Influenza-B Associated Rhabdomyolysis and Acute Renal Failure

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Received: October 16, 2012;
Initial review: November 26, 2012;
Accepted: January 01, 2013.

We present a 15-year-old boy who developed severe rhabdomyolysis and acute renal failure following influenza B infection. His renal function was restored after appropriate therapy for rhabdomyolysis. Although rapidly progressive pneumonia, respiratory failure, and acute respiratory distress syndrome are the most common severe complications of influenza B infection, clinicians should be aware that influenza B may be complicated with rhabdomyolysis and acute renal failure in children.

Key words: *Rhabdomyolysis, Renal failure, Influenza B.*

Influenza B often present with myalgia, rhabdomyolysis is rarely seen. The clinical presentation of rhabdomyolysis varies from an asymptomatic increase in creatine kinase (CK) to severe ARF and hypovolaemic shock. Few reports are available on association of rhabdomyolysis and acute renal failure (ARF) with influenza virus type B infection in children [1-5]. We present the case of a child with cerebral palsy whose renal dysfunction, caused by influenza-associated rhabdomyolysis, was restored after adequate treatment.

CASE REPORT

A 15-year-old boy, diagnosed with cerebral palsy, was in bedridden status. He had been admitted to the hospital many times for airway infection. Four days prior to presentation, he developed sudden onset of fever, decreased activity, productive cough and yellow sputum. On examination, his weight was 31 kg. The vital signs were stable. Coarse crackles were heard over bilateral lower lung fields. Laboratory investigations revealed TLC 7,600/mm^3 ($P_{61}L_{31}$ M_6E_2); serum urea nitrogen (BUN), 16 mg/dL, serum creatinine, 0.9 mg/dL; asparatate aminotransferase (AST), 33 U/L; (normal, 5-35 U/L); and alanine transaminase (ALT) 16 IU/L (normal, <40 U/L). The rapid screen test for acute influenza infection was positive for influenza B, but negative for influenza A. Chest radiography showed no active lung lesion. The electrocardiogram was normal, and blood cultures, sputum cultures, urine cultures and viral throat cultures were all negative for microbial growth. After admission, oseltamivir 60 mg bid and ampicillin and sulbactam 1.5g every 6 hours were prescribed. On day 3, chest radiography revealed an increased pneumonitis patch on right upper lung.

Shortness of breath, and dark urine with oliguria were noted on the 5th day. Laboratory test results revealed serum CK 407,421 IU/L (normal, 27-168 U/L), CK-MB 827 IU/L (normal, <16 U/L); creatinine:1.47 mg/dL; AST/ALT 3060/744 IU/L, LDH 23,880 IU/L (normal, 135-147 U/L); sodium 157 meq/L, potassium 5.1 meq/L, calcium 6.6 meq/L; uric acid 13.8 mg/dL (normal, 2.5-7.2 mg/dL). Clinical presentation and laboratory findings were suggestive of rhabdomyolysis with acute renal failure, most probably caused by influenza B infection. The patient was transferred to intensive care unit. Due to altered consciousnes, he received endotracheal intubation and mechanical ventilation. The systolic blood pressure decreased to 50-60 mmHg and poor cardiac contractility was detected. Standard management was instituted for shock including inotropic agents. Metabolic acidosis was treated by administration of sodium bicarbonate.

On hospital day 6, the blood pressure and cardiac contractility recovered to normal. However, the child developed disseminated intravascular coagulation, and had hematuria and bleeding from the gastrointestinal tract. Renal functions deteriorated and the child was started on hemodialysis. The oseltamivir treatment was shifted to peramivir because of poor GI absorption. Peramivir was discontinued 2 days later due to increasing liver enzymes, and subsequently fever subsided. After hemodialysis therapy, his renal function was improved gradually. The serum levels of the muscle enzymes CK and AST decreased rapidly to 2711 IU/L and 168 IU/L, respectively, at discharge 27 days after admission.

One week after discharge, the patient visited our outpatient department for follow-up; the serum CK level, renal and liver function had returned to normal.

DISCUSSION

Rhabdomyolysis is defined as a clinical and laboratory syndrome resulting from skeletal muscle breakdown with leakage of muscle cell contents into the systemic circulation. It is characterized by an elevated serum creatine kinase level and myoglobinuria, and may lead to renal dysfunction [2]. Rhabdomyolysis can cause life-threatening complications, including hypovolemia, hyperkalemia, metabolic acidosis, acute renal failure (ARF) and DIC [3]. ARF often results from the nephrotoxic effects of lytic myocyte components and usually presents as oligouric pigment-induced intrinsic renal failure [4]. The early and aggressive fluid repletion and bicarbonate therapy are the standard treatment to prevent ARF in such cases.

Influenza B-associated rhabdomyolysis is an infrequent and little-known complication of influenza B virus infection in children. In 2010, Wu, *et al*. [5] reviewed hospitalized children with influenza B virus infection at a university children's hospital in North Taiwan during 2000–2007 and found that 24 had presented with rhabdomyolysis; none had renal involvement. A recent review suggests that the risk of acute kidney injury in rhabdomyolysis is usually low when CK level at admission is <15, 000 to 20,000 IU/L [3]. Our patient had high level CK 407,421 IU/L. Because limited data indicate that administering oseltamivir via a gastric tube can provide systemic absorption in critically ill patients [6], our patient was treated with intravenous peramivir. It is, a neuraminidase inhibitor, authorized for emergency use for the treatment of hospitalized patients with known or suspected 2009 H1N1 influenza. Clinicians should be alert to patients with flu-like symptoms with severe muscle pain and dark brown urine (to rule out rhabdomyolysis). The high level of CK could be an indicator for the fatal complication of ARF. The early diagnosis and appropriate therapy should decrease mortality and restore renal function.

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Naxos Disease and Carvajal Variant

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Received: November 4, 2012; Initial review: December 10, 2012; Accepted: January 04, 2013.

An 11-yr-old girl, born out of a consanguineous marriage presented with recurrent exertional syncope due to ventricular tachycardia. She had woolly hair, palmoplantar hyperkeratosis and mild cardiomegaly. Echocardiogram revealed mild left ventricular dysfunction. Features were consistent with Carvajal variant of Naxos disease, an arrhythmogenic cardiomyopathy with autosomal recessive inheritance.

Key words: *Cardiomyopathy, Palmoplantar keratoderma, Ventricular tachycardia, Woolly Hair.*

Naxos disease is a recessive form of arrhythmogenic right ventricular dysplasia/ cardiomyopathy associated with a cutaneous phenotype characterized by palmoplantar keratosis and woolly hair. It is caused by mutations of the genes encoding desmosomal proteins [1]. Cardiac disease has 100% penetrance by adolescence, manifested as symptomatic arrhythmias,

heart failure and sudden death. The variant, Carvajal syndrome is characterized by younger age at presentation and more pronounced left ventricular involvement.

CASE REPORT

An 11-year-old girl of Indian origin born out of 3rd degree consanguineous marriage presented with 2 transient episodes of syncope during exertion within a period of three months. Both the times she recovered spontaneously before reaching the hospital. She was previously asymptomatic except for thickening of palmar and plantar skin with fissures noticed since early childhood. None of her family members had a similar illness. General examination revealed woolly hair and hyperkeratosis of palms and soles. In the palms, hyperkeratosis was most marked in the subungual areas. There were fissures on the plantar aspect of big toe. In addition, distal phalanges of hands appeared shorter than normal (***Fig.* 1**). Rest of the general examination including anthropometry was normal. Clinical examination of cardiovascular system revealed a resting pulse rate of 80/minute with normal volume and character of the peripheral pulses. Blood pressure was 96/44 mm Hg in the left upper limb in the sitting position. Cardiac apex was in the 5th left intercostal space in the midclavicular line with normal character, indicating cardiomegaly. First and second heart sounds were normal and there were no additional sounds or murmur.

