

Original Research Article

Spectrum of developmental anomalies of the central nervous system encountered in a tertiary care hospital

Subhasish Panda*, Subhashree Dash, Savitri Bhagat, Braja Bihari Panda

Department of Radiodiagnosis, VIMSAR, Burla, Sambalpur, Odisha, India

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***Correspondence:**

Dr. Subhashree Dash,

E-mail: dashsubhashree10@gmail.com

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ABSTRACT

Background: Congenital Central Nervous System (CNS) anomalies have typical and characteristic imaging features. Imaging plays a pivotal role in their diagnosis. This study aims to determine the prevalence and spectrum of the various congenital anomalies of the CNS diagnosed at our institution, and to classify the imaging features according to an approved classification system.

Methods: This cross-sectional study was conducted on infants and children below 12 years of age attending the Department of Radiodiagnosis of our Institution, for radiographic investigation of congenital anomalies in CNS through Computerised Tomography and/or Magnetic Resonance Imaging, over a period of one year. The spectrum of imaging features was analysed as per approved classification and corroboration with their clinical background. The prevalence of each type of congenital anomaly was also assessed.

Results: A total number of 43 developmental anomalies of the central nervous system were encountered in 33 patients over a period of one year. The most common anomalies encountered were partial corpus callosal agenesis, heterotopic grey matter and Dandy Walker malformation. The total prevalence of CNS anomalies was 4.22%. The most common clinical symptoms in these patients were seizures followed by focal neurological deficit. The imaging findings of each anomaly are discussed.

Conclusions: Developmental anomalies of CNS are encountered in 4.22% of patients in our Institution, with partial corpus callosum agenesis being the most frequent entity. Familiarity with imaging findings of these malformations is mandatory for every radiologist.

Keywords: Congenital anomalies, Corpus callosum agenesis, Heterotopia, Schizencephaly

INTRODUCTION

Congenital anomalies of central nervous system are a major cause of morbidity and mortality in neonates and infants and are a source of financial, emotional and psychological trauma for the family and the society. They occur as a result of flawed development of the brain and spinal cord, due to chromosomal abnormalities, genetic defects or intrauterine insults. The vulnerability of the fetal and neonatal brain to intrauterine insults like vascular compromise and infections stems from its rapid

growth and development during this period. Intrauterine diagnosis (which can aid in termination of pregnancy, induction of labor or surgical intrauterine intervention), although crucial, is not always possible and often major anomalies are discovered postnatally.

Postnatal clinical presentation is always nonspecific in the form of seizures, delayed developmental milestones or mental retardation which are often overlooked by the parents, thereby there occurs an inherent delay in seeking appropriate and timely physician's advice. Imaging

modalities such as Computerised Tomography (CT) of the Brain and especially Magnetic Resonance Imaging (MRI) play a leading role in clinching the diagnosis at the earliest. The anomalies of the central nervous system are varied, numerous and confusing, hence they need to be appropriately classified for the sake of comprehension and understanding. A proper classification of developmental anomalies of the central nervous system can also go a long way in throwing light on the temporal occurrence of embryologic derangements.¹

Several authors have classified the central nervous system anomalies into different types, based on either embryology or histology or tissue of origin. But a single comprehensive classification is the key to successful categorization of the anomalies and accurate reporting by the radiologist.

This study aims to determine the prevalence and spectrum of the various congenital anomalies of central nervous system (CNS) diagnosed at our institution over a period of one year, and to classify the imaging features according to an approved classification system.

METHODS

This is a cross-sectional observational study conducted on infants and children under 12 years of age attending the Department of Radiodiagnosis of our Institution, between 1st October 2015 and September 31st 2016. All infants and children under 12 years of age attending the Department of Radiodiagnosis of our Institution, between 1st October 2015 and September 31st 2016, for radiographic investigation of congenital anomalies in CNS through computerized tomography and/or magnetic resonance imaging were included in the study. Data of the patients was collected and recorded in a predesigned case record form.

