European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 09, Issue 02, 2022

Subtle changes of neuronal migrational disorder: diagnosed by non-contrast CT scans

[1]Dr. Rajeev Mudkavi, [2]Dr. Naveen Meena, [3]Dr. Naju Tanya Mudkavi

[1]Professor Department of Radiology, Jaipur National University Institute of Medical Science and Research Centre (JNUIMSRC), Jagatpura, Jaipur, Rajasthan, India
[2]Associate Professor, Department of Radiology, Jaipur National University Institute of Medical Science and Research Centre (JNUIMSRC), Jagatpura, Jaipur, Rajasthan, India
[3]Jaipur National University Institute of Medical Science and Research Centre (JNUIMSRC), Jagatpura, Jaipur, Rajasthan, India

Corresponding Author:
Dr. Naveen Meena (drnaveenmeena@gmail.com)

Abstract

Neuronal migrational disorders (NMD) offer a wide spectrum of disorders with specific diagnosis by CT and MRI of the brain. Most NMD are easily recognized on CT scans & MRI and offer little or no difficulty in their diagnosis (5, 6).
Through this article we propose to elucidate a subtle form of NMD by Non contrast CT scans of the brain. This subtle variety of NMD almost always escapes recognition on CT / MRI, always prompting a normal report on most occasions.
It is the purpose of this article to highlight the CT scan features of these nearly normal appearing images of NMD, which we propose to label as a subtle NMD (Subtle Neuronal Migrational Disorder).
30 CT scans of children ranging from 1 to 5 years were analysed retrospectively.
All had similar CT scan findings and identical clinical presentations.

Keywords: NMD: Neuronal migrational disorder. NCCT: Non contrast CT scan

Introduction

Neuronal migration disorder (NMD) is defined as a group of disorders with similar etiopathologies: namely a variable degree of disruption in the migration of neuroblasts during neurogenesis.
Neuronal migration disorders are termed cerebral dysgenesis disorders, brain malformations caused by primary alterations during neurogenesis; on the other hand, brain malformations are a broad term that refers to any insult to the brain during its formation and maturation caused by intrinsic or extrinsic causes that alters the normal brain anatomy [1].
Neural stem cells must move from the places where they are born to the areas where they will

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settle into their respective neural circuits in the growing brain. A complex array of chemical guides and signals drive neuronal migration, which begins as early as the second month of pregnancy. Neurons do not end up where they belong when these signals are missing or erroneous. This can result in brain areas that are anatomically aberrant or absent.
NMDs occur in the following conditions:

1) Neuroblasts do not migrate from all of the ventricles or migrate only part of the way.
2) Only some of the neuroblasts reach the cortical layer.
3) Neuroblasts overshoot the appropriate cortical layer and protrude into the subarachnoid space.
4) The late stage organization of the neuronal layer in the cortex is disrupted. Abnormal migration ultimately results in abnormal gyral formation [3, 4].

Symptoms of NMD

Symptoms vary according to the abnormality, poor muscle tone and motor function, seizures, developmental delays, mental retardation, inability to grow and thrive, feeding difficulties, swelling in the extremities, and a smaller-than-normal head are some of the common symptoms. Most infants with an NMD appear normal, but some disorders have characteristic facial or skull features that can be recognized by a neurologist [1, 2]. Several genetic anomalies have been discovered in children with NMDs.
The effect of environmental variables on NMDs was studied in a study. Low or subnormal mother BMI before and throughout pregnancy, maternal infection, such as rubella, and maternal smoking may have an impact on fetal brain development, including neuronal migration, according to the study [1, 2, 4].

Types of NMD syndromes

More than 25 syndromes resulting from abnormal neuronal migration have been described (14). Some of them being:

- Lissencephaly
- Schizencephaly
- Porencephaly
- Pachygyria
- Polymicrogyria
- Agyria
- Grey matter heterotopia
- Genesis of the corpus callosum and heterotopias

Treatment

Anti-seizure medicine, as well as physical, occupational, and speech therapies, may be used to treat the symptoms.

