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A Histopathologic Study of Neural tube defects in children at a tertiary care centre

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Abstract

Introduction: Neural tube defects (NTD) are one of major congenital anomalies that may cause variable morbidity in a child. Failure of normal induction during 3rd -4th week due to multifactorial reasons leads to these congenital defects. The commonly known NTDs are anencephaly and spina bifida which includes meningocele and meningomyelocele. At our tertiary care centre, we do see good number of patients with meningocele and meningomyelocele. We went back to study the different anatomical sites and morphology of meningomyelocele and meningomyelocele over the period of 12 years. Aim- To study the clinicodemographic characteristics and histopathological features of meningocele and meningomyelocele at our centre.

Material and methods: Our study was a retrospective prospective study conducted over a period of 12 years at the Department of pathology, TNMC and BYL Nair CH hospital, Mumbai. A total number of 54 cases of meningocele and meningomyelocele in children < 18 years of age received over a period of 12 years were studied. Clinicodemographic details were noted and review of histopathology slides was done. The data was analysed by the corresponding author and the co-authors.

Results: Our study comprised of 54 cases of which, 30 were meningocele and 24 meningomyelocele. The male to female ratio overall was 1.03:1. Majority of the cases were seen in less than one month followed by 1 month-6 months. The most common anatomical site was lumbosacral. Histopathology revealed, loss of epidermal appendages in 61.11%. Fibrosis, presence of immature adipose tissue and increased vascularity were more commonly seen.

Conclusion: The spectrum of histopathological aspects of spina bifida, consisting of ectoderm, neuroectoderm

and mesoderm is needed for better understanding of these defects.

Keywords: Histopathology, Meningocele, Meningomyelocele.

Introduction

Neural tube defects (NTD) are classified into cranial dysraphism and spinal dysraphism. Cranial dysraphism leads to the meningo-encephalocele or anencephaly. While meningomyelocele is a form of spinal dysraphism.(1) Meningocele is the herniation of dura and arachnoid through a defect in the vertebral column. While in meningomyelocele, spinal cord and nerve roots also becomes a part of herniated sac. (2)

The prevalence of neural tube defects is 1-2 per 1000 neonates in the world. (1) There are multiple causes of NTDs. Poor maternal nutrition and exposure to radiation leads to high chance of these congenital malformations. Others like drugs (valproate), malnutrition, low red cell folate level, maternal diabetes and obesity and genetic causes like abnormality in folate dependent enzyme pathways, mutation in folate response also have adverse effect on the CNS development. (3)

The neural tube develops in the 3rd week of development by the induction of notochordal plate and the intraembryonic mesoderm. Failure of normal induction cause NTDs and disorders of prosencephalic development. Therefore, maternal prenatal screening in the 1st and 2nd trimester identifies pregnancies at risk for NTD. (3) The screening test for NTD according to the American college of medical genetics and genomics (ACMG) is high levels of maternal serum Alpha feto protein (msAFP) in the early 2nd trimester can be done. The diagnostic test suggested is elevated AFP and acetylcholinesterase in amniotic fluid along with identifying the lesion on ultrasound examination. (4)

Grossly meningocele is a discoid partially skin covered mass. There is a smooth, glistening and membranous inner surface with a narrow pedicle representing cystocele's attachment with the spinal canal. Microscopically the sac proper is made up of collagenous tissue with meningothelial cells around the alveolar spaces, irregular clefts and in nests and cords. It may form whorls and psammoma bodies. Proliferation of nerve twigs, smooth muscle bundles and blood vessels can be seen in the sac wall. (5,6) Lipomeningocele is the accumulation of mature adipose tissue along with other findings as mentioned. (5)

Meningomyelocele is grossly seen as a translucent blue dome. The enclosed spinal cord and nerve roots can be seen through it. Contents are spinal cord, meninges, ganglia or the nerve roots, hyalinised connective tissue with blood vessels. (6) The presence of neuroglial tissue in any form with the nests of glia in the cyst wall is a feature of meningomyelocele. Similarly, lipomeningomyelocele contain mature adipose tissue, skeletal tissue and nephrogenic tissue rests. (5)

The right time for surgery is within a day or few days is the mainstay to avoid infections that can be lethal and to prevent morbidity and complications such as learning disability, seizures, meningitis or ventriculitis leading to the cognitive dysfunction. (3) The neurological manifestations in such cases are motor or sensory changes, altered bowel and bladder habits, pain and gait disturbances. Externally limb length discrepancy, equinovarus or valgus and unequal feet size can be seen. (7) Malakounides et al studied the long-term complications in 120 spina bifida patients. It was observed that only 1.6% cases had an end stage renal disease or severe renal involvement. (8) This could be

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secondary to the bladder dysfunction due to neural dysfunction.

