



Spectrum of Congenital CNS Malformations in Children with Seizure Disorder

Authors

Dr Nita R Sutay¹, Dr Shalaka Patil², Dr Priya Jhunjunwala³

¹Professor and Head of the Department, ²Assistant Professor, ³Senior Resident

Department of Pediatrics, Grant Government Medical College and Sir J.J Group of Hospitals Mumbai

Corresponding Author

Dr. Nita R Sutay

Professor and Head of the Department

Department of Pediatrics, Grant Government Medical College and Sir J.J Group of Hospitals Mumbai

Abstract

Introduction: Developmental malformations OF CNS are a complex group of congenital malformations often presenting with variable neurodevelopment dysfunction and seizures. The etiology of most of these malformations is not well known but chromosomal anomalies, monogenic disorders, maternal radiation exposure, teratogenic drugs and intrauterine infections are some of the major causes. Congenital CNS malformations are frequently associated with seizures and mental retardation. With advancement of imaging techniques (higher tesla magnetic resonance imaging and more sophisticated computed tomographic machines) it has now become possible to diagnose these malformations with precision. Hence this study has been undertaken to know incidence of CNS malformations and its clinical presentation in childhood seizure disorders.

Aims and Objectives

To study the incidence of CNS malformations and its clinical presentation in children with seizure disorder.

Materials and Methods: This was a prospective cohort study done on 102 diagnosed cases of seizure disorder conducted in department of pediatrics, Grant Govt. Medical College & Sir J J Group of Hospitals, Mumbai, India. Cohort included 102 diagnosed case of seizure disorder in children up to 14 years of age. Neuroimaging data of all patients were evaluated for a 2 year period for presence of CNS malformations, and the clinical and electrophysiological data were analyzed.

Results: Out of the studied cases 67 were males and 35 were females with a male to female ratio of 1: 0.52 . 28 (27.5%) cases of CNS malformations were reported on neuroimaging. The analysis of the CNS malformations revealed that out of the patients who were found to be having CNS malformation on either computed tomography or magnetic resonance imaging 12 (11.76%) were of Neural tube defects , 11(10.78%) were of Malformation of cortical development, 3 (2.94%) were of neurocutaneous syndrome, and 2(1.96%) were of dysgenesis of corpus collasum. Developmental delay was present in 53.6% cases and in 83 % cases age of onset of seizures was within 2 years of age. Significant association was seen with dysmorphic features (p-value<0.001), neurocutaneous markers (p-value<0.028), other congenital anomalies(p-value<0.048), and GTC convulsions(p-value<0.048). Computed tomography and magnetic resonance imaging both were done in 16/28 (57.14%). While only CT and only MRI was done in 4 and 8 patients respectively

Conclusion: CNS malformations should be suspected in paediatric patients of seizure disorder presenting with developmental delay, dysmorphic features, neurocutaneous markers, other congenital anomalies, and early onset of seizures. MRI brain is superior to CT brain for diagnosis of CNS malformations.

Key Words: Seizure in children, CNS malformations, Computed Tomography, Magnetic Resonance Imaging.

Introduction

Seizures are the one of the most common pediatric neurological disorder. 4-10% p of children suffers at least one episode of seizure in the first 16 years of life^[1]. The incidence is highest in children below 3 years of age, with a decreasing frequency in older children¹. Epidemiological studies reveal that approximately 1, 50, 000 children will sustain a first-time, unprovoked seizure each year and of these 30,000 will develop epilepsy^[2]. Many of the adolescents and adults having epilepsy had their first episode of seizures in childhood. The management of seizures or later epilepsy is more complex in developing countries like India because of ignorance, poverty, stigmatization and lack of resources and trained manpower^[3].

Incidence of epilepsy is higher in paediatric age group than with adults consequently a major portion of paediatric neurological consultation consists of patients of childhood seizure disorder or epilepsy^[4]. The etiology of seizures is paediatric age group is diverse. The common causes of seizures in paediatric age group includes febrile convulsions, seizures secondary to intracranial infections, Idiopathic partial and generalised epilepsies and seizures secondary to central nervous system malformations^[5].

The single gene disorders associated with epilepsy in childhood include Neurofibromatosis, tuberous sclerosis, Fragile X syndrome, Acute intermittent porphyria, leukodystrophies and Rett syndrome^[6]. Other Inherited metabolic conditions which may cause epilepsy in childhood include aminoacidopathies, galactosemia, Peroxismal disorders and pyridoxine dependent seizures^[7]. The common central nervous system malformations causing seizures in paediatric age group include included dysgenetic corpus callosum, lissencephaly, focal cortical dysplasia, pachygyria, poly-microgyria, schiz-encephaly holoprosencephaly, and neurocutaneous syndromes like tuberous sclerosis, Sturge Weber syndrome and hypomelanosis of ito^[8].

