The Egyptian Rheumatologist 42 (2020) 241–243

Contents lists available at ScienceDirect

The Egyptian Rheumatologist

journal homepage: www.elsevier.com/locate/ejr

A 13-year-old systemic lupus erythematosus girl initially presenting with Raccoon eyes and neuropsychiatric manifestations

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ARTICLE INFO

Article history:
Received 12 January 2020
Accepted 1 February 2020
Available online 7 February 2020

Keywords:
Systemic lupus erythematosus
Ocular involvement
Raccoon eyes
Neuropsychiatric

ABSTRACT

Background and aim of the work: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease. Although eyes are seldom affected, this case report presents a 13-year-old Iranian girl with Raccoon eyes and neuropsychiatric manifestations as an initial presentation of SLE.
Case presentation: The patient was admitted to the pediatric rheumatology inpatient, Mofid Children's Hospital, Tehran with swelling and ecchymosis around the eyes (Racoon eyes) as well as anorexia, abdominal pain, weight loss, mood disorders and hallucinations. Complete blood count showed normocytic, normochromic anemia, leukopenia, lymphopenia and thrombocytopenia. The C-reactive protein, erythrocyte sedimentation rate, liver and renal functional tests, and urine analysis were normal. The complement levels decreased, antinuclear antibody (ANA) and anti-double stranded DNA (anti-dsDNA) tests were positive. Bilateral pleural effusion and mild pericardial effusion were seen. Bone marrow aspiration showed mild hypocellularity without any evidence of malignancy. The diagnosis of neuropsychiatric SLE (NP-SLE) was held. She was treated by the pulse methyl prednisolone (30 mg/kg/d) and intravenous cyclophosphamide (500 mg/m^2), oral prednisolone and hydroxychloroquine. Her appetite improved while hallucination and aggressive behavior decreased. Peri-orbital swelling and ecchymosis decreased. After one year, her appetite became normal; mood disorders, panic, phobic attacks and hallucinations were completely remedied. Swelling and ecchymosis around the eyes were eliminated. Oral prednisolone 10 mgday and hydroxychloroquine (5 mg/kg/day) were continued.
Conclusion: SLE may present with Raccoon eyes. Rapid detection and treatment of the disease based on clinical symptoms is critical for these patients. Prednisolone and cyclophosphamide are the best choice for treatment of the disease in children.

1. Introduction

Systemic lupus erythematosus (SLE) is a complex, chronic, multisystem autoimmune disease affecting almost all body organs. The prevalence of SLE varies in different parts of the world [1,2]. The onset of clinical manifestations in SLE is variable and may have implications on the disease course, remission and clinical relapse. SLE is rarely associated with ocular involvement and may affect fewer than 5% of patients during the first year. However, more than 30% of patients may eventually present ocular involvement over the course of the disease or during the disease evolution. Lupus retinopathy is one of the most prevalent vision-threatening complications [3,4]. The initial presentation of SLE with neuropsychiatric (NP) symptom is very rare. However, over the course of the disease, 22–95% of the patients finally develop NP symptoms such as headache [5]. Gene polymorphisms of TNF-α and IL-6 were implicated in SLE while their serum levels tended to be related to the NP manifestations [6]. In this study, we reported a teenage girl with SLE who was initially presented with Raccoon eyes (peri-orbital ecchymosis), NP symptoms, and peripheral neuropathy.

2. Case report

A 13-year-old Iranian girl, who presented with ecchymosis and swelling signs around both eyes (peri-orbital), especially on the left side, was admitted in Pediatric Rheumatologic ward, Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences,

Peer review under responsibility of Egyptian Society of Rheumatic Diseases.
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https://doi.org/10.1016/j.ejr.2020.02.001
1110-1164/

Tehran, Iran. The swelling and ecchymosis around the eyes arose in the preceding 20 days and then gradually increased. After that, the left eye had blurred vision and lessened the eye sight. The patient was admitted to another hospital for a week with a diagnosis of septal cellulitis and received intravenous clindamycin. The past medical history of the patient revealed that she had anorexia, abdominal pain and constipation about 18 months ago and was treated with omeprazole as an endoscopic outpatient with gastritis. Since then, the patient had mood disorder, panic attacks, and sleep disorders. In the last few months, she had aggressive, phobic behaviors and escaped from school. The patient had also motion impairment in the right leg about 10 months ago. In the preceding two months, she developed urinary incontinence. On examination, her weight and height were 44 kg and 156 cm, respectively, with body mass index (BMI) 18.1. There was ecchymosis and swelling around both eyes, especially on the left (Raccoon eyes) (Fig. 1). Painless ocular movements, visual acuity, ophthalmoscopic and fundoscopic examinations were normal. There was right foot inversion, reduced right leg deep tendon reflex and reduced pain and heat sensation. The Babinski sign of the right foot was positive. Her greater sister was a known case of SLE.