She was evaluated further to find out the etiology of syncope. Baseline electrocardiogram (ECG) showed complete right bundle branch block with left posterior hemiblock indicating advanced myocardial disease. Transthoracic echocardiogram showed mild ventricular dysfunction. Left ventricle (LV) was predominantly involved with significant chamber dilatation and the ejection fraction was 45%. ECG obtained during subsequent episode showed ventricular tachycardia (VT) at a rate of 150/ minute (regular wide QRS tachycardia with north-west axis and deep S in V5 and V6) suggesting VT as the etiology of syncope. Magnetic resonance imaging did not reveal any fat deposits in the myocardium.

The phenotypical features and cardiac manifestations along with history of consanguinity are suggestive of arrhythmogenic cardiomyopathy with autosomal recessive inheritance. These features are consistent with Naxos disease, probably Carvajal variant. Family was counseled regarding the disease and poor prognosis. She is being managed with amiodarone and antifailure medications including carvedilol. Two years from the initial diagnosis, her disease continues to worsen with recurrent refractory episodes of ventricular tachycardia and progressive cardiac failure.

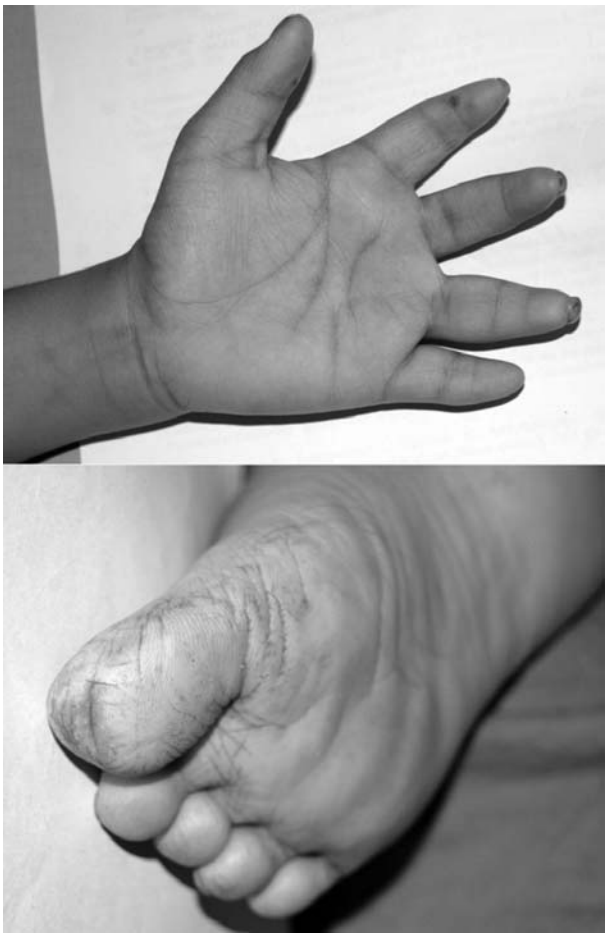

FIG. 1 *Palmoplantar keratosis. Note the subungual keratosis in the hands and fissures in the sole. Short distal phalanges of fingers are also obvious.*

DISCUSSION

Naxos disease was first reported in 1986 by Protonotarios, *et al*. [1] in patients from the Greek island of Naxos. Apart from Naxos, cases have also been reported from Italy, Turkey, Israel, Saudi Arabia and India. The variant with more pronounced left ventricular involvement and clinical overlap with dilated cardiomyopathy has been described in families from Ecuador (Carvajal syndrome) [2].

Genetic studies have located two causative genes, encoding for the desmosomal proteins plakoglobin and desmoplakin. Homozygous mutation of the *plakoglobin* gene truncating the C terminal of the protein causes Naxos disease which maps to 17q21 [3]. Homozygous mutations of another desmosomal component, desmoplakin which truncates the C terminal of the protein and maps to 6p24 is identified in involved patients from Ecuador [4]. The disease pathogenesis is linked to the specific tissue characteristics of cardiac muscle. Cardiac

muscle consists of single myocytes connected by complex intercellular contact sites called intercalated discs. Three different types of intercellular junctions are located in intercalated discs, namely adherence junctions, gap junctions and desmosomes. Adherence junctions and desmosomes secure mechanical coupling enabling synergistic contraction while gap junctions serve electrical coupling allowing rapid spread of action potentials. Plakoglobin is a common component of both adherence junctions and desmosomes. At the adherence junctions, it is connected to the actin cytoskeleton and at desmosomes to the intermediate filaments of desmin. Desmoplakin is another desmosomal protein that interlinks plakoglobin or plakophilin with desmin intermediate filaments. Defects in linking sites (C terminal) of these proteins interrupts cell to cell adhesion, particularly under conditions of increased mechanical stress leading to cell isolation and death. The result is progressive loss of myocardium and fibro-fatty replacement. Surviving myocardial fibers within fibro-fatty tissue provide a slow conduction substrate inducing re-entrant ventricular arrhythmias [5]. The degree of fatty replacement is variable.

Desmosomes are abundant in epidermis too, explaining the cutaneous manifestations. Cutaneous disease is confined to areas most exposed to pressure like the palmar and plantar surfaces, indicating the role of mechanical stress in disease expression.

In patients with Naxos-Carvajal disease, woolly hair was apparent from birth while palmoplantar keratoderma developed during the first year of life [5]. The symptomatic presentation was usually with syncope and/or sustained ventricular tachycardia during adolescence. Disease is progressive with death occurring from arrhythmia or congestive heart failure [6]. Treatment options are limited and include antiarrhythmic therapy, medical therapy for congestive heart failure, implantable cardioverter defibrillator (ICD) implantation and cardiac transplantation.

There are a few reports of Naxos disease from India earlier [7-10]. Features of this patient including presentation at younger age and left ventricular involvement are more suggestive of the Carvajal variant. However, hypoplasia of distal phalanges seen in our patient is not reported earlier.

Contributors: AA was involved in the care of the patient under supervision of KSR and preparation of the draft. AA and RPK finalized the draft. KSR reviewed the script critically and will act as guarantor of the case report. Final manuscript was approved by all the authors.
Funding: None; *Competing interests*: None stated.

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Bardet-Biedl Syndrome – A Rare Cause of Cardiomyopathy

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Received: October 23, 2012;
Initial review: November 14, 2012;
Accepted: January 09, 2013.

Bardet-Biedl syndrome (BBS) is a rare autosomal recessive condition characterized by retinitis pigmentosa, polydactyly, obesity, learning disabilities, hypogonadism and renal anomalies. Cardiomyopathy in association with BBS has previously being reported only twice in literature. We report a case of a patient presenting with features of cardiomyopathy, who was subsequently diagnosed to have BBS.

Key words: *Bardet-Biedl syndrome, Cardiomyopathy.*

Bardet-Biedl syndrome (BBS) is an autosomal recessive condition with a wide spectrum of clinical features. The principal manifestations are rod-cone dystrophy (sometimes called atypical retinitis pigmentosa), postaxial polydactyly, central obesity, mental retardation, hypogonadism, and renal dysfunction. BBS is distinguished from the much rarer Laurence-Moon syndrome, in which retinal pigmentary degeneration, mental retardation, and hypogonadism occur in conjunction with progressive spastic paraparesis and distal muscle weakness, but without polydactyly [1,2]. Significant cardiac abnormalities in isolated BBS were first reported by Elbedour, *et al*. [3] in 1994, which included 2 cases of IVS hypertrophy and 1 case of DCM with no identifiable cause. Cardiomyopathy in association with BBS has previously been reported only twice in literature.

