Anorexia Nervosa Mimicking Systemic Lupus Erythematosus
Case Report and Review of the Literature

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Abstract
Eating disorders (ED) are common psychiatric disorders with widespread prevalence especially in females between the ages of 12 and 20 years. ED was classified recently into three categories; anorexia nervosa, bulimia nervosa and binge eating disorder. Medical and psychological disturbances associated with eating disorders can lead to significant morbidity and mortality. We report a case of a 13-year-old girl presenting with signs and symptoms of anorexia nervosa that mimic signs and symptoms of systemic lupus erythematosus (SLE). She has positive Antinuclear Antibody (ANA), Anti ds DNA antibody and low complement. A multi-disciplinary team of psychiatrists, psychologists, nutritionists and cognitive-behavioral therapists managed her condition effectively. Two years after her treatment, she gained significant weight and the clinical signs in addition to the serological findings have cleared. This is the first case of nutrition deprivation symptoms involving immunological features of SLE that disappeared after treating for anorexia nervosa.

Key words: Eating disorders, systemic lupus erythematosus, children

Introduction
Eating disorders (ED) are primarily psychiatric disorders characterized by severe disturbances of eating behavior. ED most frequently occur for the first time during adolescence and usually continue into adulthood. It was proposed that the etiology of ED is multifactorial, involving developmental, biological, familial and sociocultural aspects [1]. However, the pathogenesis of ED is still unclear, and there are medical and psychological complications that may occur following ED. Eating disorders are a cause of significant mortality rate, up to 6% in anorexia nervosa (AN) and 3% in bulimia nervosa (BN) [2].

Juvenile systemic lupus erythematosus is a multisystemic autoimmune disease that most fre-
quenty occurs between the ages of 12 and 16 years and has an incidence of 0.36-0.9 per 100,000 children per year [3]. The American College of Rheumatology proposed criteria for diagnosing SLE (ACR-1997); the criteria include skin lesions, arthritis, renal disorder, neurologic disorder, hematologic changes and other clinical manifestations in addition to a wide profile of autoantibodies. However, in 2012, the Systemic Lupus Collaborating Clinics (SLCC) proposed the SLICC criteria for SLE, which gives higher regard to autoantibodies and takes into account the importance of low complement [4].

We present a case of a 13-year-old girl who had weight loss of 20 kilograms over one year due to voluntary eating of small quantities of food and exercising vigorously on a daily basis. The clinical manifestations and serological features of the case mimic the typical clinical and serological findings of systemic lupus erythematosus (SLE) disease. A multi-disciplinary team was involved in her treatment plan, which resulted in significant improvement in her condition. Two years post-treatment, she achieved considerable weight gain and her symptoms, signs and serology findings improved.

In this paper, we shed light on the pathophysiology of SLE and the effects of nutritional deprivation on the development of the disease.

**Case Description**

A 13-year-old girl presented with weight loss after she started eating small amounts of food for one year. The girl’s history involves watching television programs that showed impressive models and popular celebrities. She subsequently became obsessed about her body image and decided to become a model herself. Hence she began engaging in vigorous physical exercise such as rope jumping around 100 times per day. Her parents noticed a change in her behavior and that she had a preference to stay alone. She became depressed and aggressive. They also mentioned that her hair was falling and her menstrual cycles became scanty and irregular until there was no cycle observed at all. According to her mother’s records she lost 20 kilograms in one year’s time.

Her past medical history is irrelevant. She was the product of non-consanguineous marriage between an Arabic father and an Asian mother. The mother has rheumatoid arthritis. She has one elder sister who is healthy.

On physical examination, the girl looked apprehensive and emaciated, her weight and height were 26 kgs (< 5th Centile) and 149 cm (10th Centile), respectively (Figure 1). Her blood pressure (BP) was 90/50 mmHg. She had cold hands and feet; the peripheral pulses were of low volume. The skin and mucous membrane were intact and there was no skin rash, but her hair was thin and fragile. All other systems were normal.