Prognosis

The prognosis for children with NMDs varies depending on the kind of illness, the severity of brain abnormalities and the resulting neurological signs and symptoms.
NMD are diagnosed on imaging by MRI or CT scans. Most of the above mentioned NMD lesions are fairly obvious and have little difficulty in their radiological identifications. It is the purpose of this article to highlight a subtle form of NMD, which appears with only subtle changes on CT scans or MRI and almost always eludes diagnosis. All such cases have similar

ISSN 2515-8260 Volume 09, Issue 02, 2022

clinical symptoms common to all of them, with minor clinical variations [5, 6, 9].

Materials and Methods

Thirty patients of CT scans were retrospectively studied in the department of Radiology in JNUIMSRC (Jaipur National University Institute for Medical Sciences and Research Centre) Jaipur, India. The average age was from one to five years. All patients had similar clinical findings and were initially referred for CT scans for symptoms of mental retardation, delayed milestones and sometimes seizures. None had clinical features which predicted NMD prior to the imaging study. All scans were non contrast CT scans and were scanned in supine positions with appropriate consent and sedation.
All scans were performed on Toshiba Alexion 16 slice spiral CT scan at JNUIMSRC. Axial, coronal & sagittal scans were performed and analysed.

Results

All scans revealed similar findings on CT scans. On initial studies all scans appeared normal. However a closer look showed following findings:
1. Deep periventricular sulci bilaterally.
2. Paucity of posterior periventricular white matter.
3. Nearly parallel oriented lateral ventricles.
4. Increased interventricular distance posteriorly / colpocephaly.
5. And in very few cases, irregular indentations of the ventricular margins suggesting grey matter heterotopias.

All patients had a combination of the following clinical findings
- Premature birth.
- Delayed cry on birth.
- Blue baby/hypoxia on birth with subsequent O2 therapy for variable periods.
- Mental retardation.
- Delayed milestones including unable to sit, or stand or walk.
- Gait disturbance.
- Delayed onset seizures starting from 2-4 years after birth.

All CT scans were nearly normal on first analysis and only on closer inspection revealed the above CT findings.
The patients who presented with obvious NMD changes on CT scans like Lissencephaly, Schizencephaly and Obvious grey matter heterotopias were excluded from this study.

Discussion

NMD (Neuronal migrational disorders) embrace a wide range of disorders with the same underlying defect in the normal Neuronal Migration caused due to an episode either intrauterine or at birth. Genetic and environmental factors are the underlying etiopathologies [1, 3, 4, 10].
NMD are numerous and are easily recognized by CT or MRI. However it is through this paper, that we have sought to highlight a subtle form of NMD which does not have the specific characteristics of other NMDs and have no evidence of any Lissencephaly, Schizencephaly or obvious grey matter heterotopias.
Such pediatric patients presenting with similar clinical findings were labeled as being normal on CT Scans and MRI studies. And since they were not categorized as any form of NMD, their treatment plans were also variable.

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However on recognizing these subtle findings on CT Scans or MRI we are able to categorize their clinical symptoms as being due to a subtle form of NMD, allowing for a relevant treatment plan for such patients.
On numerous occasions in the past, such patients have been dismissed with clinical symptoms of unknown etiology. Proper diagnosis in the early years after birth would enable the treating physician as well as the family of the children to be aware of what to expect in the future and would give a proper direction to the treatment.
Early diagnosis by CT or MRI would enable us to be prepared for the inevitable delayed onset seizures, so frequently found in these patients. Proper and early physiotherapy consultations would benefit greatly, if diagnosed early by imaging studies. Hence the need to recognize this subtle variation of NMD, which could easily be mistaken for a normal brain study by CT scans or MRI.
Particularly misleading would be the delayed onset seizures which are frequently seen in these paediatric patients. If undiagnosed as NMD by CT scans or MRI, the seizures appearing anytime between 2 to 4 years would be misinterpreted by the treating physician and no correlation might be made with the underlying condition of NMD.
To recapitulate, CT scans in this study were initially dismissed as normal CT scans. On reviewing, it was found that they had subtle changes which were used to analyze the NMD. All patients came for developmental delays or mental retardation and some with seizures. All patients were of age groups of one to five years.

The scans revealed the following findings:
- Deep periventricular sulci
- Paucity of posterior periventricular white matter with absent white matter in the posterior periventricular areas.
- Parallel orientation of the lateral ventricles
- Increased interventricular distance posteriorly/ colpocephaly
- In a few cases there were small faint indentations and irregularity in the ventricular margins, representing grey matter heterotopias.

