

CASE REPORTS

Aicardi-Goutieres Syndrome – A Case Report

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Abstract:

A 4 month old male baby, who had episodes of generalized convulsion for 1^{1/2} months and microcephaly, was referred to Radiology & Imaging dept. of BIRDEM for CT scan of brain. CT scan of brain showed extensive calcifications in both cerebral and cerebellar hemispheres –The probable diagnosis was TORCH infection with mild generalized cerebral atrophy. TORCH screening was done and found negative. Patient's RBS, SGPT, S.Calcium, Parathyroid hormone, TSH, thyroxine were within normal limits. MRI of brain showed extensive T1W hypointense and T2W hyperintense areas in peri-ventricular locations represent

leukodystrophy and mild cortical atrophy of brain. CSF examination revealed WBC count 10 cells/mm³ and all the cells were lymphocytes. Aicardi Goutieres Syndrome is a rare autosomal recessive disease in which there is extensive paraventricular cerebral and cerebellar calcifications with leukodystrophy and CSF lymphocytosis. Considering history, biochemical and imaging findings the final diagnosis was Aicardi Goutieres Syndrome.

Key words: Aicardi-Goutieres Syndrome, CT scan, MRI scan, cerebral and cerebellar calcifications.

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Introduction:

Aicardi Goutieres Syndrome (AGS) is a rare autosomal recessive disorder, found in consanguineous families. The actual frequency of AGS is unknown. There is diffuse demyelination and calcification in the media, adventitia and perivascular spaces of small vessels, suggest microangiopathy, mostly affects brain. Clinical features include microcephaly, seizure, mental & developmental retardation, intermittent sterile pyrexia,

puffy swelling on fingers, toes, ears and hepatosplenomegaly. Radiological findings include calcifications of the basal ganglia, particularly in the putamen but also extending into the white matter sometimes in a paraventricular distribution & white matter changes, particularly affecting the frontotemporal regions (leukodystrophy) with temporal lobe cyst-like formation, cerebral, cerebellar and brain stem atrophy and microcephaly¹⁻³. Laboratory findings include chronic cerebrospinal fluid (CSF) leukocytosis and increased concentration of interferon-alpha (IFN- α) & neopterin.⁴

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Case Report:

A 4 month old male baby was referred to Radiology & Imaging dept. of BIRDEM for CT scan of brain with the complaints of episodes of generalized convulsion for 1^{1/2} months and microcephaly. Parents of the baby had consanguineous marriage & TORCH screening of mother was not done during pregnancy. Maternal CBC, HBsAg, VDRL, RBS, Urine R/M/E were normal during pregnancy. Antenatal USG scan at 33 weeks had shown IUGR and oligohydramnios. The baby was born by LUCS at 36 weeks of gestation due to oligohydramnios. There was no history of birth asphyxia. Birth weight of the child was 2Kg. Head circumference of baby was about 32 cm which was below 50th percentile and anterior fontanelle diameter was 4x2.5 mm. The baby had no

history of fever. Liver and spleen were just palpable, otherwise no abnormality was detected on clinical examination.

CT scan of brain showed extensive calcifications in both cerebral and cerebellar hemispheres – may suggest TORCH infection with mild cerebral atrophy (Figure-1). TORCH screening (anti-Toxoplasma gondii, anti-Rubella virus, anti-Cytomegalo virus, anti-Herpes Simplex virus) was negative for both IgM & IgG. Colour Doppler Echocardiography showed small atrial septal defect (ASD) & trivial tricuspid regurgitation (TR). As TORCH screening was negative the baby referred to paediatric neurologist. From history, clinical examination and previous reports following differential diagnoses were considered – Congenital rubella syndrome, Aicardi-Goutieres syndrome (Pseudo TORCH syndrome), hypo or hyper parathyroidism, hypothyroidism, pseudo-hypoparathyroidism. Patient's RBS, SGPT, S.Calcium, Parathyroid hormone, TSH, T₄ were found normal levels. X ray skull showed extensive calcifications (Figure-2). X ray long bones revealed no linear areas of radio-lucency at metaphyseal regions with normal bone density (Figure-3). MRI of brain showed extensive T1W hypointense and T2W hyperintense areas in periventricular locations representing leukodystrophy and mild cerebral atrophy (Figure-4). Cerebrospinal fluid (CSF) examination revealed high WBC count (10 cells/mm³) and all cells were lymphocytes. As there were dissimilar radiological, biochemical and hormonal

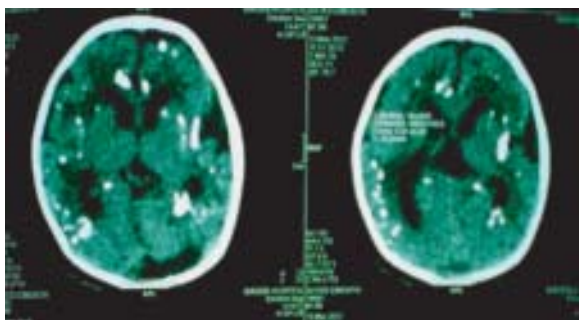


Fig-1: Multiple axial CT images of brain showing extensive calcifications in both cerebral and cerebellar hemispheres and mild cerebral atrophy with compensatory ventriculomegaly (Aicardi Goutieres Syndrome).

findings of congenital rubella syndrome and other endocrine disorders, the final diagnosis was of Aicardi-Goutieres Syndrome.



