Pediatric Lupus: Varied Haematological Picture and Presentation

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Received: 24 May 2013 / Accepted: 14 February 2014 / Published online: 14 March 2014
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Abstract Systemic lupus erythematosus (SLE) is a chronic, multisystem, autoimmune disease characterized by periods of increased disease activity caused by inflammation of blood vessels and connective tissue. Pediatric patients with SLE have a more severe clinical course when compared with adults. Patients commonly present with rash, fever, and arthritis, although the presentation may be unpredictable. Hematological findings are more predominant in children than adults. Thirty-nine percent of children with SLE will develop hematological abnormalities, one of the American Rheumatic Association criteria for classifying the disease. In our case series we found varied hematological picture and presentation. We present here four case reports of SLE cases with interesting hematological features. Our first case is a 13 month old female child who was initially diagnosed as Evans syndrome and 2 years later diagnosed as SLE. Second case is a 3 year old male child who had SLE with warm antibody AIHA. Third case is a 6 year old female child who presented with AIHA and was diagnosed with SLE 6 years later. Fourth case is a 6 year old female child diagnosed as SLE with aplastic anemia. Hematological findings should be carefully assessed and treated in order to decrease disease related morbidity.

Keywords Pediatric lupus · Hematological manifestations · SLE · Hemolytic anemia · Aplastic anemia

Introduction

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease that predominantly affects women of child bearing age. Approximately 20 % of patients present in the first two decades of life. [1] It is the most common rheumatic disease associated with significant morbidity and mortality in children. Some complement deficiencies predispose to SLE early in life. Children present with more acute illness and have more frequent renal, hematologic and central nervous system involvement at the time of diagnosis compared to adults with SLE. When comparing pre-pubertal to post-pubertal onset of pediatric SLE, the former group presents more often with hemolytic anemia and renal involvement whereas in the latter group cutaneous and musculoskeletal features are more common at disease onset [2]. Haematological abnormalities (anemia, autoimmune hemolysis, aplastic anemia, leukopenia, and thrombocytopenia) are frequently encountered in patients with SLE and are a part of the American Rheumatic Association criteria for classifying the disease. We present here four patients with age of presentation varying between 13 months and 6 years, with varied presenting complaints, involving haematological, renal and cardiovascular systems.

Case 1

A 13 month old female child was admitted with multiple ecchymotic patches over buttocks and extremities, along with pallor for 4 months. Haemogram showed Hb 6.7 gm/dL, leukocyte count was $13 \times 10^3/\mu\text{L}$ platelets 31×10^3 . MCV was 84 fl. MCH was 26 pg. MCHC 35 gm/dL. Serum ferritin level was normal (84 mcg/L). Peripheral smear showed bicytopenia with bone marrow aspiration

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suggestive of normocellular marrow with normoblastic erythropoiesis.

Serum electrolytes, coagulation profile, and liver functions were all within normal ranges. Direct coombs test was positive. ANA, RA, antiDs DNA were negative. She was diagnosed as Evans syndrome and started on oral steroids. Her hemoglobin and total leukocyte count improved. Two years later she was diagnosed as SLE, when she was readmitted with joint pains (knee, elbow, metacarpophalangeal joint) pallor along with positive ANA and Antids DNA. She was put on steroids to which she responded well. Her joint pains have subsided and her haemogram is normal.

Case 2

A 3 year old male child presented to us with fever, cola coloured urine and anasarca for 3 days. There was history of photosensitive malar rash for 2 years. Physical examination was within normal limits, except for pallor, photosensitive skin rash over face, edema and high blood pressure (BP130/96 mmHg). Haemogram showed Hb 7.9 gm/dL, leukocyte count was 6×10^3 μ /L platelets 144.1×10^3 μ /L. MCV was 72 fl. MCH was 32 pg and MCHC was 36 gm/dL. Peripheral smear showed features of hemolysis with spherocytes. Urinalysis revealed hemoglobinuria, and absence of RBC or RBC cast. Urine culture was sterile. DCT was positive. ANA was positive and antihistone antibody was positive. Antids DNA was negative. Warm antibody was positive at 37 °C. Serum electrolytes, coagulation profile, and liver functions were all within normal range. He was diagnosed as SLE with autoimmune hemolytic anaemia (warm antibody type) and started on steroids with antihypertensives along with iv immunoglobulins.

His hemoglobinuria subsided blood pressure was controlled. He was subsequently lost to follow up as he went back to his native place.

Case 3

A 6 year-old female child with no significant past medical history presented to the emergency room with breathlessness, pedal edema, hypotension and pallor. Physical examination revealed tachycardia of 124 beats per min, pallor, pedal edema, hepatosplenomegaly, crepitations and pericardial rub. On Complete blood counts a white blood cell count (WBC) of 12.5×10^3 /dL, platelets of 50,000/dL, and hemoglobin (Hb) of 3.4 g/dL. Serum electrolytes, coagulation profile, and liver functions were all within normal limits. Peripheral smear showed features of hemolysis with high reticulocyte count of 5 %. 2D echocardiography showed pericardial effusion and USG abdomen reported hepatosplenomegaly. DCT, ANA, RA,

Antids DNA, were negative. She responded well to antibiotics and was discharged on hematinics.