The study variables included the demographic profile of patients including age, sex, birth weight, whether antenatally diagnosed, parity of mother, preterm or term, mode of delivery, chief complaint of patient, examination findings, type of congenital anomaly of CNS, classification into which fitted, outcome of patient.

The spectrum of imaging features were analysed as per approved classification and corroboration with their clinical background. The prevalence of each type of congenital anomaly was also assessed.

RESULTS

A total of 33 patients with congenital anomalies of the CNS were encountered in the OPD of Department of Radiodiagnosis of our Institute over the period of one year with congenital anomalies of the CNS. Most of the patients belonged to the age group of 6 to 12 years. This age group most commonly included malformations of cortical development such as corpus callosal agenesis; as

well as abnormal histogenesis. Males outnumbered females in this study (Table 1).

Table 1: Age and gender distribution of patients at diagnosis (n=33).

Age Group	No. of Pts.	No. of Males	No. of Females
Neonate	5	3	2
Infant	8	2	6
1-5 Years	7	5	2
6-12 Years	13	11	4
Total	33	19	14

The patients were referred to our Department by the clinicians to rule out any congenital anomaly in the patients due to the presenting symptoms. The most common clinical symptoms in these patients were seizures followed by developmental delay. The other symptoms were alteration in muscle tone like spasticity, hypotonia or alteration in gait i.e. ataxia (Table 2). While spasticity, hypotonia and ataxia frequented in infants, mental retardation was reported in the age group of 6-12 years of age. Ataxia was seen exclusively in posterior fossa anomalies.

Table 2: Clinical presentation at diagnosis (n=33).

Clinical Presentation	No. of Patients	%
Seizure	22	51.1
Developmental delay	14	32.5
Mental retardation	11	25.5
Spasticity	9	20.9
Hypotonia	7	16.2
Ataxia	5	11.6

Table 3: Associated imaging findings.

Associated Findings	No. of Patients	%
Hydrocephalus	14	32.55
Altered white matter signal/density	5	11.6
Parenchymal Calcification	4	9.3
Monoventricle	3	6.9

On radiological examination several associated findings were observed. Hydrocephalus was the most frequent finding in one third of patients and was notably associated with Dandy Walker malformation, schizencephaly and alobar holoprosencephaly. Parenchymal calcification was observed in neurocutaneous disorders namely, cases of tuberous sclerosis in the form of calcified subependymal and subcortical tubers as well as in Sturge Weber syndrome (as gyriform calcification). A monoventricle (intercommunicating lateral ventricles) was seen in holoprosencephaly and schizencephaly. Altered white matter signal intensity (T2 weighted MRI)/density (CT

Scan) was observed in five patients including those diagnosed with tuberous sclerosis (foci of abnormal signal intensity or FASI), Dandy Walker malformation (due to transependymal CSF flow from hydrocephalus) and arteriovenous malformations (perilesional edema) (Table 3).

A total number of 43 CNS congenital anomalies were encountered in 33 patients included in our study, which were categorized into 21 different types (Table 4). The most common anomaly observed was partial agenesis of corpus callosum (13.9%), followed by heterotopias and Dandy Walker malformation (9.3% each). The next common were porencephaly, tuberous sclerosis, and holoprosencephaly (6.9% each). Other anomalies were observed at less 5% occurrence. These anomalies were further classified into disorders of dorsal induction, posterior fossa anomalies, disorders of diverticulation, malformations of cortical development and abnormal histogenesis. Of these classes, malformations of cortical development were the most common in this study.

Table 4: CNS congenital anomalies encountered in the study (n=43).