We herein discuss common age group, sex, anatomical site and histopathological characteristics of meningocele and meningomyelocele.

Materials and methods

This was a retrospective prospective observational study conducted over a period of 12 years in the Department of pathology, TNMC and BYL Nair CH hospital, Mumbai. An institutional ethics committee approval was obtained (ECARP-ECARP/2021/19). All the cases of meningocele and meningomyelocele in children < 18 years of age received from 1st January 2010- 31st December 2021 in the histopathology section were included. There were total number of 54 cases. Data regarding demography, clinical features and histological findings was retrieved.

Results

54 cases were studied. Following were the results obtained and tabulated under different headings and assessed under various parameters.

Meningocele constituted 55.55% and meningomyelocele 44.44% of the total cases. In our study there was a slight male predominance with meningomyelocele but with meningocele the ratio was 1:1. (Table I)

There were 26 cases (48.14%) within 1 month age followed by 11 cases (20.37%) in > 1- 6 months of age. We found 6 cases and 3 cases respectively of meningocele and meningomyelocele beyond 1 year of age. A 12-year-old female presented with a remnant of operated meningomyelocele was the oldest case. (Table II) This reflects the cruciality and urgency of treatment to prevent infections that can cause morbidity and mortality.

The lumbo- sacral site constituting 16 of 54 cases (29.62%) was the most common anatomical site followed by lumbar (25.92%) and sacral (16.66%). Some of these defects were associated with other congenital anomalies like hydrocephalus and Arnold-Chiari malformation. (Table III)

In the histopathological study of MC and MMC the significant features were inflammation, ulceration and absence of skin as seen in 51.85%, 33.33% and 11.11% of cases respectively. (Table IV) (Figure 1) These were important forerunners for infection which can have serious implications. As there is a drain of cases of MMC and MC from within city and beyond city limits for surgery, we do have a large number of cases. It was necessary to study different and common features in these lesions and to get an understanding of the morphology of these lesions.

It is important to note the presence of any immature or neoplastic mesodermal component, which however was not seen in our study. All the neuroendocrine elements seen in our study were mature. There was no evidence of malignancy.

Discussion

Meningomyelocele and meningoceles can have variable tissues within their sacs. Identifying the different tissues and observing their mature appearance is important. Sometimes within the sac, neoplastic tissue, teratomas or even developmental abnormality of fetus in fetu can be found. Infections, ulceration of skin and presence of teratomatous tissue can alter prognosis. We compare our study to the two studies published so far and have presented the comparison in a tabular form. (Table V)

In our study nearly equal number of males and females were born with MC and MMC with a M: F ratio 1.03:1. While Karabagli et al and Bangaru Sandhya et al have

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shown slight female predominance with M: F ratio of 1:1.2 and 1:1.4 respectively. [2,9] Kar et al have also shown female predominance in their study of 16 cases of spina bifida with a M: F ratio of 25:47. [10]

In literature review on myelomeningocele done by Ntimbani et al, the study of G Malakounides et al have shown slight male predominance with M: F ratio 1.1:1 in the Nigerian group which was consistent with our finding showing male predominance in MMC with a ratio of 3:2. [7, 8]

The most common anatomical site was lumbosacral, which was also seen in studies conducted by Karabagli et al, Bangaru et al, Kar A et al and Ntimbani et al. [2,7, 9, 10]

In our study the loss of epidermal appendages and fibrosis (Figure1,2) was seen in 61.11% of cases while both these histologic changes were seen more frequently in studies by Karabagli et al and Bangaru sandhya et al. Presence of inflammation and ulceration was seen only in 51.85% and 33.33% cases respectively while Karabagli et al and Bangaru et al reported inflammation in 84-90% of the cases and ulceration in 56-66% of the cases. [2,9] Neuropil like matrix and meningothelial cells were seen more frequently in studies by Karabagli et al and Bangaru et al is comparison to our study.