All had similar clinical findings:
- Delayed milestones
- Mental retardation
- Unable to sit or stand or walk in variable frequencies
- History of premature birth ranging from 32 to 34 weeks or
- Delayed birth cry/blue baby/hypoxia at birth and oxygen therapy at birth.
- Initially at birth, following the hypoxic episodes, children were normal and abnormalities were detected as the milestones were reached.
- Delayed onset seizures, occurring typically after 2-4 years of age and with initial seizure free periods.

It was hence found that all children had similar clinical and CT scan findings and the CT scan images were nearly normal and on reviewing were found to have Subtle, barely perceptible CT findings.
This article labels these findings as a subtle form of NMD (Neuronal Migrational Disorder) and allows a diagnosis for these children presenting with similar clinical findings and rules out any other etiology for their clinical conditions.

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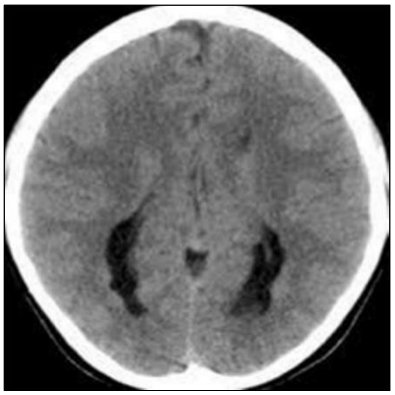

Fig 1: Grey matter heterotopias with indentations on the ventricular surface colpocephaly, however with normally visualized periventricular whit matter on both sides

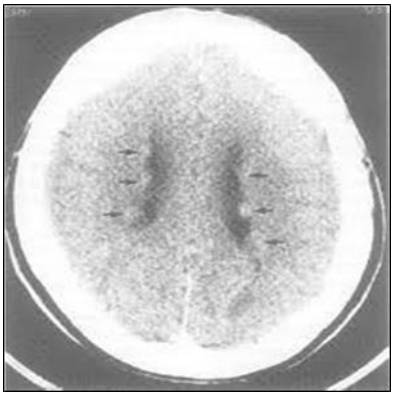

Fig 2: Grey matter heterotopia

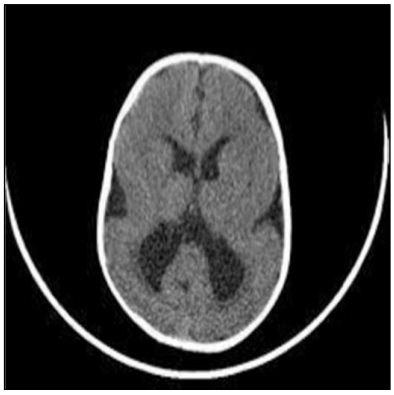

Fig 3: Lissencephaly (Pachygyria)