CASE REPORT

A 13-year male child was admitted to the intensive care unit with complaints of progressive breathlessness and cough for three months and recent swelling of his entire body. There was no history of a preceding viral illness, weight loss, haemoptysis, joint swelling, palpitations and decreased urine output. There was no past or family history of tuberculosis or cardiovascular disease. He was tachypneic and tachycardic with a low volume pulse, low BP and pitting edema. On systemic examination, heart sounds were muffled with B/L rhonchi, crepitations and hepatomegaly. Chest *X*-ray showed cardiomegaly with basal pulmonary infiltrates and ECG was normal. Echocardiography revealed dilated left atrium and ventricle with mild mitral and tricuspid regurgitation with normal sized coronary arteries and no pericardial effusion. Fractional shortening and ejection fraction were 18.5% and 0.38 respectively with no evidence of diastolic dysfunction. A provisional diagnosis of a recent myocarditis or dilated cardiomyopathy was made. Known risk factors for cardiomyopathy *i.e.* recent viral infections, rheumatic fever, congenital heart diseases, hyper-tension, connective tissue disorders, inborn errors of metabolism, muscular dystrophies, Kawasaki disease etc were ruled out and thus a possible familial/genetic cause was sought. The patient was stabilized and transferred to pediatric cardiology.

Patient had delayed motor and mental development milestones and was the second offspring of non-consanguineous marriage. There was facial dysmorphism, hypertelorism, downward slanting palpebral fissures, flat nasal bridge, long philtrum, and thick upper lip. Postaxial polydactyly and syndactyly was present in the right foot with brachydactyly in all the limbs. He had micropenis, absent axillary and pubic hair, although both testes were palpable in the scrotal sac. His height was 135.5cm, falling between 3-10 centile. On neurological examination: hypotonia, broad based gait, poor coordination, balance, dysdiadochokinesia and past pointing were present without sensory disturbance. Speech was hypernasal and slow. Fundus examination showed retinopathy, bilateral optic atrophy and ERG showed grossly abnormal retinal function in both the eyes, suggestive of atypical retinitis pigmentosa. The IQ was 56. Hearing assessment was normal. Investi-gations revealed a low hemoglobin (Hb-8 g/dL) and low calcium-(7.9 mg/dL) with raised phosphorus (5.9 mg/dL) and abnormal KFT (BU-117 mg/dL, creatinine-6.4 mg/dL, GFR-9 mL/min/m^2BSA, serum sodium-115 mmol/L and potassium-4.6 mmol/L) implying chronic kidney disease. Urine examination, GTT, LFT, ABG, C3/C4 levels, ASO and ANA were within normal limits however TSH levels were raised**.** Ultrasonography revealed bilateral shrunken kidneys with loss of corticomedullary distinction. CECT head was normal. Clinical and echocardiographic screening of other family members was normal.

The constellation of polydactyly, hypogonadism, retinitis pigmentosa, mental retardation and CKD suggested a possibility of Bardet Biedl syndrome. Other supporting features were overcrowding of teeth, gall bladder stones, and primary hypothyroidism.

DISCUSSION

Till 1970, Laurence Moon Bardet Biedl syndrome (LMBBS) was considered a single entity. However, due to the presence of two distinct phenotypic patterns, it was split into Laurence- Moon and Bardet-Biedel syndromes, with the former characterized by paraparesis and the latter by polydactyly [1]. The characteristic combination of findings in Bardet Biedl syndrome are rod cone dystrophy (93-100%), polydactyly (58-69%), obesity (72-88%), learning disabilities (41-62%), hypogenitalism in males (85-90%) and renal anomalies (25-100%) [2,4]. Bardet-Biedl syndrome (BBS) is a rare, genetic multisystem disorder; a ciliopathy secondary to the basal body dysfunction [4,5]. It is associated with mutations in 14 genes [6,7].

Our patient presented with CHF and had 5 primary and six secondary features in accordance with Beales, *et al*. [4] classification. The patient had significantly low ejection fraction with dilatation of the left ventricle suggestive of underlying cardiomyopathy. All other predisposing causes of cardiomyopathy were absent. The alliance of cardiomyopathy with this syndrome has been rarely documented.

McLoughlin, *et al*. [5] surveyed 330 published cases of LMBBS and documented 9 congenital heart diseases which included ASD, VSD, PDA, pulmonary stenosis, hypoplasia of aorta, dextrocardia, and L-TGA. Of these, 6 patients had polydactyly and may be considered as BBS patients although the presence/absence of paraparesis is not mentioned. Seven patients had acquired heart disease most commonly left ventricle hypertrophy, biventricular hypertrophy and rheumatic heart disease. All patients with acquired heart disease also had some form of renal involvement but only 3 were hypertensive [5].

Significant cardiac abnormalities in isolated BBS were first reported by Elbedour, *et al.* [2] in 1994, which included 2 cases of IVS hypertrophy and 1 case of DCM with no identifiable cause. Most of the patients studied were young, thus limiting the discovery of acquired heart disease but authenticating the reported lesions to the basic syndrome. There was no association of cardiac abnormalities with presence of renal involvement, hypertension or high creatinine levels. In these studies, male predominance was apparent and patients were asymptomatic in contrast to our patient who had symptomatic cardiac disease. In a survey of 109 BBS patients, two were found to have cardiomyopathy [4].

Dilated cardiomyopathy in our patient without an antecedent apparent viral infection might still be late sequelae of a subclinical viral infection of the myocardium. However, with no evidence of metabolic, hereditary, systemic and toxic exposure our case possibly belongs to that of "idiopathic cardiomyopathy" group. BBS thus may be a genetic/familial cause of the same. We thus report the 3rd association of BBS and cardiomyopathy. However, unlike most other documentations, CHF with cardiomyopathy was the presenting complaint leading to the first time diagnosis of this syndrome in our patient. Periodic follow up by echocardiography is required in order to monitor possible progression of heart disease [3].

Alström syndrome is a rare autosomal recessive ciliopathy, which clinically closely resembles BBS and is characterized by childhood obesity, progressive cone-rod dystrophy, sensorineural deafness, dilated cardiomyopathy, hepatic dysfunction, renal insufficiency and endocrinological features. It shares many of the complex spectrums of phenotypic features with BBS. Cognitive function is preserved in Alström syndrome and polydactyly is not a feature, thus distinguishing it from Bardet-Biedl syndrome.

BBS must be considered as a rare cause of cardiomyopathy. The association has been sparsely documented. The absence of predisposing factors and rarity of both conditions makes coincidence less likely.

Contributors: DKY: revised the manuscript for important intellectual content, supervised data collection and approved the final manuscript as submitted. He will act as guarantor of the study; MKB: carried out the initial analyses, reviewed and revised the manuscript and approved the final manuscript as submitted and AJ: drafted the initial manuscript and clinically worked up the case and approved the final manuscript as submitted.

Funding: None. *Competing interests*: None stated.

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Meningitis due to *Neisseria meningitidis* Serogroup B in India

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Received: September 29, 2012; Initial review: October 22, 2012; Accepted: January 24, 2013.

