Childhood 'Rhupus' Syndrome

Co-existence of juvenile idiopathic arthritis (JIA) with juvenile systemic lupus erythematosus (jSLE) is termed childhood Rhupus syndrome. Rhupus syndrome is diagnosed when deforming polyarthritis of JIA and symptoms of SLE co-exist along with positive serological markers [1].

We recently diagnosed Rhupus syndrome in two girls, one presented with deforming polyarthritis of bilateral wrist and knee joints for 9 months, and other with arthritis of right knee and ankle for 11 months. First child also had alopecia, malar rash and oral ulcer for last 2 months, and had hypertension, pallor, hepato-splenomegaly and myelitis, without seizures or psychosis. The other child developed malar rash, oral ulcer and skin bleeds 11 months after the onset of arthritis. Initial investigation in first child showed anemia, neutrophilic leucocytosis with raised erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Chest *X*-ray, mantoux test, and liver and renal functions were normal. *X*-ray of wrist showed juxtra-articular osetopenia. Ultrasonograpghy (USG) of knee revealed chronic synovitis. Later, she had proteinuria, positive direct coomb's test (DCT), rheumatoid factor (RF), anti nuclear antibodies (ANA), anti-dsDNA with low C3 and negative anticardiolipin and anti-UI RNP antibodies. Renal biopsy showed grade II nephritis. Whereas, initial investigation in second child revealed anemia, raised ESR and CRP with positive rheumatoid factor. Later she developed pancytopenia, azotemia, hematuria, proteinuria and positive DCT, ANA, ds-DNA with low C3, and negative antiphospholipid and anti-UI RNP antibodies. Kidney biopsy showed grade III lupus nephritis. First child was receiving methotrexate, hydroxycholoroquine and NSAIDs for 6 months for joint manifestations. Later she required pulse methyl prednisolone, followed by oral prednisolone once she developed lupus myelitis, autoimmune hemolytic anemia and nephritis. Second child was managed with NSAIDs, methotrexate, and intra-articular steroid at the beginning, required intravenous cyclophosphamide, prednisolone and azathioprine, once she developed lupus.

The girls had childhood Rhupus syndrome. Rhupus arthropathy is postulated to be either articular involvement of lupus, lupus with chronic polyarthritis or an overlap of lupus with JIA [2-4]. Children with Rhupus present with JIA and later develop lupus. In children, asymmetric erosive and or nonerosive involvements are described [5]. Previous reports showed female predominance, onset at around 8 years, polyarticular involvement, non-erosive arthritis and about 4 year of delay in diagnosis of lupus [5]. Both our patients had deforming polyarticular and oligoarticular arthritis with mean age of 9.5 years and delay in diagnosis of lupus for 9 months. Though rare, childhood Rhupus syndrome is to be considered as a differential diagnosis in patients presenting with deforming arthritis.

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Caffeine in a Term Neonate with Apnea

A term neonate with recurrent central apnea was evaluated at our neonatal intensive care unit (NICU). This male neonate, weighing 3800 g, was vigorous at birth following a caesarian delivery at 38 weeks of gestation. He required continuous positive airway pressure (CPAP) support initially for transient tachypnea but subsequently could not be weaned off as he had recurrent apneas. There was no significant antenatal history. The neonate had recurrent respiratory pauses of 10-40 seconds duration, associated

with desaturation/bradycardia, majority requiring stimulation. There was no identifiable cause for apnea in this neonate despite extensive work-up (septic work-up/biochemistry/echocardiography/CSF analysis/ neuroimaging/EEG/gastroesophageal reflux evaluation/ upper airway study/ metabolic screening). The neonate was then labelled as having primary/idiopathic apnea, and was started on trial of caffeine therapy after discussion with parents. Caffeine citrate (20mg/kg) was injected intravenously, followed by 10 mg/kg every 24 hourly. There was noticeable improvement in symptoms, and the neonate was weaned off from CPAP support after 3 days; he was discharged at 3 weeks of postnatal life on oral caffeine. Post-discharge home monitoring with pulse-oximeter recorded no apneas. Follow-up of the infant showed lag in weight velocity which catched-up after stopping caffeine at four month of age. Developmental milestones were appropriate for age.

Respiratory pauses of >20 seconds or if associated with bradycardia and cyanosis are labelled as apneas [1]. Apnea is a grave sign in term neonates and could result from sepsis, meningitis or severe brainstem dysfunction in hypoxic neonates. A term neonate with temporal lobe hemorrhage can also present with apneic seizures [2,3]. The neonate in our care was well looking with no features of encephalopathy. Caffeine therapy is extensively used in preterm neonates with apnea of prematurity [1]; however, use of this drug in term neonates is not well known. Its use is described for post-extubation management, and also for bronchiolitis related apnea [4]. We presume that the neonate had primary/idiopathic central apnea requiring intervention that gradually resolved over a period.

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Grave's Disease Following Aplastic Anemia: Predisposition or Coincidence?

A 3-year-old boy, whose mother had Grave's disease for 9 years, was diagnosed with severe aplastic anaemia in October, 2010. Bone marrow aspiration showed hypoplasia. and bone marrow cytogenetic studies were normal. He was diagnosed to be having severe aplastic anemia and was treated with immunosuppressive therapy of anti-thymocyte globulin at 5 mg/kg/d intravenously for 5 days, prednisone 1 mg/kg/d orally for 1 month and cyclosporine A 3 mg/kg/d orally. Because of neutropenia, recombinant Human granulocyte colony-stimulating factor therapy was initiated. Erythrocyte and thrombocyte infusions were also given moderately because of low blood counts. Four months after immunosuppressive therapy, cyclosporin was continued orally. The blood work-up was normal after 6 months of immunoceppressive therapy .

On follow-up, the parents informed us that the patient had a voracious appetite but had poor weight-gain, and palpitations and excessive sweating. Grave's disease was confirmed by a low TSH, elevated total thyroxine (T4), triodothyronine (T3), free triodothyronine (FT3) and free thyroxine (FT4). Thyroid-associated antibodies TRAb(+), ATG(+) and ANTI-TPO(-) were present. Thyroid ultrasound showed bilateral diffuse thyroid lesions. The patient was put on 0.5 mg/kg/d of prednisone and methimazole, which successfully improved the thyroid function later on.

Severe aplastic anemia has now been identified as a kind of bone marrow failure caused by T lymphocyte hyper-function, which induces the apoptosis of hematopoietic cells by excessive secretion of Th1 lymphokines such as IL-2 and interferon-gamma (IFN-γ) [1]. Grave's disease involving the thyroid gland is typically characterized by the presence of circulating auto-antibodies that bind to and stimulate the thyroid hormone receptor, resulting in hyperthyroidism and goiter. It is postulated that the failure of T-suppressor cells allows expression of T-helper cells, sensitized to the TSH antigen, which interact with B cells. These cells differentiate into plasma cells, which produce thyrotropin receptor-