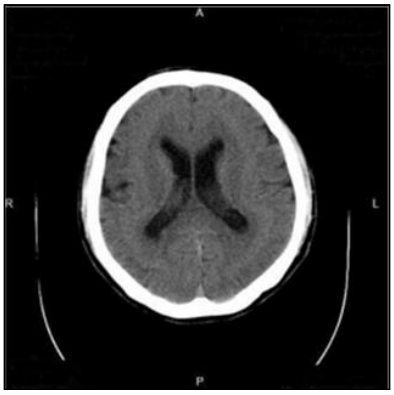

Fig 4: Band Heterotopia

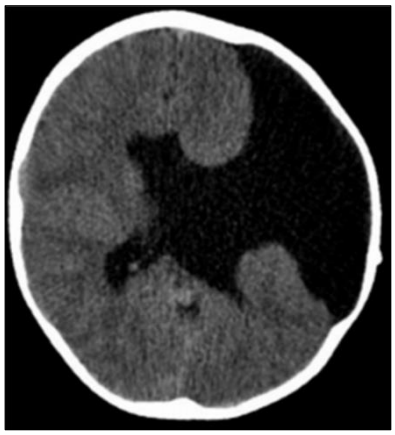

Fig 5: Schizencephaly

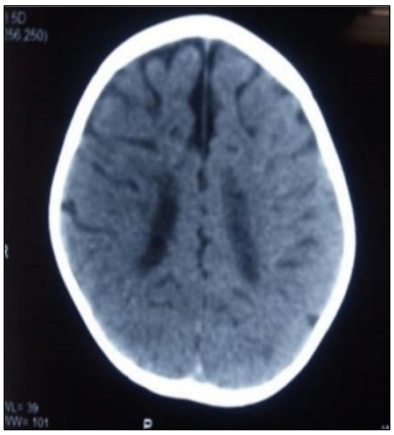

Fig 6: Subtle NMD

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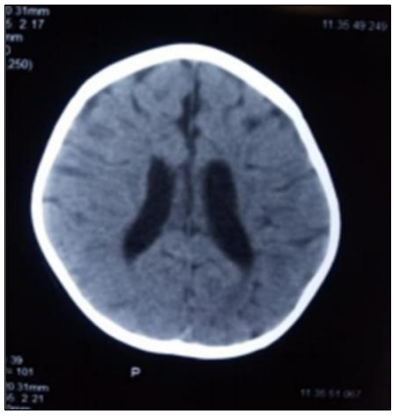

Fig 7: Subtle NMD

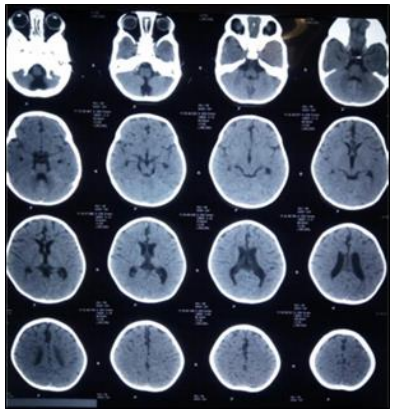

Fig 8: Subtle NMD

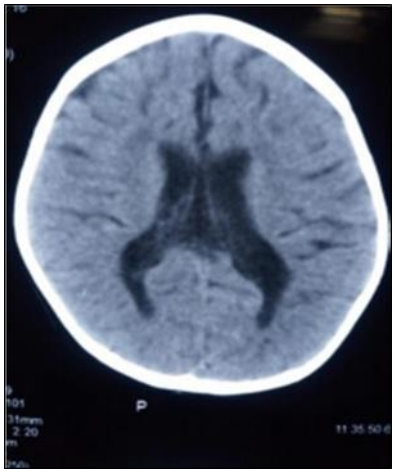

Fig 9: Subtle NMD

As seen in figures 1-5, are the obvious forms of NMD (Neuronal Migrational Disorders) presenting in the form of grey matter heterotopias, schizencephaly, lissencephaly and band heterotopias. All above lesions are obvious on ct scans and leave no doubt in the minds of the radiologists.

However figures 6-9 are the subtle NMD, referred to in this article, where at first glance the images appear normal. However a close look identifies the previously described findings of this article, namely deep periventricular sulci on both sides, paucity of the posterior periventricular white matter & relatively increased posterior interventricular distance suggesting associated colpocephaly and subtle agenesis of splenium of corpus callosum. These findings along with the clinical findings of delayed milestones, birth asphyxia with or without premature birth, gait disturbance or difficulty in standing and delayed onset seizures, clinches the diagnosis of NMD, in spite of the initial normal CT report.

Conclusion

NMD (Neuronal Migrational Disorders) encompass a wide spectrum of disorders easily identified by routine CT scans or MRI. A subtle form of NMD has been explored through this article which is almost always misinterpreted as being normal owing to the fact that the imaging findings are recognizable only on close inspection. Paucity of white matter particularly posteriorly, relatively deep sulci and parallel orientation of the lateral ventricles (with or without colpocephaly) are all findings which could easily be overlooked and through this article, we offer a diagnosis, of subtle form of NMD, and a consequent proper direction in the treatment plan for these pediatric patients presenting with clinical findings of delayed

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milestones, gait disturbance and delayed onset seizures along with a history of premature birth or hypoxia at birth. Subtle NMD is a unique addition to the wide spectrum of the pre-existing classifications of Neuronal Migrational Disorders.

Ethics approval & consent to participate

Prior written & informed consent was obtained from all patients' parents and the study was approved by the ethics review board of JNUIMSRC.

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