A child with neonatal onset multi-systemic inflammatory disease (NOMID)

***Daham de Silva[1], Kavinda Chandimal Dayasiri[2], Michelle de Silva[2], Chamidri Naotunna[2], Harendra de Silva[1]**

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Introduction

Neonatal onset multi-systemic inflammatory disease (NOMID) is also known as chronic, infantile, neurological, cutaneous, and articular (CINCA) syndrome and only around 100 cases have been identified worldwide[1]. No cases have been reported in Sri Lanka[1]. In this report, the authors present a nine years old child with NOMID syndrome.

Case report

A nine year old boy, second live born child to healthy, non-consanguineous parents with a healthy sibling, presented for further evaluation of short stature, global developmental delay and anaemia. His antenatal period was uneventful. He was born at term by elective caesarean section, weighing 2.5 kg. He had recurrent urticaria from 4 months of age up to 9 years. Recurrent febrile episodes were present up to 2 years since infancy. He was noted to have poor head control until 7 months of age. During subsequent follow up, he had global developmental delay which was accompanied by intellectual impairment.

Anthropometry revealed macrocephaly (56cm, >97th centile) and confirmed short stature (height 93 cm, <3SD and below mid-parental height range). Further clinical examination found marked pallor, clubbing, cervical, posterior auricular and inguinal lymphadenopathy, urticarial rash and facial dysmorphism. He had a 2 cm hepatomegaly. Vision assessment revealed papilloedema and optic atrophy.

[1]*Faculty of Medicine, University of Colombo, Sri Lanka,* [2]*Lady Ridgeway for Hospital for Children, Colombo, Sri Lanka,*

**Correspondence:* haresha_d@yahoo.com

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Full blood count revealed microcytic, hypochromic anaemia (Haemoglobin 4.5 g/dl, mean corpuscular volume 56fl, mean corpuscular haemoglobin 23pg, mean corpuscular haemoglobin concentration 25%), leucocytosis (white cell count 37,000 x $10^3/\mu L$), neutrophilia (28,000 x $10^3/\mu L$), and eosinophilia (2600 x $10^3/\mu L$). Blood picture showed evidence of spherocytic haemolytic anaemia, predominantly microcytic hypochromic red cells and relative eosinophilia. TORCH screening, osmotic fragility test and cryohaemolysis test were negative. Inflammatory markers were elevated (ESR 80mm first hour, CRP 87 mg/L). Serum ferritin was low (17ng/L). Renal and liver profiles were normal.

Abdominal ultrasound revealed hepatomegaly and para-aortic lymphadenopathy. Both kidneys did not show abnormal echogenicity suggestive of amyloid deposition. Bone age was delayed (4 years) at chronological age of 9 years. Electromyogram and nerve conduction studies did not show myopathy or neuropathy. Roentgenograms of both knee joints showed early arthropathy of NOMID syndrome including bony erosions and osteoporosis (Figure 1).

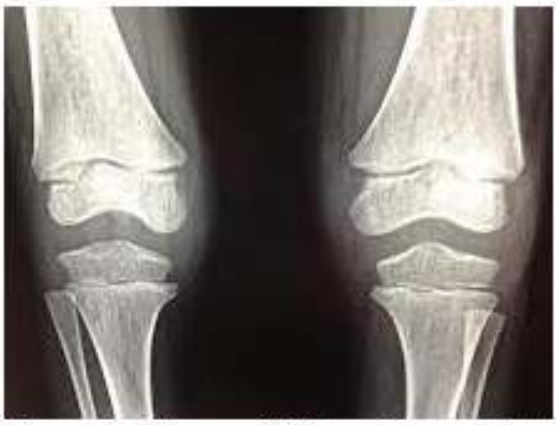

Figure 1: *X-rays of bilateral knee joints*

Echocardiogram revealed a structurally and functionally normal heart. Magnetic resonance imaging (MRI) of the brain revealed marginal communicating hydrocephalus, cerebral atrophy and delayed myelination.

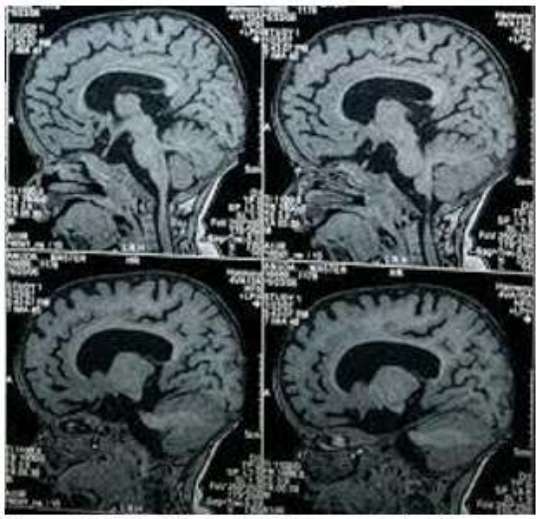

Figure 2: ***MRI of brain showing communicating hydrocephalus, cerebral atrophy & delayed myelination***

Discussion

NOMID was first described by Prieur and Griscelli[2]. Symptoms commence at birth or early infancy[3]. The disease characteristically begins with a maculopapular rash with urticarial features[4] and studies have shown that this rash appears in 100% of children with NOMID. Our patient had recurrent urticaria since 4 months of age. Failure to thrive, hepatomegaly, intermittent fever, anaemia, leucocytosis, generalized lymphadenopathy and painful arthropathy manifest with evolution of the disease[5]. Our patient had all these findings except painful arthropathy. Morphologic features include short stature, macrocephaly, and clubbing of fingers and the child reported here had all those clinical features[6]. The skeletal manifestations in this child included osteoporosis and delayed bone age, which are well described in NOMID syndrome[7]. Ocular manifestations in our patient included papilloedema and optic atrophy which are reported manifestations of NOMID syndrome. Hydrocephalus, cerebral atrophy and intellectual impairment are well described central nervous system features[7] and all were observed in the currently reported child. Reported laboratory abnormalities include neutrophil leucocytosis, persistent hypochromic microcytic anaemia, and elevated erythrocyte sedimentation rate[7] and all these laboratory features were present in our patient.

NOMID syndrome occurs following a mutation in NLRP3 gene which helps control inflammation. However, the inheritance may be heterogeneous and only up to 60% will have demonstrable mutation in the aforementioned gene[8]. Mutations in the same gene are also found in Muckle-Wells syndrome and familial cold-induced auto-inflammatory syndrome[9], but these 2 conditions can be differentiated by the clinical profile. NOMID runs a chronic relapsing course without definitive cure.

Treatment of NOMID syndrome is challenging and interleukin 1 (IL1) receptor antagonist, Anakinra, helps mitigate systemic inflammation in NOMID[10]. The outcome is better if it is commenced before the development of arthropathy[8]. Non-steroidal anti-inflammatory drugs (NSAIDS) and steroids relieve pain, fever and joint mobility temporarily as reported previously[11]. Azathioprine, colchicine, cyclosporin, etanercept, infliximab, intravenous immunoglobulin, methotrexate, penicillamine, salazopyrin and thalidomide have been tried in reported cases with no consistent response[11].

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