Type of Cong Anomaly	Total No. of patients	%
Partial Agenesis of CC	6	13.9
Heterotopia	4	9.3
Dandy Walker malformation	4	9.3
Porencephaly	3	6.9
Tuberous sclerosis	3	6.9
Holoprosencephaly	3	6.9
Schizencephaly	2	4.6
Lissencephaly	2	4.6
Sturge Weber syndrome	2	4.6
Chiari I malformation	2	4.6
Neurofibromatosis	2	4.6
Hydranencephaly	1	2.3
Diastematomyelia	1	2.3
Joubert syndrome	1	2.3
Arachnoid cyst	1	2.3
Hemimegalecephaly	1	2.3
Teratoma	1	2.3
Atypical teratoid rhabdoid tumor	1	2.3
Arterio-venous malformation	1	2.3
Cavernous angioma	1	2.3
Cerebellar hypoplasia	1	2.3
Total	43	

The MRI images of two patients with partial corpus callosal agenesis are depicted in Figure 1A and 1B. The first one is an axial MRI of the brain a four-year-old child reveal widely separated lateral ventricles which have a parallel orientation, periventricular grey matter heterotopia (Figure 1A). The second one depicts typical Viking helmet frontal horns, high riding third ventricle and non-visualisation of corpus callosum in a patient with

corpus callosal agenesis. Corpus callosal agenesis was associated with diastematomyelia, schizencephaly, lissencephaly and heterotopia in this case (Figure 1B).

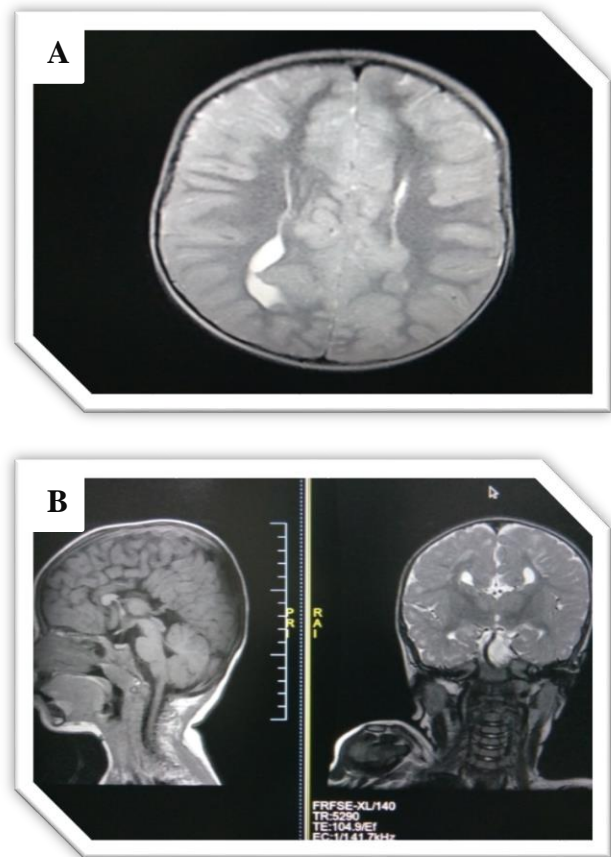


Figure 1: A) Axial MRI of the brain showing Corpus Callosum agenesis and subependymal heterotopia. B) Sagittal and Coronal MRI of a case with Corpus callosum agenesis.

The next common anomalies were heterotopic grey matter and Dandy Walker malformation. In Figure 2A, the axial MRI T2 W image depicts a wide transcerebral cleft lined by grey matter in a patient with open lip schizencephaly and Figure 2B shows another patient with pachygyria as well as a thick band of subcortical grey matter diagnostic of lissencephaly with band heterotopia. Dandy Walker malformation of a patient is shown in Fig 3 where axial CT scan shows a wide communication between a dilated fourth ventricle and enlarged cisterna magna with nonvisualisation of vermis.

The next common anomalies found were holoprosencephaly (Figure 4A and 4B) and tuberous sclerosis (Figure 5). In Figure 4A, the CT scan shows a holovertricle communicating with a dorsal cyst and fused deep gray nuclei and frontal lobes. Figure 4B reveals fused basal ganglia and frontal lobes without a dorsal cyst or holovertricle and the diagnosis was semilobar holoprosencephaly. In this study, a case of alobar holoprosencephaly was also encountered.