Invasive meningococcal disease has a fulminant course and high mortality. *Neisseria meningitidis* serogroup A is predominantly responsible for meningococcal disease in India and the developing countries. Group B meningococcus, which is prevalent in the developing world is uncommon in India. We herein report the second case of group B meningococcal infection from the country, two decades after the reporting of the first case. Ineffective vaccines against serogroup B warrant the need for close surveillance of this disease.

Key words: *Child, India, N. meningitides serogroup, Surveillance.*

Invasive meningococcal disease commonly follows a fulminant course and has high mortality [1]. Thirteen serogroups of *Neisseria meningitidis* have been identified, but six of these serogroups (A, B, C, W135, X and Y) are responsible for majority of the infections worldwide [1]. Serogroup A strains are predominantly responsible for meningococcal disease in developing countries, including India [2]. Serogroup B strains are responsible for outbreaks of meningitis in the developed world where vaccines against serotypes A,C,Y and W135 are extensively used [3]. Group B meningococcus is not prevalent in India, with only one previous report [4]. We herein report the second case of group B *N. meningitidis* infection from the country.

CASE REPORT

The patient was a one-year-old, boy weighing 7kg who presented to the pediatric emergency with seizures, history of high-grade fever, vomiting, lethargy and decreased oral acceptance since three days. He had multiple episodes of generalized tonic clonic seizures in last 24 hours. He was delivered at full term through an uneventful vaginal delivery. Immunization history was appropriate for age. No history of similar illness was present in the family and immediate contacts. On examination, child was conscious, had no cyanosis and had bilaterally constricted pupils with sluggish reaction to light. He was febrile (101^0F) with heart rate of 172 beats per minute and respiratory rate 42 per min. Capillary filling time was less than 3 sec. Anterior fontanelle was full and pulsatile. Neck rigidity was present. There was increased tone in all four limbs, deep tendon reflexes were brisk with bilateral extensor plantars. He had no skin rash. Initial clinical diagnosis of meningitis was made and therapy with intravenous ceftriaxone and anticonvulsants was started, in addition to supportive management.

Laboratory reports revealed that the child had hemoglobin of 8.1 g/dL with total white blood cell count of 10,610/mm^3 (56% neutrophils, 38% lymphocytes, 3.9% monocytes and 1.2 % eosinophils), and platelet count of 5.9 lakh/mm^3; C-reactive proteins was raised (178.97 mg/L). The blood pro-calcitonin levels were 118.23 ng/mL (≥10 ng/mL and plasma lactate levels were also raised (30.5 mg/dL). Renal function tests and serum electrolytes were within the normal range. The cerebrospinal fluid showed raised protein levels (113 mg/dL), and low levels of glucose (26 mg/dL). CSF cytology could not be reported because of hemmorhagic nature of tap. CSF lactate levels were increased at 83.93mg/dL and CSF chloride levels were 123 nmol/L. Latex agglutination was performed on the CSF sample and was

reactive for *N. meningitidis* group B (Pastorex Meningitis*, BIO-RAD*). Blood and CSF culture grew *N. meningitidis* as identified by Vitek 2 Compact system (BioMerieux, France). Serogrouping was done by *N.meningitidis* antisera (Remel Europe Ltd. UK) and was confirmed was as *N.meningitidis* serogroup B. The strain was found resistant to penicillin (MIC, 0.5 µg/mL) and ciprofloxacin (MIC, 0.5 µg/mL), and sensitive to ceftriaxone (MIC, 0.094 µg/mL), chloramphenicol (MIC, 0.19 µg/mL), azithromycin (MIC, 0.5 µg/mL), rifampicin ((MIC, 0.032 µg/mL), and meropenem (MIC, 0.032 µg/mL) as determined using E test and interpreted in accordance with CLSI guidelines. Blood and CSF samples tested positive for *ctrA* gene for *N.meningitidis* by Real time PCR assay. DNA extraction from blood and CSF samples was performed using the Magnapure Compact automated nucleic acid extraction system. (Roche Diagnostics, Basel, Switzerland) as per manufacturer's protocol. A 111 bp region of *ctrA* gene was amplified using ctrA specific primers, with slight modification [6]. *N. meningitidis* ATCC 13090 was used as the positive control.

The cranial ultrasonography showed slight ventricular prominence with normal cerebral parenchyma. The patient was placed under isolation and chemoprophylaxis with ciprofloxacin given to the close contacts of the patient. The patient was continued on intravenous ceftriaxone and phenytoin. He was put on mechanical ventilation because of repeated seizures and declining oxygen saturation. High grade fever and seizures were persisting till the 5th day of admission despite midazolam infusion (2µg/kg/min). Intravenous dexamethasone 1 mg 8 hourly was initiated along with other therapy on day 5. The patient started showing clinical improvement from the 7th day onwards with no fresh seizures, repeat blood culture showing no growth, and improved blood counts. Midazolam was discontinued on 9th day of admission. After 16 days of antibiotic therapy, repeat CSF examination was within normal limits and culture did not yield any growth. Despite the clinical and laboratory improvement, the antibiotic therapy was maintained for a total of 21 days. Dexamethasone was discontinued after 10 days of therapy. By day 29, the child had recoverd and was discharged on oral anticonvulsants from the hospital. Meningococcal carriage screening of the patient and the parents did not yield any positive results.

DISCUSSION

Meningococcal meningitis is a serious infection and if untreated, may be fatal with case fatality rates reaching 5-10% in developed countries and upto 20% in developing countries [7]. The neonate in the previous study had died within 6 hours of admission. However, in our study, the child survived and recovered after a prolonged hospital stay. The source of Group B meningococcus could not be ascertained in this case. The reason for very low prevalence of serogroup B in India is not known. It may be postulated that predominance of serogroup A might lead to suppression of serogroup B in the Indian population similar to the phenomenon observed in pre-vaccine era in developed countries. In addition to the varying geographical distribution, the proportion of cases caused by each serogroup may also vary by age. US studies describe serogroup B to be causing 30-50% of cases in infants younger than 1 year of age, while serogroups C, Y, and W135 causing 75% of meningococcal disease in those 11 years and older [7,8]. Both the cases from India (including the present case) were below one year of age.

Effective vaccines are available for meningococcal serogroups A, C ,Y and W135. Consequently, serogroup B, *N. meningitis* has become the major cause of bacterial meningitis especially in countries where vaccine for other serotypes has been introduced [4]. Vaccine against serogroup B strains for global use has been challenge. This is due to frequent antigenic variations among this serogroup. Antigenic mimicry of serogroup B polysaccharide with human neurologic tissues is also a problem [9]. Vaccines based on other bacterial cell components have shown poor protective immune response in children under 24 months of age [10]. Thus, the occurrence of even a single case Group B meningococcal meningitis in India has important public health implications.

Indian data on meningococcal disease is sparse and is limited to the studies undertaken during or immediately after suspected outbreaks. Studies during inter-epidemic period and constant surveillance of the invasive meningococcal disease can help understanding the epidemiology of this highly fatal disease. Though there is a gap of two decades between the first and the second case report, there is a strong need for close surveillance and documentation for further group B meningococcal infections in India. With recent licensing of conjugated quadrivalent vaccines in the country, it will be interesting to observe changing epidemiology of invasive meningococcal disease in India.

Contributors: All the authors have prepared, designed and approved the study.
Funding: None; *Competing interests*: None stated.

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Myxoid Lipoblastoma

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Received: December 10, 2012;
Initial review: December 21, 2012;
Accepted: January 24, 2013.