Spina bifida is not always seen as a isolated lesion. It can be associated with other congenital anomality at the same or different levels in the spinal cord. Chiari malformation shows association with spina bifida. In this there is a caudal displacement and herniation of cerebellar part, medulla oblongata with a brain stem. This occurs through the foramen magnum which is followed by cerebrospinal fluid outflow obstruction causing hydrocephalus in MC and MMC cases. [1,2]

Thus, in our study hydrocephalus was associated in 3.33% of MC cases. While it was associated in 33% cases of MC in study by Karabagli et al and 22.22% cases of MC in study by Bangaru et al. Chiari malformation was also seen in higher percentage of the cases in studies by Karabagli et al and Bangaru et al. [2,9] In a study of 68 cases of NTDs by Schoner et al 75% of the lumbosacral cases were associated with Chiari II malformation, of which hydrocephalus was seen in 85.4% of cases. [1]

Table 1: Distribution of meningocele and meningomyelocele w.r.t sex.

	M	F	Total	M: F
Meningocele	15	15	30	1:1
Meningomyelocele	14	10	24	3:2
Total	29	25	54	

Table 2: Distribution of meningocele and meningomyelocele w.r.t age.

	< 1month	> 1-6 month	> 6 month- 1YR	> 1 YR	N=54
Meningocele	14	5	5	6	30
Meningomyelocele	12	6	3	3	24
Total	26	11	8	9	54

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Table 3: Distribution of meningocele and meningomyelocele w.r.t anatomical site.			
	MC (n=30)	MMC (n=24)	TOTAL (n= 54)
CERVICAL	01	02	03
CERVICO-THORACIC	01	00	01
THORACIC	03	03	06
THORACO-LUMBAR	01	04	05
LUMBAR	09	05	14
LUMBO-SACRAL	08	08	16
SACRAL	07	02	09
TOTAL			54
ASSOCIATED ANOMALIES			
Hydrocephalus	01	00	
Arnold-chiari	01	01	

Table 4: HISTOPATHOLOGICAL CHARACTERISTICS OF MC AND MMC			
1) EPITHELIAL CHANGES	MC (n=30)	MMC (n=24)	% of 54 cases
Normal thickness	22	22	81.48%
Papillomatous	00	01	1.85%
Hyperplastic	01	01	3.70%
Inflammation	12	16	51.85%
Ulceration	08	10	33.33%
Loss of epidermal appendages	18	15	61.11%
Hyperkeratosis	00	00	-
Absent skin	04	02	11.11%
2) MESODERMAL CHANGES			
Fibrosis	18	15	61.11%
Myxoid change	02	00	3.70%
Subepithelial edema	03	02	9.25%
Increased BV	16	14	55.55%
Smooth muscle bundle	05	02	12.96%
Skeletal muscle	01	00	1.85%
Mature cartilage	02	01	5.55%

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Calcification	00	00	-
Mature adipose tissue	15	08	42.59%
3) NEUROENDOCRINE			
Glial/ neuropil like matrix	00	21	38.88%
Normal ependymal lining	00	08	16.66%
Meningothelial cells	11	13	44.44%
Nerve fibres	11	04	27.77%
Ganglion cells	00	00	-

Table 5: Comparison of MC and MMC.

	OUR STUDY (2023)	KARABAGLI et al (2014)	BANGARU SANDHYA et al (2021)
GENDER	F<M 1:1.03	F>M 1.2:1	F>M 1.4:1
COMMON SITE	Lumbosacral	Lumbosacral	Lumbosacral
HISTOPATHOLOGICAL FEATURES			
Loss of epidermal Appendages	61.11%	93%	91%
Fibrosis	61.11%	90%	89%
Inflammation	51.85%	90%	84%
Ulceration	33.33%	66%	56%
Peripheral nerve fibres/ roots	27.77%	83%	73%
Abnormal/ increased Blood vessels	55.55%	79%	78%
Neuropil like matrix	38.88%	79%	76%
Mature adipose tissue	42.59%	62%	67%
Ependyma/ choroid Plexus	16.66%	35%	-
Meningothelial cells	44.44%	25%	62%
Arrector pili hyperplasia/ hypertrophy	-	18%	29%

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Myxoid changes	3.70%	7%	-
Subepithelial edema	9.25%	7%	11%
Skeletal muscle	1.85%	4%	09%
Calcification	-	4%	-
Mature hyaline cartilage	5.55%	2%	-
ASSOCIATED ANOMALY			
Hydrocephalus	3.33% (MC)	33% (MC) 91%(MMC)	22.22% (MC) 86.6%(MMC)
Chiari II malformation	3.33% (MC) 4.16%(MMC)	22% (MC) 88%(MMC)	6.66% (MMC)

