Case Report

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Systemic lupus erythematosus and Down syndrome: a case report and literature review

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Introduction: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can involve any organ system, and may lead to significant morbidity and even mortality. Down syndrome (DS) is the most frequent genetic cause of intellectual disabilities, typically caused by the presence of an extra chromosome 21.

Case presentation: A 47-year-old Syrian female of DS who complained of low-grade fever, oral aphthae, fatigue, and arthralgia three months before presentation. Although the patient was diagnosed with phenotypically and gynogenically DS, a milder mosaic type was identified. She appeared fatigued with a blood pressure 110/70 mmHg, pulse 104/min, temp 100 F, having oral ulcers, tenderness of joints on palpation, haemoglobin 9.4 g/dl, white blood cells 10.9/mm^3, platelets 87 000 × 109/cm with C-reactive protein of 2,3 mg/dl, and an erythrocyte sedimentation rate of 68. Urea 33 mg/dl with creatinine 0.9. The rest of the tests were unremarkable. Urine analysis was normal.

Discussion: The prevalence of SLE in DS in the literature was found only in five cases, with different presentations, in the last 36 years. In our case the patient presented with mild lupus manifestations and responded well to steroids and hydroxychloroquine. Also, In our case, an onset of SLE in an old DS (DS female patient), whereas SLE is more frequent in childbirth-aged women, in addition to that DS patients had a short life expectancy.

Conclusions: DS is associated with a predisposition to developing connective tissue disorders, especially in young females. unfortunately, patients were not diagnosed in all five cases until later with a flare because of the cognitive defect.

Keywords: case report, down's syndrome, systemic lupus erythematosus

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can involve any organ system and may lead to significant morbidity and even mortality. The pathogenesis of SLE includes a complex interaction between the environmental influence and genome to produce an epigenetic change that alters the expression of specific genes that contribute to disease development. Exposure to environmental factors such as UVB radiation, infections, and toxins triggers a loss of immune tolerance in genetically susceptible individuals and leads to aberrant activation of autoimmunity[1].

HIGHLIGHTS

- The manuscript describes a case of a 47-year-old Syrian female of Down syndrome (DS).
- The patient was diagnosed with phenotypically and gynogenically DS, a milder mosaic type was identified.
- Also the patient was diagnosed with systemic lupus erythematosus.
- Our case report is very special and important because the prevalence of systemic lupus erythematosus in DS in the literature was found only in five cases, with different presentations, in the last 36 years.
- We compared our results with the 5 original published studies.

Down syndrome (DS) is caused by a random error in cell division that results in the presence of an extra copy of chromosome 21. Studies found an autoimmunity-prone state in DS, in which a cytokinopathy, hyperactivated CD4 T cells, and ongoing B-cell activation contribute to a breach in immune tolerance, predisposing these patients to autoimmune disease. also open therapeutic paths, as we demonstrate that T-cell activation is resolved not only with broad immunosuppressants such as Jak inhibitors, but also with the more tailored approach of IL-6 inhibition[2,3]. DS presents with a constellation of cardiac, neurocognitive, and growth impairments. DS is also prone to infectious, inflammatory, autoimmune, and connective tissue conditions. DS associated with connective tissue disorders is hypothesized but is still rare[4].

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This case report has been reported in line with the SCARE Criteria[5].

Case report

We reported a case of a 47-year-old Syrian female of DS who presented in March 2023, complaining of low-grade fever, oral aphthae, fatigue, and arthralgia three months before presentation.

She had the typical face of DS and knocked knees (Figure 1) and (Figure 2).

She was able to communicate in short simple obvious sentences.

Although the patient was diagnosed with phenotypically and gynogenically DS, a milder mosaic type was identified. There was no family history of DS in the patient's pedigree. The patient's medical history was otherwise unremarkable.

On physical examination, the patient appeared fatigued, with a blood pressure 110/70 mmHg, pulse 104/min, temp 100 F, having oral ulcers and tenderness of joints on palpation.

Laboratory tests showed a haemoglobin 9.4 g/dl, white blood cell count of 10.9/mm^3, platelet 87000 × 109/cm, C-reactive protein of 2.3 mg/dl, and erythrocyte sedimentation rate of 68. Urea 33 mg/dl with creatinine 0.9. The rest of the tests were unremarkable. Urine analysis was normal.

Immunological profile was done ANA; 323Au/ml (normal:0–25), homogenous, Anti double-stranded DNA was 1.84 which is considered positive. The remaining immunological profile was negative.

Echocardiogram showed an ejection fraction of 60%, and pericarditis.

Also, abdominal echo shows peritonitis.