Her basic laboratory results were Hb: 13.2 g/dl, WBC: 4.5 10⁹/l; Poly.: 78% Lymph: 18%, Mono: 8%, Platelets: 292 10⁹/l, liver function test: total protein 70 g/dl. Alb: 34, g/dl, Globulin: 36 g/dl with normal liver enzymes. ESR and CRP were within normal limits.

She was reassured and referred to the psychology clinic for psychological assessment. Multi vitamin and iron therapy were started. Two months later, she presented with joint pains and an occasional headache with blurred vision. A repeated blood count showed Hb: 10.1 gr/dl, WBC: 3.2 10⁹/l, Poly: 81%, Lymph: 10% and Mono: 9%. Renal function tests (RFT): Urea: 9.7 mmol/l, Creatinine: 99 mmol/l, K: 5.0 mmol/l. Na,
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Cl and HCO3 were normal. Urine analysis revealed RBC 5-7 cells/HPF, epithelial cells and Bacteria++, while urine culture showed no pathogen.

At this stage, the girl was investigated for rheumatic disorders such as SLE. Serology results revealed ANA+ (titer 1/640) speckled pattern, with positive anti-ds DNA antibody and anti-Centromere antibody. Complement values were: C3:69 mg/dl (N: 90-170) and C4:18.4 mg/dl (N: 20-40). Serial urine analysis revealed occasional microscopic hematuria but urine cultures were always negative.

After rehydration, her urea and Creatinine turned back to baseline values. In view of blurred vision and headache, magnetic resonance imaging (MRI) brain scan was performed and no abnormalities reported.

In her regular follow-up visits, this girl was referred to a multi-speciality team that involved a psychiatrist who started regular psychotherapy sessions, a psychologist and a cognitive-behavioral therapist who suggested different modalities of treatment towards positive thinking.

In spite of all efforts to improve our patient’s thinking and behavior, she persisted on eating small amounts of food that to her thinking met her goals of being slim and attractive. However, in spite of her difficult physical situation, her school performance had remained excellent.

One year after her presentation, she gained only 3 kilograms (Figure 1), and at this time she complained of abdominal pain for two months but no vomiting or change in bowel habit.

H-pylori tests were done and revealed negative results. Upper and lower gastrointestinal endoscopies were performed and showed healthy mucosa with unremarkable histopathology findings. Anti-smooth muscle antibody (SM) and anti-liver kidney microsome antibody (KLM) were negative.

18 months after the start of her illness and extensive psy-

Figure 2. Patient’s growth parameters during 30 months follow up period.
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Table 1. Patient’s serological data during the course of illness.

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<tr>
<td>ANA</td>
<td>+,1/320</td>
<td>+,1/640</td>
<td>+,1/160</td>
<td>+,1/160</td>
<td>+,1/80</td>
<td>-</td>
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<tr>
<td>Anti ds DNA antibody</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Anti Centromere antibody</td>
<td>+</td>
<td>±, Equ</td>
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<tr>
<td>C3 (N:90-170 mg/dl)</td>
<td>69</td>
<td>77.8</td>
<td>69</td>
<td>61</td>
<td>85</td>
<td>120</td>
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<tr>
<td>C4 (N:10-40 mg/dl)</td>
<td>18.4</td>
<td>15.2</td>
<td>14.6</td>
<td>13</td>
<td>18</td>
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Two years after her presentation, our patient’s weight increased to 46.4 kgs (10th-25th centile) while her height was only 152.6 cm (5th-10th centile) (Figure 1). The girl’s behavior gradually changed to be more friendly and interactive. Moreover, her menstrual cycles returned to normal and clinical examination revealed strong hair, warm hands and normal BP and peripheral pulse volumes. Serial serology screening revealed gradually declining ANA titer and negative for both Anti-ds DNA antibody and anti-centromere antibody. C3 values had increased. (Table 1) Urine analysis showed no more abnormality. Six months after being clinically stable, she continued to gain weight normally.