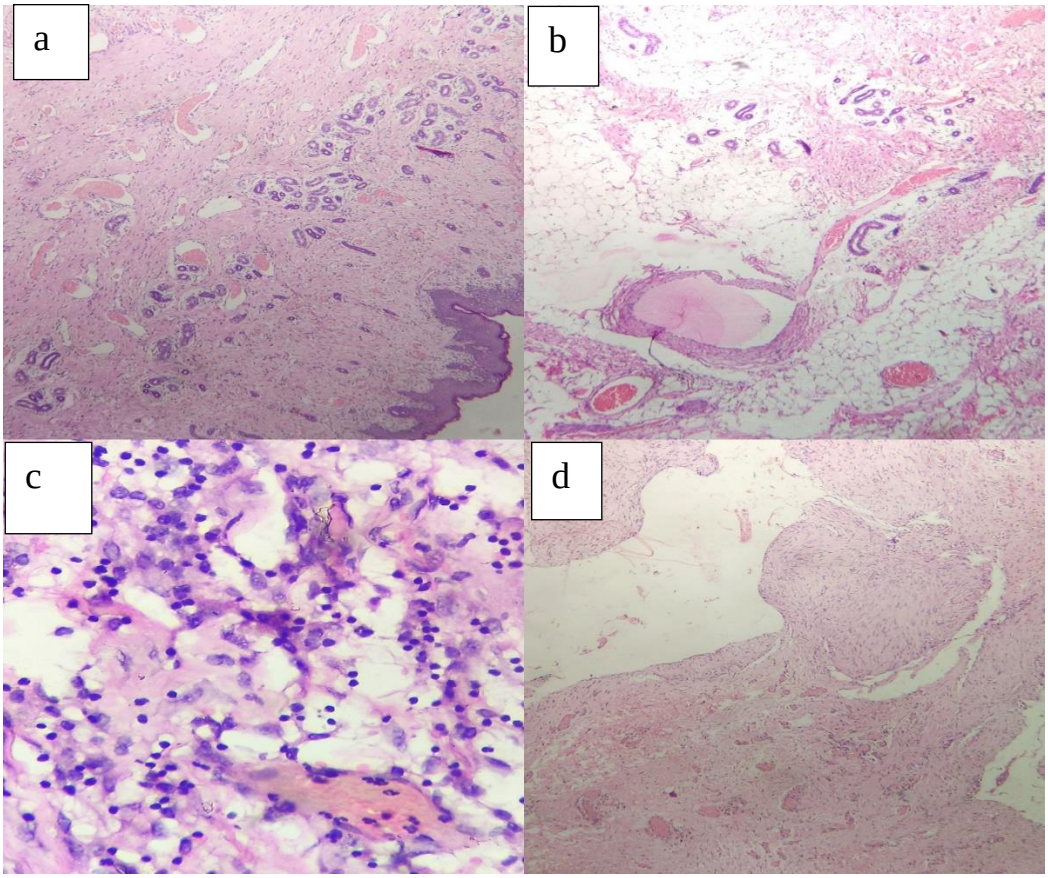

Figure 1: Meningocele, H & E. (a) (10X) and (b) (40X) keratinised stratified squamous epithelium with lobules of mature adipose tissue with adnexal structures. (c) chronic inflammation with increased blood vessels, 10X (d) Fibrous tissue, 10X.

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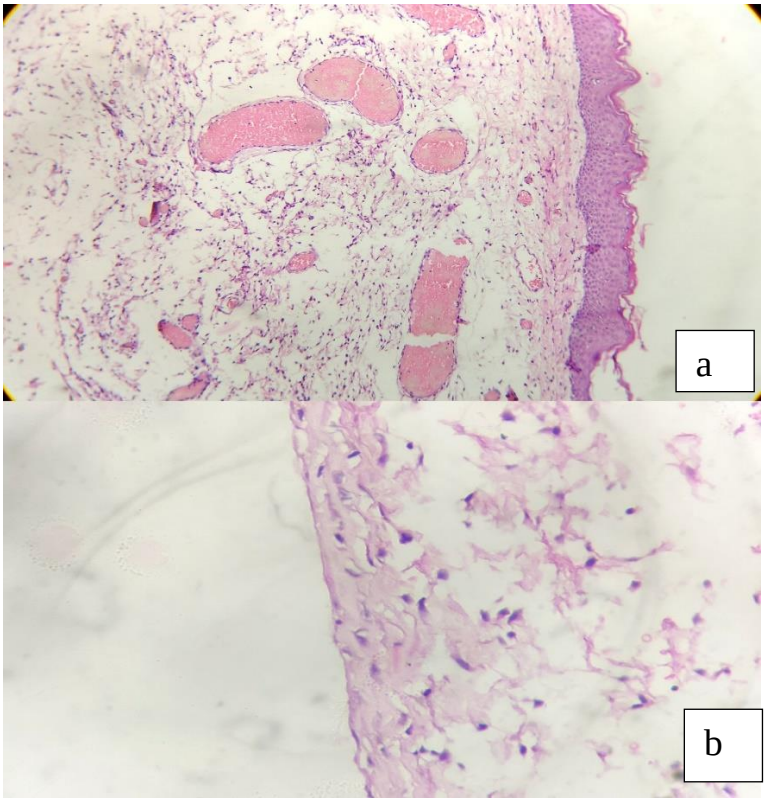