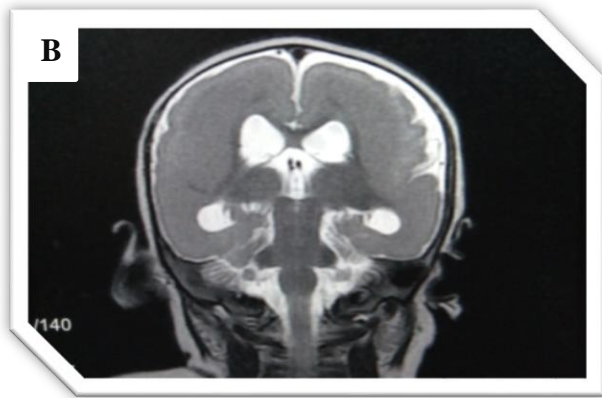
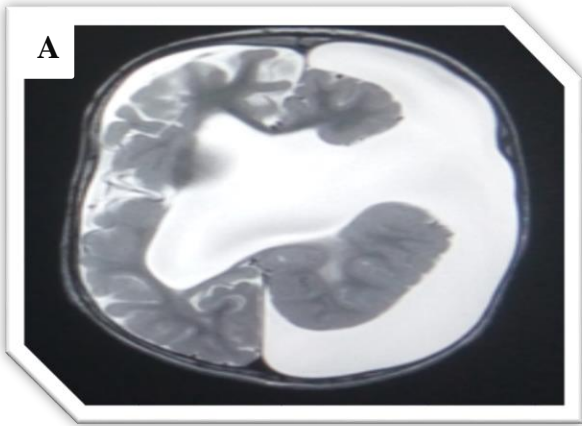


Figure 2: A) Axial MRI T2 W image showing open lip schizencephaly. B) Axial MRI showing lissencephaly with band heterotopia.

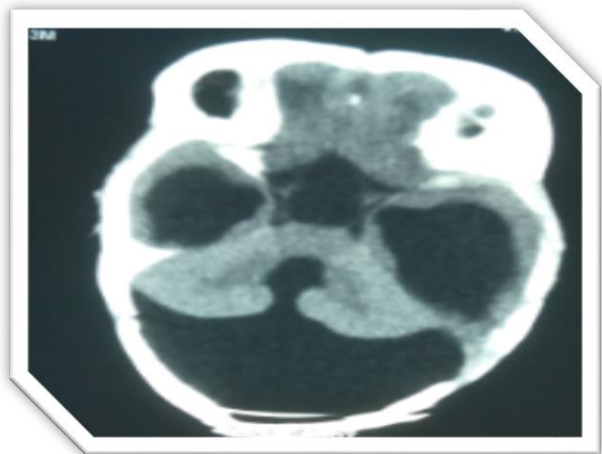


Figure 3: Axial CT Scan showing Dandy Walker malformation.

Typical images of tuberous sclerosis are seen in Figure 5A where MRI brain shows multiple subcortical tubers and subependymal nodules which are T1 hyperintense and CT of abdomen shows bilateral renal angiomyolipomas (Figure 5B). The total prevalence of CNS anomalies was 1.6 %

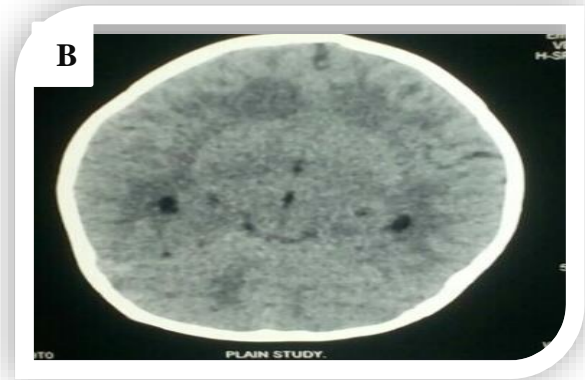


Figure 4: A) CT scan showing semilobar holoprosencephaly. B) CT scan in another patient showing semilobar holoprosencephaly.

