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VAN DER KNAAP Disease – A Case Report

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Abstract:
Van der Knaap disease or Megalencephaly with Leukoencephalopathy and cysts is a rare autosomal recessive inborn genetic disorder seen in children below one year. Despite of abnormal MR findings these infants present with delayed development of motor dysfunction. We present one such case of a one and half year child who presented with delayed milestones and classical MRI findings.

Keywords: *Van der Knaap disease –delayed milestones – cystic changes in brain*

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I. Introduction :

Van der Knaap disease is a rare genetic disorder that is attributed to mutations of MLCI and GLIALCAM genes [1]. It is also known as Indian Agarwal megalencephalic leukodystrophy. The most common clinical presentation is macrocephaly at birth with slow deterioration of motor function which can occur within one year. The other clinical symptoms include delayed development and decreased cognitive function, cerebellar ataxia, seizures and clinical deterioration after mild trauma. The most prominent pathological change noted in the brain specimen is vacuolization in subcortical white matter and spongiform leukoencephalopathy11 On CT scan the affected white matter shows hypoattenuation with enhancement on contrast administration. The MRI findings are very characteristic . There will be diffuse white matter involvement including subcortical U fibers. On T1WI the white matter signals are reduced and show abnormal high signals on T2WI and FLAIR sequences. The affected areas are mostly cerebral white matter , posterior limb of internal capsule , brain stem with sparing of corpus callosum. Subcortical cysts are seen mostly in anterior temporal and fronto parietal lobes. On DWI there is decreased anisotropy and increased ADC values. MR Spectroscopy shows decreased NAA in white matter and other metabolites in cystic areas. There will be no enhancement with contrast .

II. Clinical History :

17 months old child presented to pediatric OPD with complaints of developmental delay as noticed by the mother in the form of head lag even at 6 months of age, eventually could not sit without support , stand or walk. There was no history of seizures or birth trauma or post natal complications. There was no difficulty in feeding the child. On examination there was global developmental delay affecting gross motor , fine motor , speech and language and social domains severely. Family history of consanguineous marriage present. History of mental retardation , intellectual disability and congenital blindness in father's aunt present. On clinical examination the child had microcephaly (head circumference of 42 cms) and generalized hypotonia. Anthropometry OFC 42 cms < 3rd centile. CC 44 cms. Higher functions are normal with repetitive behavior. Lab investigations showed Hb 11.0g/dl , RBC count 6.05 M/ml, TLC 9.88 10 3/mm2. CRP > 6mg/L negative. Serum electrolytes normal . Thyroid profile and creatine phosphokinase were normal. MRI brain showed T2 and FLAIR hyperintensities involving the deep white matter of cerebral hemispheres including subcortical U fibers with sparing of frontal lobes. Both temporal lobes showed symmetrical cystic areas which are not restricted on diffusion restricted .The capsule ganglia , thalami and cerebellar hemispheres are normal.

III. Discussion:

Vander Knaap disease (vanishing white matter disease) is often reported from Agarwal community in India , though seen in other communities also [2] . Most of these cases present with epilepsy within two years. Ankush Sharma [3] reported it in a 27 yr old male with seizures and ataxia since the age of eight . Koray Koc [4] reported it in siblings aged 6 years and 10 years. Vander Knaap disease presenting with atypical findings like absence of seizures predicts poor Prognosis [5] . The youngest child reported was a 24 day neonate with seizure [6]. The most common clinical presentation in this condition is macrocephaly within one year of birth with delayed onset of motor dysfunction. Cognitive functions also will be delayed. Our child also presented with the classical symptomatology described as seen in other reported cases. The MRI findings in our case was very characteristic of Van der Knaap disease. The differential diagnosis include metachromatic leukodystrophy, Alexander disease, Canavan disease, X linked adrenoleukodystrophy. The presence of subcortical cysts in temporal lobes and involvement of subcortical U fibers differentiates it from metachromatic leukodystrophy. In Canavan disease the basal ganglia are involved and MR spectroscopy shows marked elevation of NAA which is not a feature in this condition. Alexander disease shows enhancement of frontal white matter and involvement of basal nuclei. X linked adrenoleukodystrophy shows contrast enhancement of peritrigonal white matter . The presence of subcortical cysts in temporal lobes along with diffuse dysmyelination of white matter of cerebral hemispheres is very typical of Van der Knaap disease. The treatment of this condition is by anticonvulsants and physio therapy for the loss of motor function

Conclusion: The treating pediatrician should be aware of this condition in infants with macrocrania with delayed development of motor dysfunction with typical MRI findings for proper management.