Complete blood count (CBC) showed leukopenia and mild lymphopenia. Other blood parameters or indices (e.g. serum electrolytes, ammonia and lactate, coagulation tests, kidney and liver function tests, and urine analysis) were normal. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum immunoglobulins (Igs) and complement tests were normal. Rheumatoid factor (RF), anti-nuclear antibody (ANA), anti - double stranded DNA (anti-dsDNA) and anti-phospholipid antibodies were negative. To rule-out neuroblastoma, Vanillin-mandelic acid (VMA) was measured in 24-hour urine and was negative. Chest X-ray and echocardiography were normal. Orbital computerized tomography (CT), total spinal magnetic resonance imaging (MRI), brain MRI were normal. Electromyography (EMG) and nerve conduction velocity (NCV) tests showed right foot peripheral neuropathy. Serological tests were negative for human immunodeficiency viruses (HIV), herpes simplex virus (HSV), Epstein–Barr virus (EBV), Cytomegalovirus (CMV), brucella and mycoplasma. Based on the historical, clinical, and laboratorial findings, there was a probable diagnosis of SLE in view of the neurological and hematological disorders and positive family history. She was recommended to be followed, and oral gabapentin and amitriptyline were prescribed for symptomatic treatment.

2.1. Second hospitalization

After eight months, the patient was re-admitted with chief complaints of anorexia, abdominal pain, weight loss, mood disorders and hallucinations, as well as increased ecchymosis and swelling around the eyes. On physical examination her weight and height were 35 kg and 157 cm respectively, (BMI 14.2). The patient was pale with hepatosplenomegaly. The rest of clinical examinations did not change and remained constant compared to the preceding admission. The CBC showed normocytic, normochromic anemia, leukopenia, lymphopenia and thrombocytopenia (pancytopenia). The patient had hypokalemia and hyponatremia. CRP, ESR, coagulation tests, serum ammonia and lactate, liver and renal functional tests, and urine analysis were normal. Complement levels (CH50, C3, and C4) were clearly decreased, and ANA and ds-DNA were positive. Chest x-ray showed bilateral pleural effusion and echocardiography revealed mild pericardial effusion. Her abdominal-pelvic CT revealed mild hepatosplenomegaly. Bone marrow aspiration showed mild hypocellularity in all blood patterns without any evidence of malignancy. Based on the American College of Rheumatology and Systemic Lupus International Collaborating Clinics Classification Criteria for SLE [7], the diagnosis of neuropsychiatric SLE (NP-SLE) was held: neurological and hematological manifestations, serositis, ANA and anti-dsDNA positive. She was treated by pulse methyl prednisolone (30 mg/kg at a max of 1 g/dose) and intravenous cyclophosphamide (CYC) (500 mg/m^2) monthly for 6 months, then every 3 month, oral prednisolone and hydroxychloroquine (HCQ).

2.2. Outcomes and follow-up

After treatment with first pulse methylprednisolone and CYC, her appetite and energy improved and her hallucination and aggressive behaviors decreased. Finally, the swelling and ecchymosis around her eyes were beginning to decrease. Treatment with oral prednisolone (2 mg/kg/day; max 60 mg/day) and HCQ (5 mg/kg/day) was continued and the patient received pulse CYC for 6 months. The oral prednisolone was tapered after 2 months of treatment with decreasing 5 mg every two weeks until 20 mg daily was reached at the 6th month of treatment. HCQ (5 mg/kg/-day) continued during this period.

Subsequently, CYC pulse was infused (500 mg/m^2) every month for 6 months, then every 3 months along with the continuation of oral medications. One year after the second admission and above mentioned therapies, her appetite reached back to normal; her weight and height increased to 47 kg and 160 cm, respectively. Also all of her mood disorder symptoms, panic and phobic attacks, and hallucinations were completely remedied. The antidepressant and antipsychotic drugs were discontinued and the patient had no problems at school. Swelling and ecchymosis around the eyes were eliminated (Fig. 1). Oral prednisolone 10 mg daily and HCQ (5 mg/kg/day) were continued.