Fig- 2: X ray skull (lateral view) showing extensive calcifications.



Fig-3: X ray long bones show normal bone density with no linear areas of radio-lucency at metaphyseal regions .

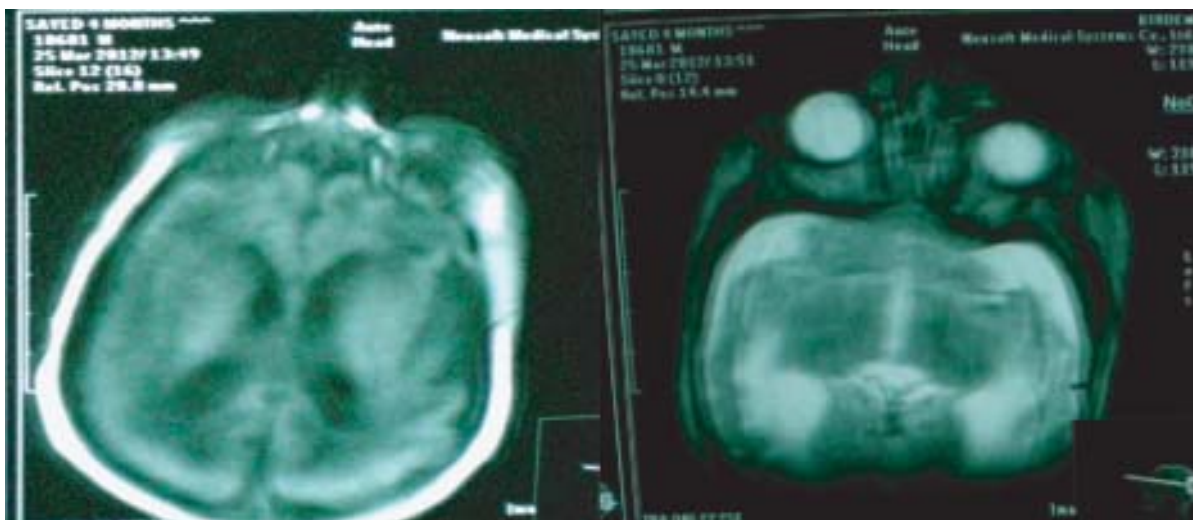


Fig.-4: MRI of brain showing T1W hypointense and T2W hyperintense areas in peri-ventricular locations represent leukodystrophy with mild cerebral atrophy (Aicardi Goutieres Syndrome).

Discussion:

Aicardi-Goutieres syndrome (AGS) also known as Pseudo-TORCH syndrome/Cree encephalitis was described by Jean Aicardi and Francise Goutieres in 1984⁵. The actual frequency of AGS was unknown. But it is rare disease. It is caused by mutation of one of five genes such as TREX1, RNA SEH2A, RNA SEH2B, RNA SEH2C & SAMHD1⁶. It is autosomal recessive in nature and isolated in consanguineous families.

The pathogenesis is diffuse demyelination and calcification in the media, adventitia, and perivascular spaces of small vessels.

Its clinical manifestations are progressive decline in cranial growth (microcephaly), seizure, mental & developmental retardation, intermittent sterile pyrexia, puffy swelling on fingers, toes, ears and hepatosplenomegaly. In our case, there were generalized convulsion and microcephaly which are common finding in AGS. Imaging findings of both CT scan and MRI of our case were similar to the previous reported cases of AGS which were evident by calcification of the basal ganglia extending into the white matter, white matter changes (leukodystrophy)⁷ and cerebral atrophy except cerebellar and brain stem atrophy and temporal lobe cyst formation.⁸ In our case we found 10 lymphocytes/mm³ CSF which was diagnostic. But thrombocytopenia and elevated liver enzymes were not found. Interferon-alpha (IFN- α) & neopterin may be found in CSF which was

not done because of lacking of laboratory facilities in our country.

The major differential diagnosis of Aicardi Goutieres Syndrome is congenital rubella syndrome though both IgG & IgM for rubella are negative. Because in immunodeficiency syndrome that reduce the antibody response to the organism. In congenital rubella syndrome the calcifications are periventricular locations rather than paraventricular seen in Aicardi Goutieres Syndrome with leukodystrophy.

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