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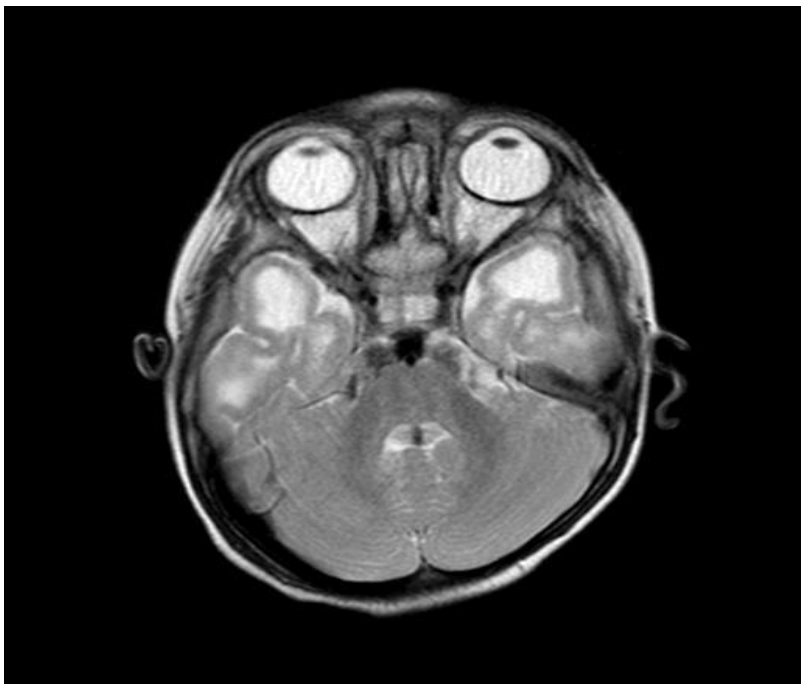
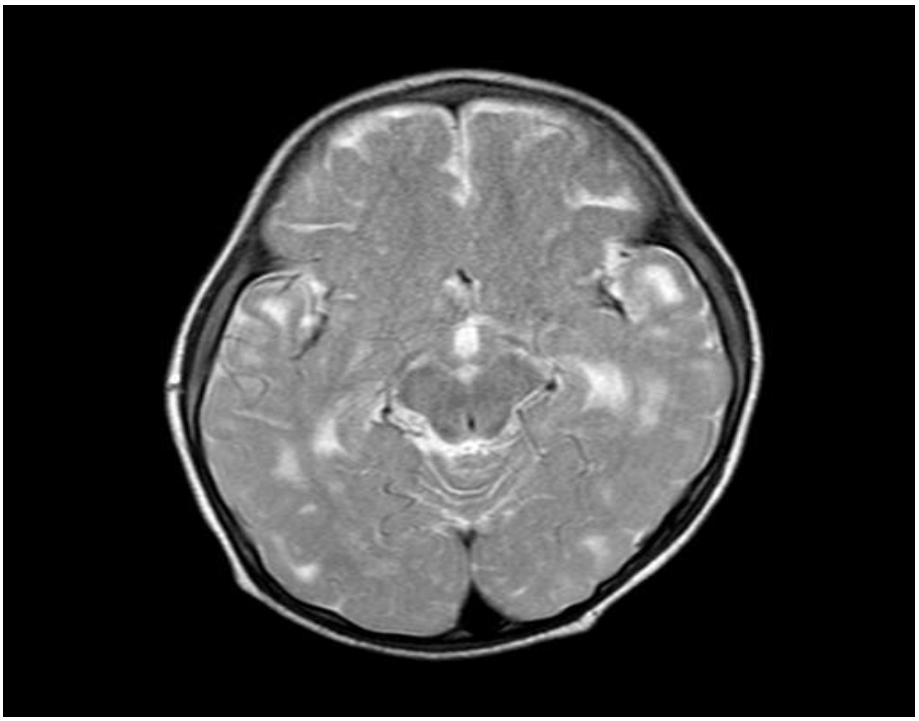
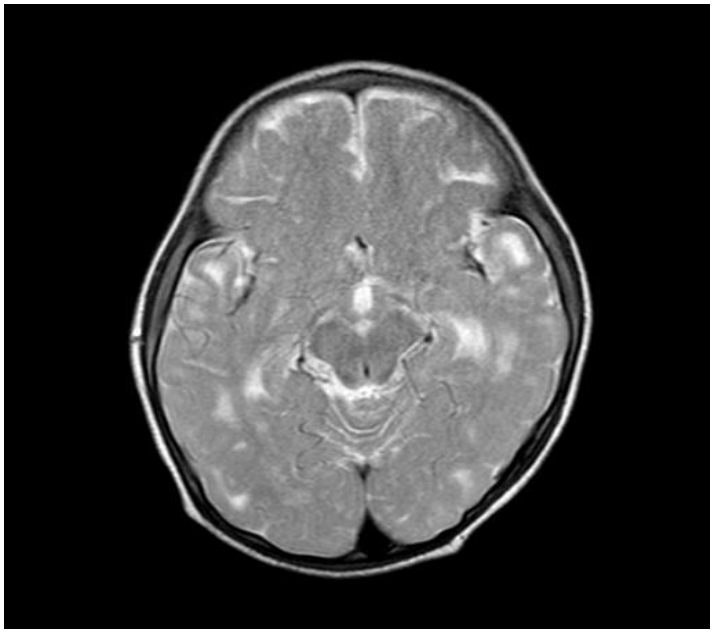
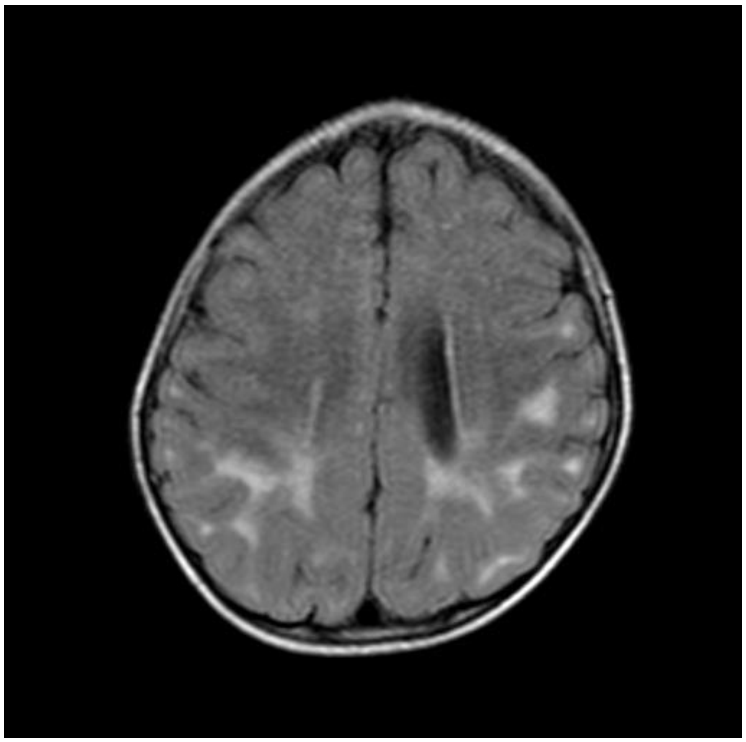
LEGENDS:

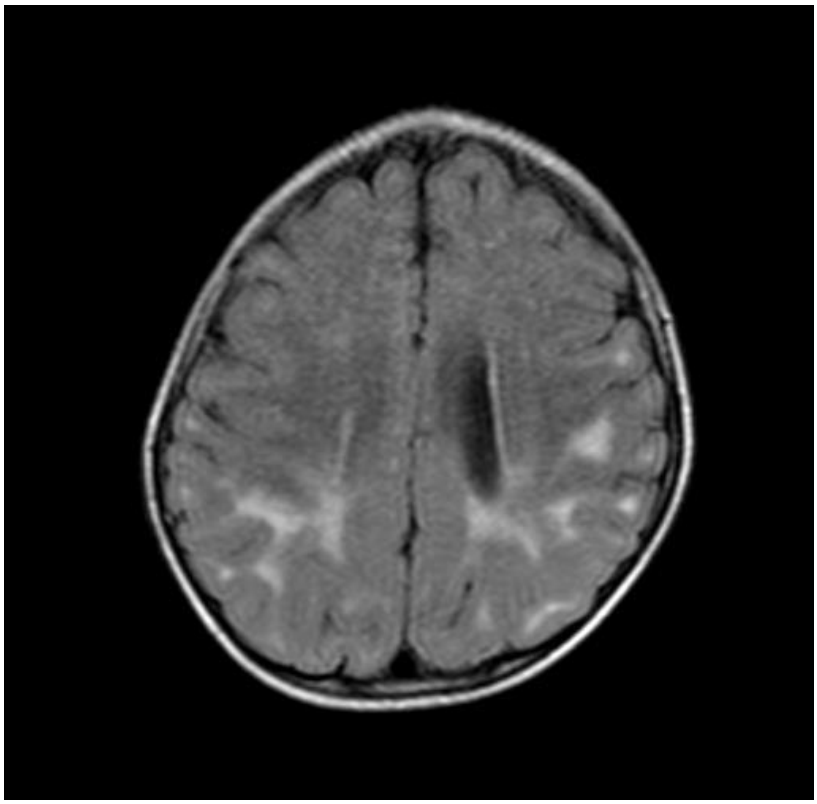
AXIAL MR IMAGES OF BRAIN show T2, FLAIR hyperintensities in temporo parital white matter including subcortical U fibers along with cystic changes in bilateral temporal lobes .

