Administration of oral calcium and calcitriol remains the mainstay of treatment. The goals of therapy are to maintain serum calcium levels within the reference range so as to avoid hypercalciuria. Thyroid function tests should be evaluated periodically even in absence of features of AHO, as hypothyroidism develops rarely, as seen in our patient.

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Chronic Myeloid Leukemia in a Child with IgA Nephropathy

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We report an 11 year old boy with IgA nephropathy developing chronic myeloid leukemia on follow-up. This association suggests that a B cell defect might be involved in the pathogenesis of these two conditions.

Key words: *Chronic myeloid leukemia, IgA nephropathy.*

There is increasing evidence of abnormal glycosylation of immunoglobulin A1 (IgA1) subclass due to B-cell defect in the pathogenesis of immune-complex mediated IgA nephropathy [1]. The occurrence of IgA nephropathy and leukemia has been reported rarely in children [2]. Here we report a child with IgA nephropathy developing chronic myeloid leukemia (CML) on follow-up.

CASE REPORT

An 11-yr-old boy was diagnosed acute nephritic syndrome at 3 year back in view of hypertension, hematuria, proteinuria (spot urine protein to creatinine ratio 0.75), mild renal insufficiency (serum creatinine 1.1 mg/dL), and normal serum albumin and cholesterol. He had no anemia, leukocytosis or electrolyte disturbances. He was treated with salt and fluid restriction and oral nifedepine for hypertension. Serum complement C3 level was normal, anti nuclear antibody and anti double standard DNA was negative. In view of persistent hypertension, renal insufficiency, microscopic hematuria and proteinuria he was referred for evaluation. On examination, the patient was well nourished (weight 46 kg, and height 157 cm) with periorbital edema and blood pressure140/84 mm Hg. Systemic examination was normal. Urinalysis showed 2+ albumin, red blood cells and Up/Uc ratio of 0.33. Blood investigations showed a creatinine of 1.0 mg/dL, albumin 4.2 g/dL and potassium 5.1 mEq/L. Ultrasonogram of the kidneys showed normal size kidneys. Renal biopsy showed seven glomeruli of which two were completely sclerosed and one showed segmental sclerosis and proliferation. Remaining

glomeruli were normal-sized with increase in mesangial cellularity and thin capillary walls; tubules, interstitium and blood vessels were unremarkable. Immunofluorescence examination showed mesangial granular deposits of IgA, and C3c and IgM. A diagnosis of class III IgA nephropathy was made [3]. The patient received treatment with angiotensin converting enzyme inhibitors and fish oil supplements without steroids. Later, he received therapy with an angiotensin receptor blocker. Ten months later, he was admitted with fever, generalized edema, anemia, hepatosplenomegaly and a soft systolic murmur. The blood pressure was 130/80 mm Hg. Investigations showed a serum creatinine level of 0.9 mg/dL, urea 28 mg/dL, uric acid 6.8 mg/dL, sodium 134 mEq/L, potassium 3.4 mEq/L and albumin 3.9 g/dL. The hemoglobin level was 8.5 g/dL, with leukocytes 237200/cu mm, and differential count of 6% polymorphs, 5% lymphocytes, 9% eosinophils, 10% basophils, 8% stab neutrophils, 6% myelocytes, 9% metamyelocytes, 10% promyelocytes, 32% myeloblasts and 5% nucleated red cells; platelets were normal. A diagnosis of CML with blast crisis was made (***Fig* 1**), and the patient received intravenous and oral fluids of 3 L /day along with alkalization of urine and allopurinol. BCR-ABL translocation assay showed hybrid transcript in leukocytes suggesting chronic phase of CML. Genomic breakpoint observed at e14a2 corresponds to p210. The patient was treated with Imatinib 400 mg once a day [4, 5]. After 1 month follow-up, there was no hepatosplenomegaly, and leukocyte counts and renal functions were normal.