Figure 2: Meningomyelocele, H & E, (a) Loss of epidermal appendages with increased blood vessels, 10X (b) Meningothelial lining, 40X.

Conclusion

Histopathology of spinal congenital malformation can be complex. Awareness about the spectrum of histopathological changes with respect to epidermal, mesodermal and neuroectodermal tissues in cases of spina bifida will help in diagnosis and detailed histopathology reporting in such cases.

Abbreviations:

CNS- central nervous system

NTD- Neural tube defects

MC- Meningocele

MMC- Meningomyelocele

H & E- Haematoxylin and eosin

References

1. Schoner K, Axt-Fliedner R, Bald R, Fritz B, Kohlhase J, Kohl T, Rehder H. Fetal Pathology of Neural Tube Defects - An Overview of 68 Cases. Geburtshilfe Frauenheilkd. 2017 May;77(5):495-507. doi: 10.1055/s-0043-103459. Epub 2017 May 24. PMID: 28579621; PMCID: PMC5444532.
2. Karabagli, Pinar & Gurcan, Tugba & Celik, Esin & Karabagli, Hakan. (2014). Myelomeningoceles and Meningoceles: A Clinicopathologic Study of 43 Cases. Journal of Neurological Sciences. 31. 335-345.
3. Robert M. Kliegman, Joseph W. St. Geme III, Nathan J. Blum, Samir S Shah, Robert C. Tasker, Karen M. Wilson. Nelson textbook of pediatrics. 21st edition. Vol 2. Elsevier Inc., Philadelphia, PA, 2020. Page no.3064-3068.
4. Palomaki GE, Bupp C, Gregg AR, Norton ME, Oglesbee D, Best RG; ACMG Biochemical Genetics Subcommittee of the Laboratory Quality Assurance Committee. Laboratory screening and diagnosis of

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open neural tube defects, 2019 revision: a technical standard of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2020 Mar;22(3):462-474. doi: 10.1038/s41436-019-0681-0. Epub 2019 Nov 8. PMID: 31700163.

5. John R. Goldblum, Laura W. Lamps, Jesse K. McKenney, Jeffrey L. myers. Rosai and Ackermans surgical pathology 11th edition, vol 2. Elsevier Inc.,Philadelphia, PA, 2018. P. 1949-1950.
6. Pant I, Chaturvedi S. Spectrum of histopathology in spinal lesions. Astrocyte 2016; 2:187-99.
7. Ntimbani J, Kelly A, Lekgwara P. Myelomeningocele - A literature review. Interdisciplinary Neurosurgery: Advanced Techniques and Case Management. 2020 Mar; 19:100502. doi: 10.1016/j.inat.2019.100502.
8. G. Malakounides, F. Lee, F. Murphy, S.A. Boddy, Single centre experience: long term outcome in spina bifida patients, J. Pediatr. Urol. 9 (2013) 585–589.
9. Sandhya B, Sabitharani SS, Niharikareddy Y. Spinal Dysraphism- A Histopathological Study of 45 Cases. Journal of Clinical and Diagnostic Research. 2021 Jun, Vol-15(6): EC01-EC04. 10.7860/JCDR/2021/47341.14978.
10. Kar A, Kar T, Kanungo S, Guru L, Rath J, Dehuri P. Risk factors, organ weight deviation and associated anomalies in neural tube defects: A prospective fetal and perinatal autopsy series. Indian J Pathol Microbiol. 2015 Jul-Sep;58(3):285-91. doi: 10.4103/0377-4929.162832. PMID: 26275247.

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