These CNS malformations constitute some of the important causes of seizures in childhood. Advancement in imaging techniques has imme-

nately changed the scenario as far as diagnosing these conditions are concerned^[9]. This study was conducted to know the incidence of CNS malformations and its clinical presentation in children with seizure disorder.

Materials and Methods

This was a prospective cohort study conducted over a 2 year period. 102 children of seizure disorders were enrolled from pediatric department of Grant Government Medical College & Sir J.J. Group of Hospitals, Mumbai. Informed consent was taken from parents of all those who met the criteria of the study. Permission of Institutional ethical committee was taken. Basic Demographic data like sex, age at present and age t onset of seizures was noted. A detailed birth history with an special attention towards birth asphyxia ,History of developmental delay, family history of seizures was noted. General examination with an emphasis on diagnosing neurocutaneous markers, other congenital anomalies, dysmorphic features, and dystonia was done. EEG, Computed tomography and MRI was done. In each patient an attempt was made to correlate the seizure disorder with type of CNS malformations, its clinical presentations and EEG features.

Inclusion Criteria

1. Patients presenting with seizures.
2. Age less than 14 years.

Exclusion Criteria

1. Age more than 14 years.
2. Febrile seizures.
3. Provoked seizures like those caused by meningitis, hyperpyrexia, head injury and electrolyte imbalance.
4. Those who denied consent to be part of the study.

Results

Out of 102 patients of seizure disorder 67(65.69%) were males and 35(34.31%) were females. There was a male preponderance with M: F ratio being 1: 0.52 (Figure 1)

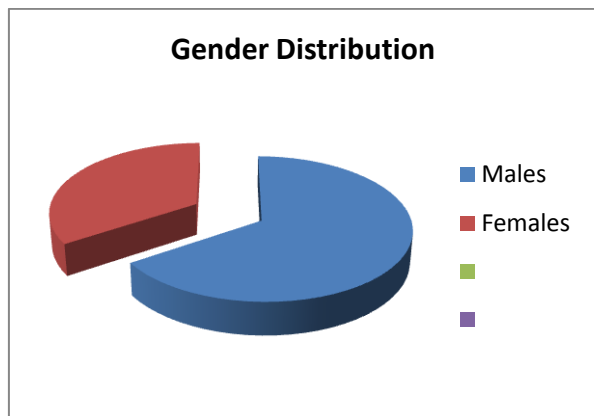


Fig 1 : Gender Distribution of the studied cases.

The analysis of age of onset of the seizures revealed that most of the patients had their first episode of seizures before 2 years of age. Out of 102 patients 83 (82.35%) patient had their first episode of seizures before they completed 2 years. While 12 patients had their first episode between 2-5 years. 5 and 2 patients had their first episode of seizures in between 5-10 years and more than 10 years respectively (Figure 2).

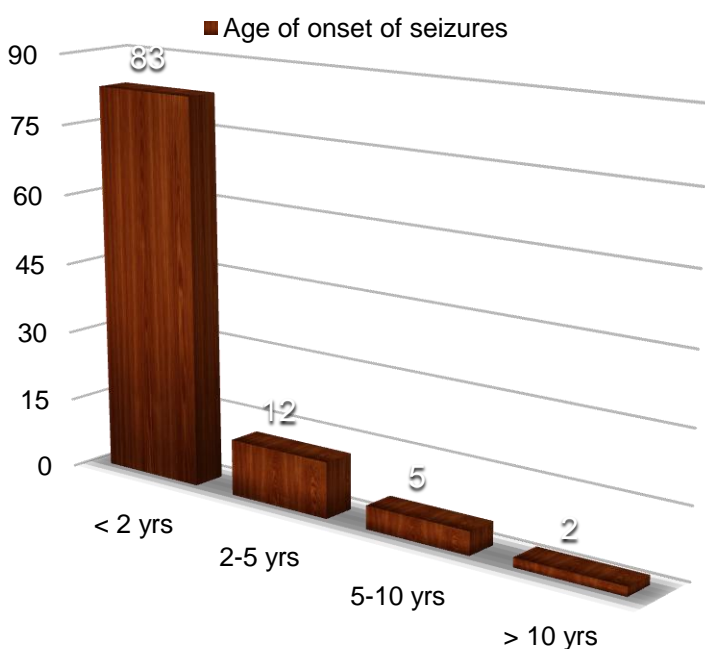


Figure 2: Age of onset of first episode of seizures.