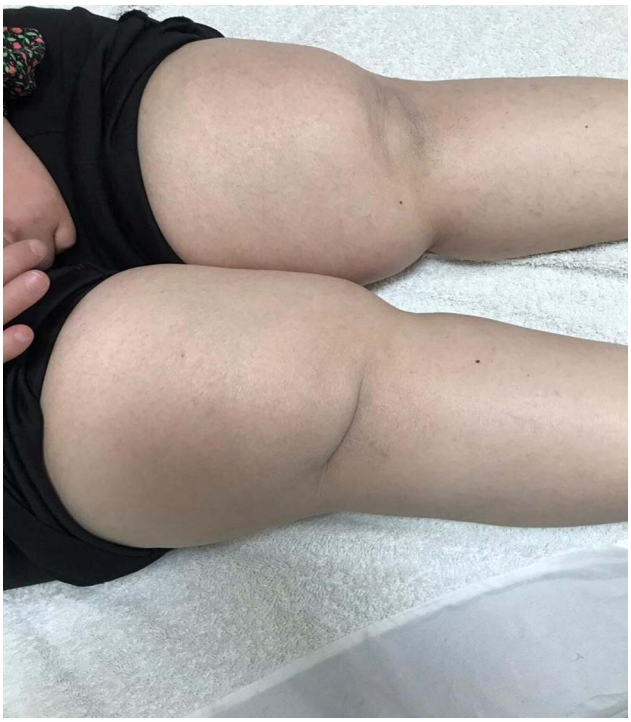

Figure 1. Shows the patient's knocked knees.

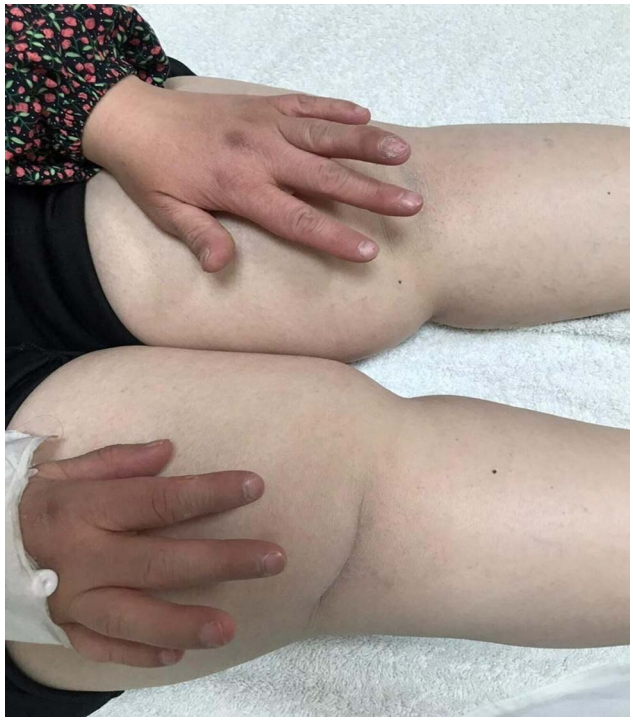

Figure 2. Shows the patient's fingers and knocked knees.

The patient was diagnosed with SLE, according to ACR/EULAR 2019 criteria[6]; as ANA;1/640, in addition to fever, pericarditis, peritonitis, anaemia, thrombocytopenia, and positive Anti double-stranded DNA.

She was given prednisolone 40 mg, hydroxychloroquine 200 mg. The patient showed significant clinical improvement in 1 week with an improvement of the oral ulcer, and arthralgia. Increasing platelet count up to 123000 × 109/cm. There was effusion at the echocardiogram (Figure 3).

Her steroids were gradually tapered and stopped after 3 months. The patient is doing well on regular follow up.

Discussion

The prevalence of SLE in DS in the literature was found only in five cases, with different presentations, in the last 36 years. The first case was reported by Franklin *et al.*[7] in a 20-year-old female who presented with fever, rash, arthritis, and haematological involvement. Positive ANA, Anti-ds DNA, and lupus cells were found. She was treated with NSAIDs.

The second case that was reported was an 8-year-old boy by Bakkaloglu *et al.*[8] previously diagnosed as having SLE 7 years ago and presented with oral lesions, cutaneous findings, positive coombs haemolytic anaemia, positive ANA titre, and anti-DNA. Renal involvement and cerebral vasculitis were developed within 5 years, and treated with cyclophosphamide and steroids, leading to the death of the patient due to respiratory failure.