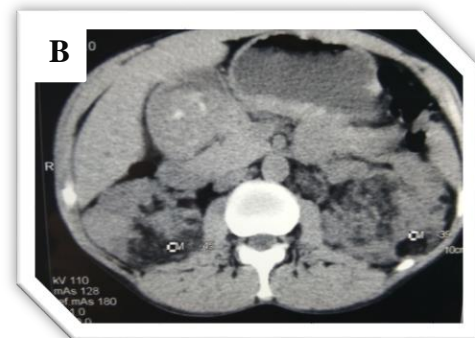
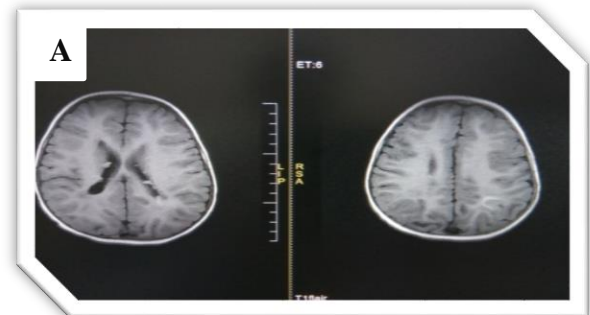


Figure 5: A) MRI brain of a case of tuberous sclerosis. B) CT abdomen with bilateral renal angiomyolipomas.

DISCUSSION

Most common CNS anomaly discovered during the study period was that of partial agenesis of corpus callosum followed by Dandy Walker malformation. Cases of holoprosencephaly, lissencephaly, schizencephaly, heterotopia and a variety of others such as diastematomyelia and Chiari malformations were also encountered. These anomalies can be classified as follows.¹

Disorders of dorsal induction

These include disorders of primary neurulation such as neural tube defects and secondary neurulation namely diastematomyelia.

Chiari malformation

Chiari I malformation is characterized by caudal herniation of cerebellar tonsils at least 5mm below the level of foramen magnum seen on midsagittal MRI.² An association with other abnormalities of the craniovertebral junction such as basilar invagination, platybasia and Kippel-Feil deformity has been reported. Chiari II malformation denotes caudal herniation of cerebellar tonsils as well as vermis with crowding of posterior fossa and effacement of cistern magna. Thinning and elongation of the fourth ventricle as well as beaking of tectum are other features.³ A lumbosacral meningocele is usually associated.

Encephaloceles

The term refers to herniation of brain parenchyma along with meninges through a defect in the calvarium-most commonly occipital followed by parietal and frontal. These are often associated with Chiari 3 malformation involving the upper cervical spine as well.⁴ Only occipital encephalocele was encountered in the present study.

Diastematomyelia

This is otherwise known as split cord malformation and describes a longitudinal split in the spinal cord with or without an intervening fibrous or osseous septum.⁵ Most common location is lumbosacral spinal cord as was the case in one of the patients in the study. An association with corpus callosal agenesis has been described and was encountered in one case in our study.⁶

Posterior fossa anomalies

Dandy Walker malformation

This most common posterior fossa anomaly is characterized by an enlarged posterior fossa, with a posterior fossa cyst communicating with a dilated fourth ventricle and associated with hypoplasia of the inferior vermis is consistent with this condition (Figure 3).

Hydrocephalus often ensues and macrocephaly is the most common clinical feature.⁷

Joubert Syndrome

An autosomal recessive disorder characterised by variable agenesis of the inferior vermis. Molar Tooth Appearance on Axial MRI is typical.⁸

Posterior fossa arachnoid cyst

Extra-axial CSF density cystic SOL without communicating with fourth ventricle.