The analysis of the patients who had been admitted with seizures revealed that the most common type of seizures were generalised tonic clonic seizures which were seen in 52 (50.98%) patients. The next common type of seizures were

complex partial seizures which were seen in 20 (19.60%) patients followed by absence, myoclonic and simple partial seizures which were seen in 10 (9.80%), 8 (7.84%) and 8 (7.84%) respectively. Least common form of seizures in studied cases were secondary generalized type of partial seizures which were seen in 4 (3.92%) patients (Table 1).

Table 1: Types of seizures seen in studied cases

Types of seizures	Subtype	No Of Cases	Percentage
Generalised Seizures	Absence	10	9.80 %
	Tonic clonic	52	50.98 %
	Myoclonic	8	7.84 %
	Total	70	68.62 %
Partial Seizures	Simple	8	7.84 %
	Complex	20	19.60%
	Secondary Generalized	4	3.92%
	Total	32	31.37 %
Total		102	100%

The neuroimaging of these patients was done. Out of 102 studied cases neuroimaging was normal in 45 (44%) patients while abnormal neuroimaging was found in 57 (56%) patients. Being imaging modality of choice magnetic resonance imaging was done in all patients except in 4 patients who were either non-cooperative or had some or the other contraindication to undergo MRI. Computed tomography and magnetic resonance imaging both were done in 16/28 (57.14%). While only CT and only MRI was done in 4 and 8 patients respectively (Figure 3).

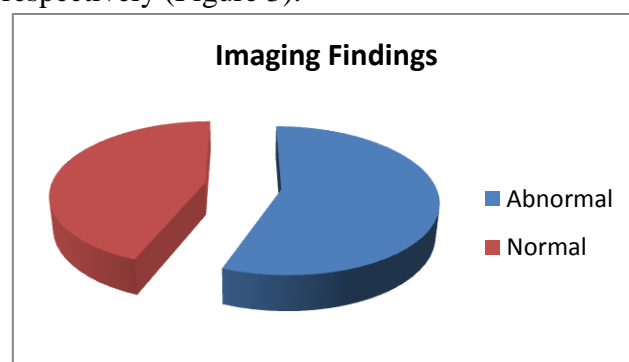


Figure 3 : Normal and Abnormal neuroimaging.

The analysis of patients revealed with neuroimaging abnormalities revealed that out of 57 patients having abnormal neuroimaging CNS

malformations were present in 28 (27.5%) patients, Hypoxic ischemic encephalopathy /Hypoglycemic insult was seen in 26(25.5%) patients, other anomalies like. subarachnoidhaemorrhage, sagittal sinus thrombosis, cerebral atrophy were seen in 3(2.9%) of cases, and study was normal in 45(44.1%) patients (Figure 4).

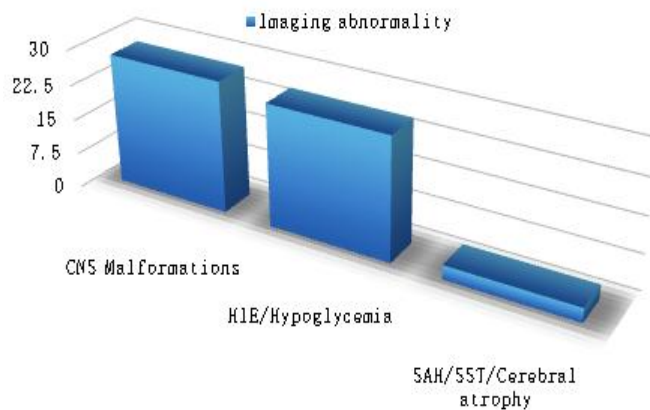


Figure 4 : Neuroimaging of the cases revealing abnormalities

Out of 28 patients with CNS malformations 12(11.76%) were of Neural tube defects, 11(10.78 %) were of Malformations of Cortical Development, 3(2.94 %) were of Neurocutaneous syndrome, 2(1.96 %) were of Dysgenesis of corpus callosum (Table 2).

Table 2 : Neuroimaging abnormalities observed in studied cases.