A rapidly growing soft tissue mass in the axilla of an infant raises the suspicion of a lipoblastoma or a liposarcoma. Excisional/incisional biopsy is vital in confirming the diagnosis and hence avoiding aggressive extirpation. This case report highlights the role of histopathology and immunohistochemistry as the gold standard in differentiating a lipoblastoma from a liposarcoma. In some cases where the histopathology is inconclusive, genetic rearrangement of the PLAG1 (pleomorphic adenoma gene 1) oncogene on chromosome 8q12 helps in confirming the diagnosis of lipoblastoma.

Key words: *Axillary mass, Lipoblastoma, Infant.*

The presence of an axillary mass in infancy entertains the diagnosis of a cystic hygroma, hamartoma or a soft tissue neoplasm. Lipomatous tumors, namely lipoblastomas are rare, benign tumors of infancy and early childhood. They arise from the embryonal fat cells which persist and continue to proliferate into postnatal life. They are characterized by their rate of rapid growth, local invasion and increased incidence of local recurrence of 14-25% [1]. The diagnosis of a liposarcoma in infancy should be made with caution, owing to its rarity and the aggressive treatment involved. The role of excisional biopsy, histopathology with immunohistochemistry and cytogenetics in the establishment of an accurate diagnosis, is highlighted in the following case report.

CASE REPORT

An 8-month-old female child presented to us with a swelling in the right anterior chest wall, extending through the axilla to the back (***Fig.* 1**). It was noticed since the age of 5 months, with rapid increase in size over the last one month, to the present size. The mass was non tender, soft to firm in consistency, bosselated surface, with no skin changes. The differential diagnoses included a vascular hamartoma, cystic hygroma, a soft tissue tumor such as lipoblastoma or a liposarcoma, or a matted lymph node mass.

The ultrasound examination showed an 8×7.5×4.5cm iso- to hyperechoic, lobulated solid mass, with posterior border extending beneath the lower margin of the scapula. MRI chest confirmed an 8×5×4cm right shoulder girdle,

well encapsulated soft tissue mass probably arising from the subscapularis muscle and probably of neoplastic etiology. There was no intrathoracic or bony involvement. In view of the well encapsulated nature of the tumor, an excisional biopsy was planned. The rapid growth in the tumor size warranted immediate excision to prevent mass effect and rule out malignancy which is rare, but not unknown.

Surgical exploration revealed an 8×5×6 cm vascular fleshy mass arising from the subcutaneous tissue in the axilla, closely adherent to the muscles of the chest wall and the axillary neurovascular bundle. The use of a nerve stimulator and bipolar diathermy facilitated fine dissection. The mass was completely excised. On histopathology, gross examination showed an encapsulated lobulated mass with pale cut surface with myxoid changes. On microscopy, lobular architecture with interspersed myxoid and mature adipose tissue was seen. Each lobule contained vacuolated adipocytes in various stages of maturation. Maturation of the adipocytes was more in the centre than in the periphery. There was absence of invasion in the surrounding skeletal muscle. The wide CD34, focal S100 positivity, Mib negativity and morphology rendered the diagnosis of a myxoid lipoblastoma. A PLAG1 gene analysis for determining the aggressiveness of the tumor was recommended, but was unavailable. No recurrence has been noted 2 years postoperatively.

DISCUSSION

Lipoblastoma is a tumor of infancy, with 90% before 3 years of age and 40% in the first year of life [3] A male preponderance of 3:1 has been noted [1]. Though most commonly found in the extremities -70% [4], it can also be seen in the head and neck area, trunk, mediastinum, retroperitoneum, and various organs like lung, heart and parotid gland [5]. It is recognized as a benign neoplasm with tendency of local recurrence of 14% to 25 % [1]. They can be locally invasive making complete surgical excision difficult and hence increasing the risk of local recurrence.

Histopathology with immunohistochemistry in conjunction with the morphology remains the gold standard in differentiating a lipoblastoma from a myxoid liposarcoma. Myxoid morphology in lipoblastoma is not very common. Characterstic features and lipoblastoma have been previously described [1,3,6].

In cases where these features are inconsistent, cytogenetic advancement has led to the confirmation of LPB, where consistent rearrangements in the PLAG1 oncogene on chromosome 8q12 have been noted [7].

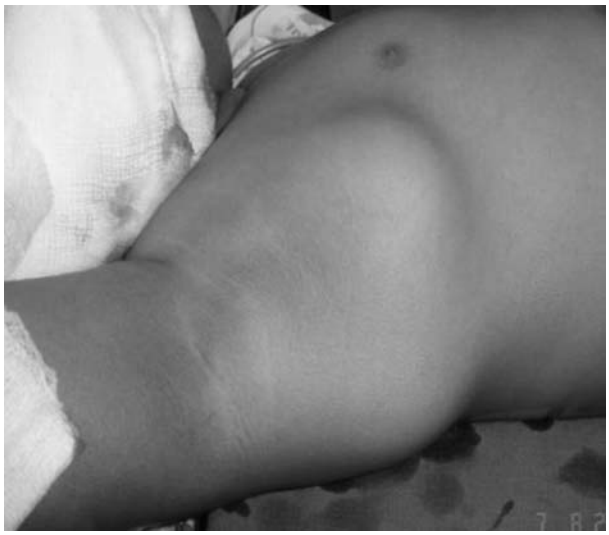

FIG. 1 *An 8×5 cm swelling in right axilla extending to the back.*

It has been found that 70% of lipoblastoma have *PLAG1* gene rearrangement on chromosome 8q12 and up to 18% are associated with polysomy for chromosome 8 [7]. *PLAG-1* is involved in mitogenesis, proliferation, apoptosis and IGF-2 up-regulation. In humans it is expressed mainly in fetal tissues and in low levels postnatally [7, 8].

Surgical resection is the treatment of choice except in those infiltrating tumors requiring mutilating excision [1]. The aim of surgery is complete gross excision without sacrificing the surrounding vital structures or extirpation of tissue that could lead to major deformity. Incomplete gross excision, infiltrating LPB, is notorious for its recurrence. Hence, sequential close postoperative follow up with MRI is essential. A follow up of at least 2 years postoperatively is recommended [9].

Contributors: All authors contributed to writing the report.
Funding: None; *Competing interests*: None stated.

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Rhizomelic Chondrodysplasia Punctata With Maternal Systemic Lupus Erythromatosus

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Received: December 27, 2012;
Initial Review: January 28, 2013;
Accepted: January 29, 2013.

We report Rhizomelic Chondrodysplasia Punctata (RDCP), a rare, autosomal recessive disorder with rhizomelic shortening of limbs, congenital cataracts and seizures but without any biochemical abnormality. The mother of the baby developed Systemic Lupus Erythromatosus (SLE) with Ro/SSA antibodies 11 months after delivery. Ro/SSA antibodies may generate calreticulin antibodies causing characteristic skeletal changes.

Key words: *Anti Ro/SSA, Punctate epiphyseal calcification.*

The classic form of rhizomelic chondrodysplasia punctata (RCDP) a rare, autosomal recessive peroxisomal disorder is characterized by proximal shortening of the limbs, cataracts, distinct facial appearance, growth failure, psychomotor retardation and seizures[1]. Common radiological features are punctate epiphyseal calcifications, metaphyseal abnormalities, coronal clefts in vertebral bodies [1]. RCDP is usually lethal with 60% deaths occurring by age 1 year. [2] The characteristic biochemical profile has been previously described [3]. Recently, patients with RCDP phenotype but without abnormal peroxisomal function have been reported usually secondary to teratogen exposure or maternal diseases [4]. We report a neonate with features of RCDP without biochemical abnormality but whose mother was diagnosed having SLE 2 months prior to delivery.