DISCUSSION

IgA nephropathy is a common chronic primary glomerular disease, which rarely presents as acute nephritic syndrome. Systemic diseases with IgA deposits include systemic lupus erythematosus, Henoch-Schonlein purpura, cystic fibrosis, ankylosing spondylitis, dermatitis herpetiformis, inflammatory bowel disease, celiac disease, chronic liver disease, infections like mycoplasma, leprosy and toxoplasmosis, as well as neoplasms like non-Hodgkin lymphoma, monoclonal IgA gammopathy and carcinoma of the lung and colon [1]. Various hypotheses suggested in the pathogenesis of IgA nephropathy are predisposing genetic factors, IgA immune complex disease due to abnormal IgA glycosylation and adhesion molecules on mononuclear cells and lymphocyte subpopulation [1,6,7]. Chromosome aberrations identified by genome-wide linkage analysis in families with IgA nephropathy cases is suggested to be predisposing genetic factor for development of disease [1]. Abnormal galactosylation in the hinge region of IgA1 subclass results in formation of circulating immune complex and its deposition in mesangium. These deposits release cytokines, growth factors and adhesion molecules, which lead to proliferation of mesangial cells, inflammation and sclerosis [1,7]. The recognition of B-cell defect and the role of adhesion molecules/growth factors enables targeting treatment with bone marrow transplant or neutralizing antibodies [6,7]. Findings that predict progression to end stage renal disease include heavy proteinuria, diffuse mesangial proliferation, a high proportion of glomeruli showing sclerosis, crescents or capsular adhesions, and the presence of moderate or severe tubulointerstitial changes [8]. There are increasing reports of association between chronic glomerulonephritis and leukemia in adults [9,10]. Renal infiltration by leukemic cells is rare and presents with abdominal pain or hematuria with renal biopsy showing presence of abnormal cells as seen in peripheral blood. The present patient had acute nephritic syndrome, which was followed three years later by the occurrence of CML. This association suggests that a B-cell defect might be involved in the pathogenesis of IgA nephropathy and CML.

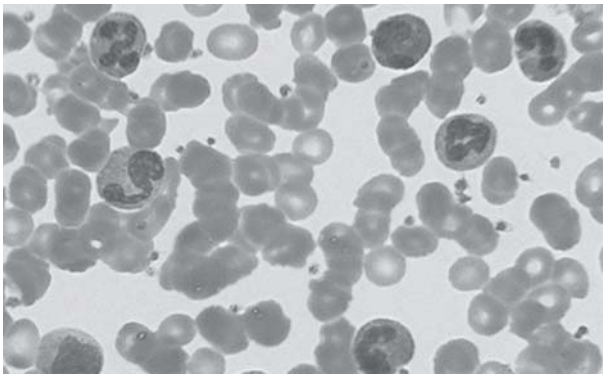

FIG.1 *Peripheral smear showing features of chronic myeloid leukemia.*

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Facio- Auriculo- Vertebral Sequence in association with Congenital Hypoparathyroidism

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Although, Facio-auriculo-vertebral sequence (FAVS) is a well recognized condition with cranio-facial, ocular and vertebral anomalies, extreme variability of expression is characteristic. Association of cardiac, CNS, lungs, kidneys and limb defects are described. We report a neonatal case with FAVS in association with congenital hypoparathyroidism.

Key words: *Branchial arch anomaly, Congenital hypoparathyroidism, Embryology, Facio-auriculo-vertebral sequence.*

Facio-auriculo- vertebral sequence (FAVS) is a spectrum of developmental disorders involving oculo- auriculo- vertebral disorder, Hemifacial microsomia, FAV syndrome and Goldenhar syndrome [1,2]. FAVS consists of facial asymmetry, maxillary and mandibular hypoplasia, cleft palate, macrostomia, microtia or anotia and pre- auricular ear tags or pits, in addition to vertebral anomalies. Goldenhar syndrome consists of above defects plus epibulbar dermoids and/ or lipodermoids. Association of anomalies of heart, kidneys, CNS, lungs, limbs have been described [3,4]. There is only one fetal autopsy case report of FAV sequence with associated DiGeorge sequence (with hypoplasia of parathyroid glands) [5].

CASE REPORT

A 15-day-old neonate, second child of a non-consanguineous marriage, presented to us with two days history of multiple brief episodes of seizures. On clinical examination, baby had facial asymmetry with hypoplasia of the right mandible and right macrostomia, cleft palate, small deformed and very low set right pinna with a pre-auricular tag and atresia of the right external auditory canal (***Fig.* 1**). Apart from anti-mongoloid slant and hypertelorism, both the eyes were normal. The neonatal reflexes (including Moro's, sucking, rooting, etc) and other systemic examination were normal.

On evaluation, his sepsis screen (including total white cell count, band count, random blood sugar, C- reactive proteins, blood culture and CSF study) was negative. Biochemical evaluation revealed a serum calcium concentration of 6 mg /dL, the serum phosphorus concentration of 11 mg /dL and serum alkaline phosphatase concentration of 150 U/L. The serum concentration of magnesium was 1.8 mg /dL, the serum concentration of 25-hydroxyvitamin D was 7 ng /ml (normal range- 5-42) and the serum concentration of