Neuroimaging	Number Of cases	Percentage
Normal	45	44.11%
Neural Tube Defects	12	11.76%
Malformations Of cortical Development	11	10.78%
Neurocutaneous syndrome	3	2.94%
Dysgenesis Of corpus collasum	2	1.96%
HIE/Hypoglycemic insult	26	25.49%
Subarachnoid hemmorrhage,Sagittal sinus thrombosis, Cerebral atrophy	3	2.94%
Total	102	100%

Out of 28 patients having neuroimaging abnormalities of CNS malformations 16 patients were male and 12 were females with male:female ratio of 4:3. Significant association of CNS malformations was found with dysmorphic features(p-value<0.001), generalized tonic clonic seizures (p-value<0.048). Though association was found non-significant, most patients with CNS malformations had developmental delay(53.6%) and early onset of seizure disorder that is within 2 years of age(83 %). Out of those 28 patients with CNS malformations both MRI and CT scan brain was done in 16 patients,only MRI brain was done in 8 patients and only CT scan brain was done in 4 patients. Out of 16 patients with CNS malformations in which both MRI and CT scan brain were done, CT brain was found to be normal in 6 patients,while MRI brain in same patients had shown CNS malformations, 3of these patients were having malformations of cortical development. In 2 patients CT scan brain had shown hydrocephalus while MRI brain had shown Dandy Walker malformation and Arnold Chiari malformation type 2 in same patients.

Discussion

The current study was carried out on 102 patients of seizure disorder out of which 28 (27.5%) patients were diagnosed to have central nervous system malformations diagnosed by neuroimaging with relevant clinical features.

Among those 28 patients of seizure disorder with CNS malformations neural tube defects were the most common(11.76 %) malformations followed by malformations of cortical development (10.78%) while neurocutaneous syndromes were less common and isolated dysgenesis Of corpus collasum was least common (1.96%) malformations. These results are in agreement with that Dolk et al^[10], who reported that neural tube defects were among most common human malformations. This is also in agreement with a study done by Girgis et al^[11].

In this study males had more preponderance over females for convulsions with male: female ratio

was 1:0.52. CNS malformations were also more commonly seen in males with female ratio being 4:3. These results are in agreement with that of Girgis et al. who reported male: female ratio of 6:4 and Adeyemo et al. who reported the male: female ratio to be 1.6:1^[12].

In this study age of onset of seizures in majority of patients was within first two years of life (83%). Girgis et al., reported age of onset of seizures in majority of the patients to be in first year of life (79% of cases). Gungor et al reported that seizures started in first year of life in (48.6%) of the cases in general^[13].

Developmental delay is also found more common in seizures disorder with central nervous system malformation but p- value was found to be non-significant. In this study, Development delay was reported in 53.6% patients of study group i.e. in patients with central nervous system malformations. This result is in agreement with that of Leventer et al., who reported developmental delay or intellectual disability in 68% cases^[14]. In a study conducted by Sanghvi et al 19% of the studied patients had normal neuro-developmental assessment, 64% patients had global delay in milestones and 17% had motor delay^[15].

In 28 patients of seizure disorder with CNS malformations on measuring the head circumference it was found that 17.9% were microcephalic and 21.4% were macrocephalic. While Girgis et al, reported that (39%) were microcephalic and (9.1%) were macrocephalic, Leventer et al., reported macrocephaly in 8.3% And microcephaly in 5.5% while Sanghvi et al., reported that 22 (28.9%) out of 76 patients had microcephaly.

In this study generalized seizures were found in 68.62% patients of seizure disorder and other types in 31.37% patients. Girgis et al. reported that most common type of seizure was generalized in (33%). Focal type was less common and was reported in patients with dysgenesis of corpus callosum and less extensive form of (MCD) as polymicrogyria and heterotopia. Sanghvi et al. reported that seizures were generalized in 31/76 cases (40.7%) and partial in 27/76 (35.6%)".

Serdal et al., reported that in 101 cases included in his study; epileptic seizures were present in (71.3%). Generalized seizures were present (32.7%), complex partial in (25.7%) and secondary generalized in (11%)s.

Conclusion

In conclusion the incidence of central nervous system malformations diagnosed by neuroimaging in childhood seizure disorder is 27.5%. Neural tube defects were the most common type of malformations diagnosed followed by malformations of cortical developments, neurocutaneous syndromes and isolated dysgenesis of corpus callosum.

Our study concludes that central nervous system malformations should be suspected in patients of seizure disorder presenting with developmental delay, microcephaly, macrocephaly or dysmorphic features or other congenital anomalies or neurocutaneous markers especially when age of onset of seizures is early during first two years of life. Neuroimaging is required for accurate anatomic diagnosis. Magnetic Resonance Imaging is superior to Computed tomography scan for diagnosis of central nervous system malformations, especially for malformations of cortical development.

Conflict Of interest: None

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