CASE REPORT

This male baby was the first child of healthy unrelated Indian Hindu parents born at term by spontaneous vaginal delivery. His mother and father were 25 and 29 years old, respectively. There was no history of spontaneous abortions or antenatal teratogen exposure. His birthweight was 2459 g (10-25th percentile), length was 42.5 cm (<10th percentile), and head circumference was 33 cm (50th percentile). His upper segment to lower segment ratio was 1.8:1. He was a disproportionately

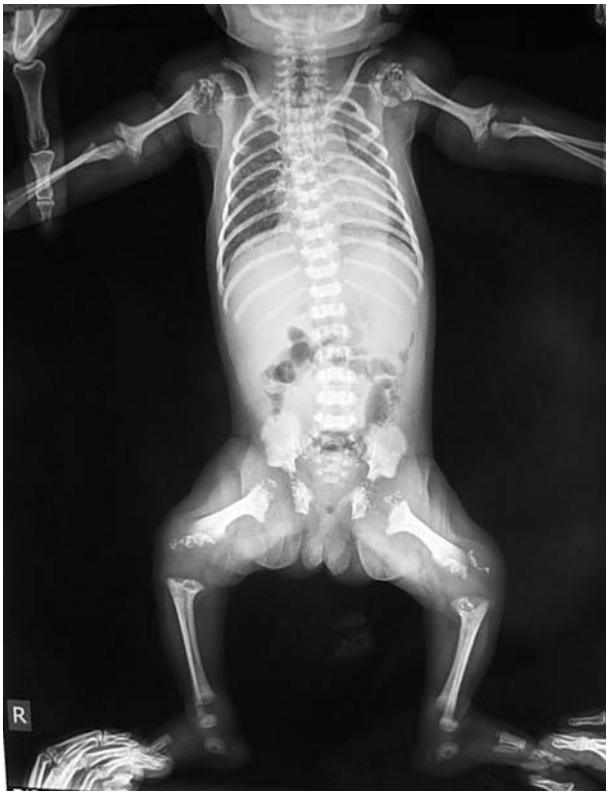

FIG. 1 *Skiagram showing punctate epiphyseal calcification of shoulder, elbow, hip and knee joints with metaphyseal flaring of humerus.*

short infant. He had proximal shortening of both upper and lower limbs, midfacial hypoplasia with a depressed nasal bridge. and anteverted nares with a short neck with nuchal fullness, a barrel-shaped chest. There were no skin lesions. Ophthalmological examination showed cataract in both eyes.

A skeletal survey showed rhizomelic shortening of extremities. Bony stippling was noted in shoulder, elbow, hip and knee joints with metaphyseal flaring in humerus and femur (***Fig.* 1**). The pelvis appeared normal, but the spine exhibited minimal ossification and coronal clefts of the vertebral bodies.

Cranial and abdominal ultrasonography and echocardiography were normal. CT Brain revealed stippled anterior arch of foramen magnum. A diagnosis of rhizomelic chondrodysplasia punctata was made. Red blood cell plasmalogen content was performed as dimethylacetals (DMAs). The mean levels of C16:0DMA/C16:0 fatty acid, C18:0 DMA/ C18:0 fatty acid, VLCFA and phytanic acid levels were within the reference range.

Cataract extraction was done. Genetic assay could not be done due to financial constraints. Genetic counseling was given to the parents. The infant was discharged from the nursery at 10 days of age and is receiving regular physiotherapy.

Two months later, the mother had joint pain of the hands and the feet and photosensitive malar rash. Maternal serology results were diagnostic of SLE with positive antinuclear antibody with a 1:640 titer in a speckled pattern; positive for extractable nuclear antigen with an anti-SM level of 42.10 EU/mL [reference:<20 EU/mL] and anti-RNP level of 192.50 EU/mL [reference: <20.01 EU/mL]; positive for anti- SSA[Ro] 155.4 EU/ mL (reference:<25.1 EU/mL). Other antibodies were negative with normal C4 complement level. The mother was started on low dose prednisolone 10 mg/day.

DISCUSSION

Chondrodysplasia punctata (CDP) is characterized by punctuate calcification of cartilage. It includes peroxisome biogenesis disorders (Zellweger syndrome, neonatal adrenoleukodystrophy, infantile Refsum disease, and RCDP Type1), maternal conditions and teratogen exposure. CDP has four main types, the autosomal dominant (Conradi-Hunermann's type), autosomal recessive (rhizomelic type), the X-linked dominant form (Happle) and the X-linked recessive form.

There are three types of RCDP. RCDP Type 1 involves mutations in the PEX7 gene [3]. RCDP Types 2 and 3 are phenotypically similar to RCDP Type 1, but result from deficiencies of dihydroxyacetone phosphate acyltransferase and alkyldihydroxyacetone phosphate synthase, respectively[1].

Though our patient presented with many characteristic features of RCDP but he differed from other patients in that there was no abnormality of red blood cell plasmalogens and phytanic acid levels. Antenatal history of teratogens like rubella infection, and warfarin or dilantin use was negative. There are case reports of maternal autoimmune diseases like SLE and phenylketonuria with CDP in their babies [5-9]. Our patient is the eleventh reported RDCP patient born to a mother with SLE. Only 3 have had the characteristic skin lesions of neonatal lupus erythematosus (NLE) and none had congenital heart block.

The proposed mechanism for stippling in CDP-associated maternal lupus is immune mediated by maternal autoantibodies crossing the placenta in early to midgestation. These antibodies inhibit a high-affinity calcium-binding protein of endoplasmic reticulum, calreticulin. Anti Ro/SSA is an autoantigen complex that may include calreticulin. Auto-antibodies to calreticulin and Ro/SSA are involved in the pathogenesis of congenital heart block and the cutaneous lesions of SLE and may be responsible for the skeletal changes by inhibiting calcium binding. Animal model studies showed that immunization of mice with Ro resulted in the production of anti-Ro, anti-La, and anti-calreticulin antibodies [10] Our patient's mother was positive for Ro/ SSA. Alternatively maternal autoantibodies affect the infant's vitamin K metabolism [8] resulting in bleeding into the epiphyseal cartilage, which produces the stippled appearance.

Autoantibodies may be the largest single risk factor for the development of CDP in the neonate but the presence of autoantibodies cannot be the only determining factor to predict the occurrence of CDP, because the incidence of CDP in infants of mothers with SLE is very low. Management of these babies is mainly supportive. Cataract extraction and physiotherapy may help. Genetic counseling is necessary. Monitoring growth and development, seizure control, vision, hearing, contractures and orthopedic complications need regular assessment on follow up.

Contributors: AR and PKD: managed the patient, reviewed the literature and drafted the manuscript; PKD will act as guarantor of the study; AR: collected the data. SP: critically reviewed the article and helped in drafting the paper. The final manuscript was approved by all the authors.
Funding: None; *Competing interests*: None stated.

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Very Low-dose Intravenous Immunoglobulin for Treatment of Immune Thrombocytopenic Purpura

Treatment of immune thrombocytopenic purpura (ITP) is a controversial subject. The management varies widely, ranging from observation only, to aggressive management with corticosteroids, intravenous anti-D rhesus, intravenous immunoglobulin (IVIG), rituximab, splenectomy, etc. The British Society for Hematology and American Society of Hematology have developed ITP management guidelines [1].