Discussion

A recent classification of eating disorder phenotypes in children and adolescents using latent profile (LP) analysis was proposed as: LP1, characterized by binge eating and purging, LP2, characterized by excessive exercise and extreme eating disorder cognitions and LP3, characterized by minimal eating disorder behavior and cognitions. LP1 represents bulimia nervosa and LP2 and LP3 represent anorexia nervosa with relaxed weight criterion. [5] Our patient manifests behavior represented by LP2 in terms of excessive exercise and extreme eating disorder conditions.

Serious medical complications were reported secondary to anorexia nervosa and bulimia: e.g., acute kidney failure and electrolyte disturbances were a result of nutritional deprivation in a 40-year-old woman. Starvation-induced acute psychosis in a 19-year-old girl who presented with abnormal behavior after being on 100 kcal/day diet and an elevated anti-nuclear antibody (ANA) [6-7]. Similar to the aforementioned cases, our teenage girl suffered acute kidney injury as a result of dehydration. Moreover, she presented with anemia, lymphopenia, arthralgia, depression and amenorrhea, positive ANA, anti-ds DNA antibody and anti-centromere antibody and low complement that raised the suspicion of SLE diagnosis according to the ACR 1997 criteria for SLE diagnosis [4]. However, in view of the significant improvement in our patient’s health after being on a higher calorie diet, we point to the potential causal relationship between nutritional deficiency and appearance of SLE features.

Systemic lupus erythematosus is a complex autoimmune disease resulting from a loss of tolerance to multiple self-antigens that is characterized by autoantibody production and inflammatory cell infiltration in target organ such as kidneys and brain. T lymphocytes are critical players in SLE pathophysiology as they regulate B cell response and infiltrate target tissues, leading to tissue damage [8].

Abnormal expression of key signaling molecules and defective functions of T cells play a significant role in the pathogenesis of SLE. Current research on lymphocyte signaling abnormalities in SLE has been directed towards investigating various factors that contribute to abnormal tyrosine phosphorylation, intracellular calcium response, and cytokine production. Moreover, DNA hypomethylation affects a number of genes in T cells in SLE patients, which may be of genetic
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Vitamin D has been shown to modulate the immune system and has anti-inflammatory properties; the immune regulatory role of vitamin D affects both innate and adaptive immune responses contributing to immune tolerance of self-structures. Vitamin D deficiency skews the immunologic response toward loss of tolerance [10].

Recent years have brought a paradigm shift for the role of the essential element zinc in immunity. The activity of virtually all immune cells is modulated by zinc in vitro and vivo. Zinc has been shown to bind and affect the activity of several signaling molecules, such as protein tyrosine phosphatases (PIPs). In addition, zinc acts as an intracellular signaling molecule. That is, a molecule whose intracellular status is altered in response to an extracellular stimulus and that is capable of transducing the extracellular stimulus into an intracellular signaling event [11].

Autophagy (self-digestion) is a physiological cellular mechanism that degrades and recycles proteins and other molecules to maintain an adequate amino acid level during nutritional deprivation of the cells. According to certain experimental data, autophagy may be implicated in autoimmunity by delivering the peptide from autophagic vacuoles via lysosomes to MHC molecules and thereby access the cell surface (immunophagy), consequently activating and regulating CD4+ T cells by antigen-presenting cells (APC). The proposed effects of autophagy in development of autoimmunity were: generation of autoantigen, molecular mimicry, presentation of intracellular autoantigen, regulation of antigen-presenting cells (APC), and impact on CD4+ T cell regulation and macrophage activation. Thus, autophagy can be relevant to the induction or loss of tolerance to intracellular molecules [12].

Abnormality in lymphocyte signaling pathway induced by zinc deficiency and breaking down of immune tolerance to self-structure by conditions such as vitamin D deficiency, or by autophagy process induced by nutritional deprivation could contribute to SLE pathogenesis. Clearance of ANA and other antibodies and disappearance of symptoms in our patient after being on a diet with sufficient calories should focus physicians’ attention on the importance of linking such complications to ED behavior.

Conclusion

We present a case of a female teenager in whom significant clinical and serological findings correlate with the diagnosis of SLE as a result of an eating disorder.

Acknowledgment

We would like to thank our patient for her agreement to publish her case.

References