. found at least one shunt malfunction in 45.9% of patients (78/170) during the 1-year postoperative observation period (8). Regarding the aspect of reducing shunt infection rate, Mohamed Moussa et al. stated that injection of prophylactic vancomycin and gentamicin in and around the shunt hardware significantly reduced the incidence of postoperative shunt infection in congenital HC patients who underwent VP shunt insertion (34). In our series, we detected shunt-related complications in 20 patients (45.5%), excluding a case of wound dehiscence that was repaired under local anesthesia. Although this rate is similar to those reported in the literature, it was found to be slightly higher. This could be due to simultaneous MCD repair and VPS placement in 75% of our patients in our study. According to the literature, the timing of VPS placement in patients with midline closure defects is controversial (4,28). However, this will be the subject of another planned study.

■ CONCLUSION

The duration of operation, length of stay, and morbidity rates in Group 1 MCD patients were lower than those of Group 2 MCD patients, according to the number of MCD-affected vertebrae. The neurological findings in Group 1 were closer to normal. In Group 2 (patients with an anomaly involving three or more levels of vertebrae), complications such as infection and CSF leakage were found to be increased, causing increased length of stay and morbidity rates. In M and MM, the density of the neural tissue in the sac and the number of affected vertebrae were negative prognostic factors. In pediatric cases, the major points of concern are avoiding hypothermia and maintaining hemostasis while preserving neural tissue, closing the defect as soon as possible, and placing VPS if there is accompanying hydrocephalus during the same session. This study represents a limited sample of newborns with MCD. Multicentered prospective studies, including a larger patient series, are required.

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