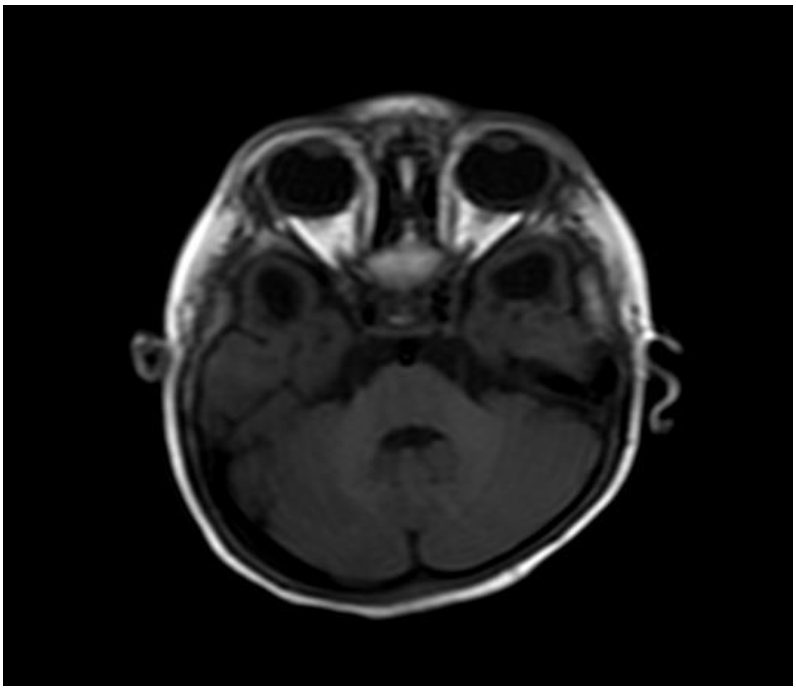












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