3. Discussion

Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease characterized by excessive inflammatory and immune responses and tissue damage and involves various organs and systems [8]. Measuring organ damage in SLE is important with special concern to juvenile-onset patients to allow for designing

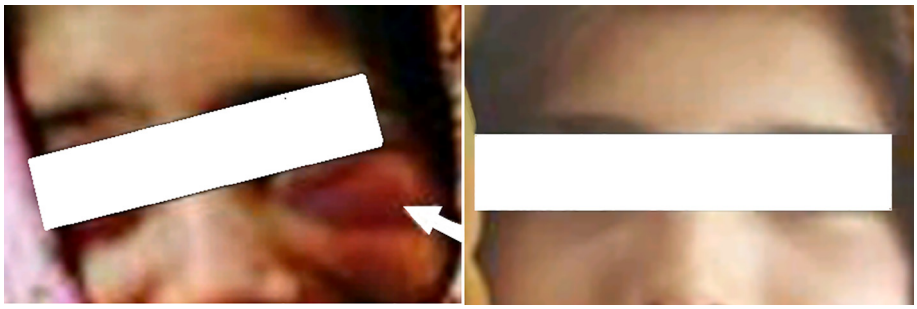

Fig. 1. Ocular involvement of the patient before (left: Racoon eye) and after (right) treatment.

new treatments that improve control of disease activity and minimize the development of irreversible damage [9]. Since about 20% of cases are diagnosed before age 16, SLE in children under 5 is really rare. There are multiple risk factors involved in its development and sex is the first and the strongest disease determinant with about 90% being females [1–4]. Estrogen plays an important role in disease exacerbation stimulating B cells to produce autoantibodies. C1q, C2, and C4 deficiencies are associated with disease development. A family history of other autoimmune diseases and a genetic background are also effective factors [10,11]. Furthermore, environmental factors (e.g. sunlight) and viruses (e.g. EBV) raise the risk of SLE development [10].

Clinical symptoms of the juvenile patients are different from the adults [9]. The most common primary clinical symptoms in children with SLE include fever, fatigue, loss of appetite, musculoskeletal pain, hair loss, and painless oral ulcers [12]. LN is very common in childhood-onset SLE and begins early in the disease course [13]. Neuropsychiatric manifestations of SLE may be associated with the disease activity or could be misdiagnosed and treated as a mood disorders, anxiety or psychosis. Musculoskeletal pain may also be misdiagnosed in children as nonspecific growing pain for a long time [12].

Ocular involvement of SLE is rare and could be orbital, periorbital edema, keratoconjunctivitis sicca, episcleritis and retinopathy [14]. Eye affection in SLE is very rare at the onset of the disease and it is thus important to reveal [4,14]. Other ocular features in SLE include involvement of the anterior and posterior segments, proptosis, orbital pain, blurred vision, chemosis, enophthalmos, and movement restrictions. Vasculitis is a potential key player in SLE [15] and associated myositis may contribute to the eye affection and may be initially misdiagnosed as bacterial cellulitis [4]. Peri-orbital edema is seldom present at disease onset and may occur in 4.8% throughout the course of the disease which may be due to the increased vascular permeability, renal involvement, secondary angioedema, and mucin substitution in the skin [4,16]. Raccoon eyes in our patient may be due to increased vascular permeability. Ocular involvement in SLE should be treated promptly with systemic corticosteroids [4,14].

Neuropsychiatric lupus is rare in children at the onset of the disease and is an indication of severity [17]. In spite of its controversy in children's NP-SLE, pulse CYC still seems to be an alternative of choice [17,18]. The diagnosis of SLE in a patient with initial ocular involvement is a clinical challenge [4]. Raccoon eyes may be caused by trauma to the surrounding eye or soft tissue around it, fracture of the skull, malignancies, amyloidosis, rhinoplasty or severe and prolonged intravenous pressure following long-term coughing or sneezing [19,20].

Diagnosis of SLE with initial NP manifestations is a hindrance issue for a physician with an old hand at clinical problems and is delayed in many cases [17]. However, it is necessary to rapidly diagnose and treat SLE with rare symptoms such as ocular and NP to control the disease promptly and prevent further damage and progress [4,17].

In conclusion, ocular involvement in the form of Racoon eyes could be the initial presentation in juvenile SLE. Neuropsychiatric manifestations could be associated with the eye affection at the disease onset. Prompt diagnosis and management of the disease is critical for these patients. Prednisolone and cyclophosphamide are effective treatment options.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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