It was first reported in 1981 by Dr. Paul Imbach that high doses of IVIG promote fast recovery of ITP in children. The mechanism of action of IVIG remains as yet incompletely understood [2]. For pediatric patients requiring treatment, a single dose of IVIg (0.8 to 1 g/kg) can be used as first line treatment [3]. We report a case of ITP treated with very low-single dose of IVIG (100 mg/kg).

A nine-year-old boy presented to us with complaints of fever, cough and pin point red spots over the body for 2 days. He also had one episode of bleeding from nose. On examination he had petechial spots scattered all over the body. There was no hepato-splenomegaly. Complete blood count showed haemoglobin of 11.4 g/dL, white blood cell 8000/mm^3 and platelet 8,000/mm^3. Peripheral blood smear was normal other than severe thrombocytopenia and large platelets. The bone marrow examination showed megakaryocytes, which were present in increased numbers. Patient was started on IV methylprednisolone (20 mg/kg/day) for 3 day then switched to oral prednisolone. With this treatment, platelet count increased to 45000/mm^3. Patient again presented after 10 days with platelet counts of 10,000, multiple petechial spots and gum bleeding. Patient was started on intravenous anti-D rhesus (75 µg/kg) but no response was noted. At this stage it was planned to give IVIG but due to cost constraints, patient was given single very low dose of IVIG (100 mg/kg). Bleeding stopped and platelet count increased to 26,000/mm^3 after 1 day, 68,000/mm^3 after 2 days, 140,000/mm^3 after 3 days of IVIG therapy. Four weeks after therapy platelet count was 72,000/mm^3.

Till date there is only one paper concluding that treatment with very low-dose (200mg/kg) IVIG according to individual clinical response is effective and safe in childhood acute ITP [4]. With 1 g/kg dose itself, only 2/3rd of responders will have a sustained response. The remaining 1/3rd will relapse after 6 weeks. Whether the sustained response rate is going to be further lower with 100 mg/kg dose is a question to be explored.

ITP behaves differently in different children. Some respond to steroids, some to IVIG and some to neither. Presumably this is related to the amount of antiplatelet antibody production. We hypothesize that some children may have a relatively lower antibody load and may hence respond to lower doses of IVIG. Further studies are needed to evaluate the efficacy of very low dose IVIG in children with ITP.

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Ventricular Ectopic Beats in a Child Receiving Carbamazepine

Hematopoetic, hepatic and dermatological toxicity of Carbamazepine is well-known, but cardiac side-effects are not that widely recognized. Its use has rarely been reported to cause conduction abnormalities, predominantly in elderly women, with therapeutic (or moderately elevated) plasma concentrations of the drug [1]. We herein report a child with syncopal attacks following carbamazepine use.

An 8-year-old child presented with history of fainting attacks while playing, which lasted for a few seconds, followed by spontaneous recovery. He had two such witnessed episodes in the preceding week, which prompted the present consultation. He was developing normally, studied in class III, and never had any previous episodes of dizziness, syncope, breathlessness or cyanosis. He did not report any other associated cardiac symptoms. He was on regular treatment with carbamazepine (15 mg/kg/d) for Idiopathic generalized epilepsy from another institution since past one year, with no non-compliance, or missing a dose in the last 24-hours. Contrast-enhanced CT head done at that time was normal.

On detailed history, these episodes of fainting did not resemble the seizures that he had experienced in the past, and during this episode he did not have any other neurologic symptoms. The fainting attacks were transient and the child recovered immediately after the fall. On examination, the patient was alert and cooperative with blood pressure of 98/76 mmHg. He was noted to have an irregularly irregular pulse, and ectopic heart beats after every 8 to 10 beats, with a heart rate of 70 to 80 beats per minute. A 12-lead electrocardiogram showed ventricular premature beats (***Fig.* 1**). Child was admitted and started on tablet atenolol, 25 mg daily . An echocardiogram ruled out structural heart disease. Holter monitoring for 24 hours showed frequent ventricular ectopic beats though the child did not have further fainting episodes during the hospital stay.

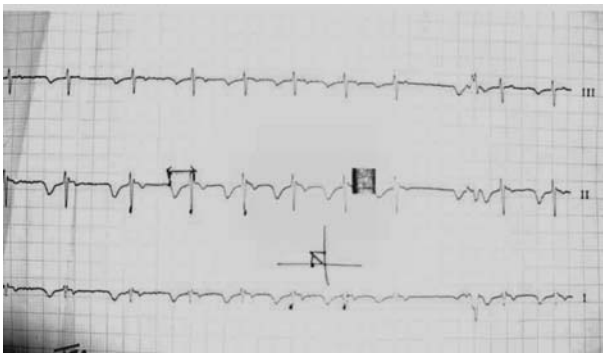

FIG. 1 *Ventricular premature beats seen in the child's electrocardiogram on admission.*

In the background of reports of carbamazepine causing conduction disturbances, it was replaced with tablet valproate 15 mg/kg/day. Atenolol was stopped. Serum carbamazepine level six hour after the last dose of the drug was 10.6 µg/mL (therapeutic range 8-12 µg/mL). The patient was discharged on day 5, after documenting a normal ECG. Repeat holter study at 3 months of follow-up, did not show any abnormality. On follow-up at one year, he was asymptomatic without any complaints of fainting attacks or giddiness.

Carbamazepine exerts its effect by acting as a sodium channel blocker, and is known to produce negative chronotropic and dromotropic effects on the heart; thus, it may sometimes lead to conduction disturbances, including Sinus bradycardias, sinus pauses, junctional bradycardias, and AV blocks, ranging from first degree to complete [2]**.** A recent review of these reports showed that elderly women, particularly those with a pre-existing conduction abnormality, were mostly involved [1], though reports in young also exist. Usually brady-arrhythmias occur at therapeutic doses, whereas sinus tachycardia is the main arrhythmia in massive CBZ overdose [3]. An increase in ventricular premature beats over next five days has also been reported in patients who abruptly discontinued CBZ because of cardiac side-effects [4]. Our patient, however, did not have any history of discontinuation of the drug prior to presentation. Another possibility could have been arrhythmia-related seizures [5]; however, there was no recurrence of the ECG abnormality after stopping carbamazepine. Using the Naranjo Adverse Drug Reaction Probability Scale classified the event as a 'possible' adverse drug reaction.

We wish to highlight that cardiac side-effects may sometimes occur after prolonged carbamazepine therapy, and may be associated with normal or slightly high serum levels. As seen in this child, rapid resolution of symptoms occurs on discontinuing the drug.

Acknowledgement: Dr Priyanka Solanki, Department of Pediatrics, Lok Nayak Hospital; and Dr. Sanjiv Kathuria DM, Department of Cardiology, GB Pant Hospital.

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Management of Severe Scorpion Sting at a Rural Hospital

Severe scorpion sting is a life threatening accident not uncommon in Western Maharashtra [1]. Scorpion venom delays closing of sodium neuronal channel resulting in liberation of endogenous catecholamines into circulation, manifesting as "autonomic storm" [2]. In the past, upto 30% fatality due to refractory heart failure due to *Mesobuthus tamulus* envenoming has been reported. Since the advent of prazosin, a postsynaptic alpha blocker, the fatality due to refractory heart failure has reduced to less than 4-8% in pediatric age group [3].

Cottage Hospital is a public health institute situated on Mumbai-Goa highway. The mono specific scorpion antivenom against the *Mesobuthaus tumulus* is prepared at Haffkine Institute, Mumbai has been available at our Institution since 2010. We retrospectively analyzed details of 12 children who suffered autonomic storm due to scorpion sting (***Table* I**). Of these, six (2 males) had received scorpion antivenom plus prazosin and the remaining (3 males) received only scorpion antivenom. All gave history of scorpion sting and relatives brought the killed specimen.