Six years later she was readmitted with malaise, reduced appetite with pain in bilateral knee joints. On examination she had pallor, malar rash and hepatosplenomegaly. Routine haemogram showed Hb 4.7 gm/dL, leukocyte count was 4×10^3 / μ L platelets 310×10^3 / μ L. ESR 70 mm/h. Reticulocyte count 3 %. Peripheral smear showed mild anisocytosis, predominantly microcytic hypochromic cells, with elliptocytes. DCT, ANA, antiDs DNA were positive. RA factor, antiphospholipid antibodies were negative. C3 level was 30 mg/dL (90–180 mg/dL). Urine examination revealed proteinuria, RBC 10–12/hpf along with RBC cast when she had presented to emergency our initial diagnosis was severe sepsis with pericardial effusion in congestive heart failure. She was started on antibiotics, gradually when worked up further diagnosis of active lupus was made for which she was put on steroids.

Renal biopsy report was suggestive of lupus nephritis for which iv cyclophosphamide was given. She was discharged after course of cyclophosphamide completed, her disease flare was under control.

Case 4

A 6 year old female child presented to us with off and on fever for 5 months, joint pains (bilateral knee joint, metacarpophalangeal joint) with pallor for 4 months. She also had skin bleeds just 2 days prior to admission. Physical examination was within normal limits, except for pallor and petechiae. Routine haemogram showed pancytopenia, with a WBC of 1.98×10^3 /dL, platelets of 3 L/dL, and hemoglobin (Hb) of 4.6 g/dL. Peripheral blood smear showed pancytopenia with normoblastic erythropoiesis. The bone marrow aspiration was dry tap and biopsy showed decreased cellularity with normoblastic reaction. Myeloid series showed maturation arrest. No megakaryocyte or abnormal cells were seen ANA, antiDs DNA were positive. RA was negative. C3 was low. Serum electrolytes, coagulation profile, liver functions and urine analysis were all within normal limits. She was diagnosed as SLE with aplastic anaemia. Her hematological profile has shown improvement joint pains have subsided. Currently she is on alternate day steroids along with cyclosporine (Table 1).

Discussions

Pediatric systemic lupus erythematosus (pSLE) is a chronic multisystemic autoimmune disease with complex clinical manifestations. Although the presentation, clinical manifestations, immunological findings and treatment issues of pSLE are similar to those of adult SLE patients, there are

Table 1 Comparison of all four cases, there presentation and final diagnosis

Case	Age	Sex	Presenting complaints	CBC			Final diagnosis	Treatment	Outcome	SLEDAI index	ACR criteria
				Hb ^a	Tlc ^b	Plt ^c					
1	13 month	F	Eccymotic patches	6.7	13	0.31	Evans ↓ SLE	Steroids	Improved	9	4
2	3 years	M	Fever, anasarca, hemoglobinuria with malar rash	7.9	6	4.1	SLE with warm antibody hemolytic anaemia	Steroid and IVIg	Improved	18	5
3	6 years	F	Pallor, pericardial effusion, joint pains, malar rash and haematuria	4.7	4	3	SLE with hemolytic anaemia	Steroid	Improved	36	8
4	6 years	F	Fever, pallor, petechiae, joint pains	4.6	1.98	0.3	SLE with aplastic anaemia	Steroid and cyclosporine	Improved	13	4

SLEDAI SLE disease activity index

^a gm/dL^b × 10³/UL^c L/UL

special issues which need to be considered when dealing with SLE in children. In general, children with SLE tend to have a more severe disease at onset with higher rates of organ involvement and a more aggressive clinical course than adult-onset SLE patients. At onset, 40–90 % of children will present with constitutional symptoms (fever, fatigue or weight loss), 20–82 % will have renal involvement, 20–74 % musculoskeletal symptoms, 22–74 % malar rash, 15–45 % lymphadenopathies and 15–74 % visceromegaly

Thirty-nine percent of children with SLE will develop hematological abnormalities, one of the ACR diagnostic criteria for SLE, during the course of the disease. [3] During the course of their illness, 70 % of patients with SLE will have anemia, 65 % will have leukopenia, [4] and 25 % will have thrombocytopenia. [5] The majority of the anemia in SLE is thought to be secondary to the underlying chronic inflammatory disease, with only 2–3 % of the cases caused by autoimmune hemolytic anemia. When AIHA occurs it is due to warm antibodies, this is the predominant type of AIHA in SLE patients. Red blood cells coated by warm IgG antibodies are removed from circulation by spleen. [6] SLE patients uncommonly present with pancytopenia. Feng et al. [7] evaluated pancytopenia in 23 patients with SLE by performing bone marrow biopsies. In this case series, only 4 patients had received cytotoxic drugs, and the majority of patients were on corticosteroid treatment only. Thrombocytopenia is often associated with antiplatelet and antiphospholipid antibodies and can also be secondary to hypersplenism.

In our case series two patients had hemolytic anemia, one had aplastic anemia. Fourth patient had bicytopenia.

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