Disorders of diverticulation/cleavage

Holoprosencephaly

An anomaly of ventral induction of the brain where the forebrain (cerebral hemispheres) fails to separate. It can be of three varieties-lobar, semilobar and alobar, in increasing order of severity depending upon the degree of separation (Figure 4A and B). It is the most common congenital anomaly of the brain to be associated with facial abnormalities such as presence of proboscis, cyclopia, hypotelorism, absent nasal bridge, cleft lip and palate.⁹ Facial anomalies were associated with all the cases of holoprosencephaly in this study, the most severe -proboscis observed in the Alobar variety. Ventricular septal defect was present in a patient of semilobar holoprosencephaly who was later diagnosed as Patau Syndrome using Karyotyping.

Malformations of cortical development

Lissencephaly

It is the most severe form of abnormal migration characterized by paucity of gyri and sulci termed as agyria and pachygyria.¹ Two types of Lissencephaly have been recognized: Type I-Smooth cortical margin with thick subcortical band of heterotopic gray matter and intervening cell sparse layer (Figure 2B). Type II-Nodular cortical surface.

Schizencephaly

CSF filled transcerebral clefts lined by gray matter resulting in communication of lateral ventricle with subarachnoid space (Figure 2A). They can be unilateral or bilateral and open or closed lip. No case of closed lipped schizencephaly was encountered in our study.

Corpus callosal agenesis/dysgenesis

The white matter tracts which usually cross the midline, instead are oriented vertically, separating the lateral ventricles widely, with the frontal horns depicting a Viking helmet configuration (Figure 1). The third ventricle is often high riding.

Heterotopias

This term denotes location of normal neurons at abnormal locations due to impaired neuronal migration.¹ They may be of several types:

- Periventricular or subependymal-nodular gray matter foci in a subependymal location were seen associated with a case of corpus callosal agenesis (Figure 1A).
- Subcortical-Nodular, curvilinear or mixed.
- Laminar-Bilaterally symmetrical and circumferential subcortical layer of gray matter appearing as double cortex with an intervening thin ribbon-like altered signal intensity white matter was noted in cases of lissencephaly (Figure 2B).

Disorders of histogenesis

Tuberous sclerosis

Tuberous Sclerosis (TSC) is an autosomal dominant neurocutaneous disorder with documented neurological, cardiac, renal, pulmonary and cutaneous manifestations (Figure 5).¹⁰ Classic clinical triad of epilepsy, mental retardation and skin manifestations such as adenoma sebaceum are seen in only half of the patients.^{10,11}

Sturge Weber syndrome

Characterised by Gyriform intracranial calcification with or without volume loss. Usually diagnosed between 2 and 7 years of age.¹² Associated enlargement of choroid plexus and facial haemangiomas manifest as portwine stain is typical (absent in only 5 % of patients) and situated ipsilateral to the intracranial lesion as was the case in both of our patients.^{12,13}

Neurofibromatosis (NF)

Unlike Neurofibromatosis type I, type II is not associated with neurofibromas. Instead, patients with this disease have bilateral vestibular schwannomas (which are diagnostic) as well as CNS meningiomas and spinal ependymomas.¹⁴ One case of NF II with bilateral vestibular schwannomas alone was found in our study.

Congenital Tumors

According to Wakai et al, only patients diagnosed with intracranial neoplasms before 2 months of age should be included in this category.¹⁵ Atypical teratoid rhabdoid tumor and teratomas (one each) were diagnosed in this study.

CONCLUSION

Developmental anomalies of CNS are encountered in 1.6% of patients in our institution. The classification described in this study clearly demarcates these anomalies into broad subtypes of which malformations of

cortical development were most common. Partial corpus callosum agenesis was the most frequent anomaly. Familiarity with imaging findings of these malformations is mandatory for every radiologist.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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