Alpha receptor stimulation plays important role in the pathogenesis of acute pulmonary edema. Prazosin, by blocking alpha receptors corrects the abnormal hemodynamic, and metabolic effects of circulating catecholamines [3,4]. Patients treated with prazosin alone are reported to recover in 10-24 hours, till the venom is metabolized by body. In such situation victims needs close monitoring in intensive care [8]. 10-20% of children, irrespective of oral prazosin, were found to develop tachycardia, hypotension and pulmonary edema [8]. Scorpion antivenom neutralizes the circulating venom and it has no action in reverseing the effects of already raised catecholamine and tissue-bound venom [5]. Cold extremities occur due to alpha receptor stimulation as a result of vasoconstriction, and delay the venom absorption in circulation from site of sting, which acts as depot. Simultaneous use of oral prazosin, which antagonizes the catecholamine actions and improves the peripheral circulation and rapid absorption of venom in circulation that becomes accessible to already circulating antivenom, thus recovery is shortened in prazosin pluse antivenom group as compared to scorpion anti venom grop alone [5]. Rapid recovery of victims treated with prazosin and antivenom prevent the extra load of these cases to intensive care unit, which is beyond the reach of poor people.

TABLE I CHARACTERISTICS OF CHILDREN WITH AUTONOMIC STORM (*N*=12)

Treatment	*Anti-scorpion venom (AScV)*	*AScV + Prazosin*
Age (y)	9 (7-12)	8.8 (3-13)
Time between sting to hospitalization (hours)	2.41 (1-3.5)	1.5 (1-2.5)
Blood pressure (mm Hg)		
Systolic	140 (80-190)	123 (90-170)
Diastolic	80 (60-100)	80 (70-100)
Pulse rate (per min.)	89 (68-110)	89 (84-100)
AScV dose* ((1.2)vial)	2.33 ((2-5)vial)	1.33
Pulmonary edema	3	0
Recovery	3	6
Time for recovery (h)	7.1 (4-8)	3.75 (2-5)

**1 vial=10 mL; Values in mean (range); Ascv-Anti-Scorpion venom.*

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Childhood Catatonia

Catatonia is a syndrome of motor dysregulation that is rarely recognized in pediatric age group with an estimated incidence of 0.16 million per year [1,2]. In any patient presenting with catatonia, neurological or other general medical conditions, neuroleptic induced side effects, substance intoxication or withdrawal should be ruled out before considering psychiatric etiology [3]. We report a rare case of childhood catatonia due to psychosis.

Master A, 11-year-old male, a fourth standard student, presented with abrupt onset and gradually progressive course of decreased interpersonal interaction and decreased self care for 3 months. He was evaluated in pediatrics, pediatric neurology and endocrinology OPD. Personal and developmental history was uneventful. There was no history of seizure, fever, drug use preceding onset of illness. Apart from BMI of 28, physical examination did not reveal any abnormality. Slit lamp examination did not reveal K-F ring. Hemogram, renal function tests, liver function tests, MRI brain, thyroid profile, serum insulin, fasting blood glucose, post-prandial blood glucose and serum cortisol did not reveal any abnormality. As no organic cause was found, he was referred to child and adolescent psychiatry OPD.

On mental state examination, patient fulfilled syndromal diagnosis of catatonia and had psychotic signs. He was not clinically depressed. He was diagnosed to have psychosis unspecified (F 29) and treated with risperidone (upto 4 mg/day) and lorazepam (upto 4 mg/day). He gradually improved over 8 weeks. Lorazepam was tapered and stopped. He was discharged on risperidone 4 mg/day. At 3 months follow up, he was mildly inactive as compared to his usual self but was doing well otherwise.

Dysregulation of γ-aminobutyric acid (GABA)-A, glutamate, and dopamine systems are hypothesized to be involved in catatonia [4]. Deprivation, abuse and trauma can precipitate catatonia in paediatric patients without clear medical cause [5]. Acute management of catatonia involves lorazepam challenge test, identifying and correcting underlying medical cause, maintaining adequate nutrition, fluid and electrolyte balance, and avoiding postural immobility which may lead to complications like bed sores or muscle contracture [4]. Electroconvulsive treatment (ECT) is considered as the last choice [4]. As our patient responded well to pharmacotherapy, ECT was not necessitated.

Catatonia is poorly recognized in children and adolescents due to overshadowing by medical or neurological or pervasive developmental disorders [5]. Accurate diagnosis is important because catatonia responds readily to benzodiazepines and electro-convulsive therapy.

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Further Considerations on The So-Called Rowell Syndrome

The recent article by Solanki, *et al*. [1] described a further case of Rowell Syndrome (RS), that is a long debated nosological entity, historically defined as a unique clinical association between cutaneous lupus erythematosus (CLE) with erythema multiforme (EM) like lesions and characteristic immunologic pattern. Last year we reviewed all the 71 cases reported as RS up to 2011, and questioned its framing as separate entity [2].

The 13-years old female child described by Solanki, *et al*. [1] apparently fulfilled the diagnostic criteria suggested first by Rowell, *et al.* [3] in 1963 and then classified as major and minor by Zeitouni, *et al*. [4] in 2000. However, as already pointed out in our review, in the majority of cases, different entities were reported as RS, misdiagnosing association between subacute CLE (SCLE) annular polycyclic type, described for the first time in 1977 by Gilliam and better defined by Sontheimer et al. in 1979, and other specific type of CLE as discoid LE (DLE), acute CLE or chilblain lupus variant.

In our opinion, the case reported by Solanki, *et al*. [1] should be considered as SCLE, since it shows annular-polycyclic lesions on the upper chest (different from symmetrical typical raised targetoid lesions of EM) with erosive lesions of the hard palate, frequently reported as non-specific lesions of SCLE, representing a clinical marker of active disease (American College of Rheumatology Criteria). Other features, including photosensitivity and malar rash, strongly support our hypothesis, despite the negativity of anti-Ro antibodies, that are absent in about one third of the patients with SCLE.

In conclusion, we reiterate our critical opinion about RS, stressing the concept that different entities have been wrongly reported under this name. In particular, annular-polycyclic type of SCLE is often misdiagnosed as EM-like rash. Moreover, the real association between LE and EM, as happens for other associations (*i.e.* CLE and lichen planus or psoriasis), should be considered a mere coincidence, that does not justify the framing of a separate syndrome as originally suggested by Rowell, *et al*. [3]

Acknowledgments: Professor P. Fabbri and Doctor E. Antiga.

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Effect of Infliximab 'Top-down' Therapy on Weight Gain in Pediatric Crohn's Disease

I would like to make certain comments on recent article by Kim, *et al.* [1] on growth facet of Crohn's disease [1]. Azathioprine was started at the outset of treatment itself that in a group had mild to moderate disease though it is recommended only in those with severe disease or those with frequent relapses [2]. Also, authors have not mentioned the frequency of disease flare-up in follow-up and their management. Since present study takes into account growth parameters as major outcome, inclusion of nutritional intake assessment in all study groups at 0, 2, 12 month time interval and their comparison would have added to results of study. Finally, there is a significant difference noted between increment in weight *Z* scores of steroid and azathioprine group at 2 months however in both groups steroids were used in induction phase and azathioprine effect is generally seen after 3 month of start. For such a difference no plausible explanation is given in text.

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Editor's Note: Authors of the original paper did not respond to this letter.

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