The third case reported in 1998 by Feingold & Schneller[9], was a 30-year-old female, who presented with chest pain due to pericarditis, arthralgia, and photosensitivity further investigations revealed chronic persistent hepatitis with a positive ANA

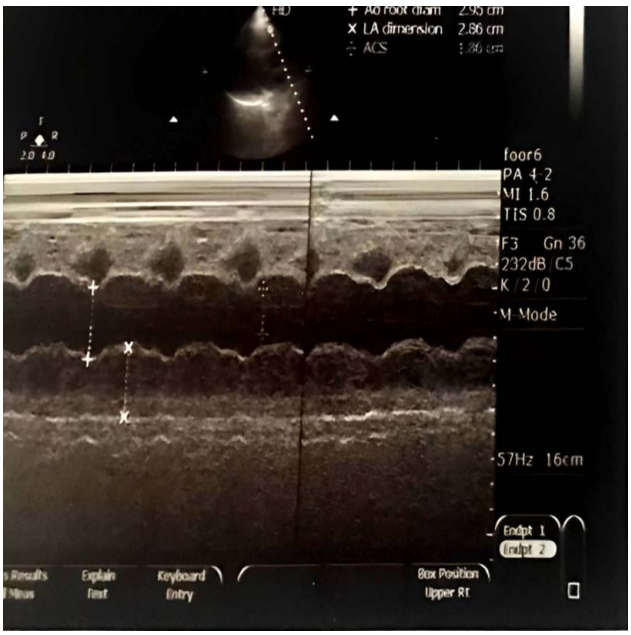

Figure 3. Shows effusion at the echocardiogram.

and ds DNA, treated with steroids and non-steroidal anti-inflammatory drugs (NSAIDs) with discontinuation of therapy one year later.

Suwa *et al.*[10] reported the fourth case in 1999 when a 42-year-old Japanese female presented with fever, rash, arthritis, and pleuritis, she was found seropositive with ANA and Lupus Erythema cells and responded well to low-dose prednisone 20 mg.

In the fifth case reported by Kidwai *et al.*[11], in 2020, 14-year-old female presented with arthralgias, rash, haematological and immunological manifestations, and a probable cerebral involvement earlier in the course before the diagnosis was made, successfully treated with steroids, hydroxychloroquine, and azathioprine.

Our case is 47 a years old female with DS, presented with mild lupus manifestations and responded well to steroids and hydroxychloroquine.

Table 1 summarized the cases.

SLE is characterized by aberrations that involve hyperactive B cells, T cells, and cells of the monocytic lineage, resulting in polyclonal B-cell activation, increased numbers of antibody producing cells, hypergammaglobulinemia, autoantibody production, and immune complex formation. Increased interleukin (IL) 6 and IL-10 may promote B-cell aberrant activity. However, some studies have suggested abnormalities in IL-6 and IL-10, but these studies are not reproduced in all ethnicities[12].

There is a growing interest in how trisomy 21 disrupts immune tolerance and promotes autoimmune disease in individuals with DS, and researchers have begun to identify the key immune genes, pathways and cell types that are dysregulated. There is an extensive autoimmunity-relevant remodelling of the immune landscape DS individuals, particularly in cytokines, immune subsets, and the enhanced interferon signalling. Too much interferon signalling is known to be harmful in medical conditions such as systemic lupus erythematosus.IL-6 was implicated as an independent driver of T-cell dysregulation in individuals with DS. Together, these results highlight various molecular changes in individuals with DS that resemble those seen in autoimmune and rheumatic diseases. DS-related cellular changes include increased frequencies of T helper 1 (TH1) cells, TH17 cells and CD11c + B cells[2,3].

Undiagnosed cases of connective tissue disorders, including SLE may be dismissed because of the presence of other mimicking diseases such as infections, and hypothyroidism[11,12]. The inability of the patient to explain their complaints, and the short life expectancy of these patients[13] may confuse the clinicians, whereas adulthood is the frequent age in most SLE patients[14].

NSAIDs are effective for symptom relief in lupus-associated arthritis and myalgias. Almost all patients will be treated with corticosteroids at some point, and hydroxychloroquine should be used in all patients with lupus unless contraindicated, as we did. Immunosuppressants and biologics are used in unresponded SLE or severe SLE presentations[15].

In our case, an onset of SLE in an old DS female patient, whereas SLE is more frequent in childbirth-aged women, in addition to that DS patients had a short life expectancy[13].

Conclusion

DS is associated with a predisposition to developing connective tissue disorders, especially in young females. To date, there are only 5 case reports documented in this aspect; unfortunately, patients were not diagnosed in all five cases until later with a flare because of the cognitive defect.

The question of whether the association of DS with SLE is coincidental or whether there is a predilection for autoimmune disorders in DS is still being investigated. Further investigations of this disorder will improve the understanding of the correlation

Table 1

Summarizing of the data from the previous studies

Case author	Age of the patient	Sex	Presentation	Treatment
Franklin *et al.*[7]	20	Female	Fever, rash, arthritis, and haematological involvement. Positive ANA, Anti-ds DNA, and lupus cells	NSAIDs.
Bakkaloglu *et al.*[8]	8	Boy	Oral lesions, cutaneous findings, haemolytic anaemia, positive ANA titre, and anti-DNA. Renal involvement and cerebral vasculitis were developed within 5 years	Cyclophosphamide steroids
Feingold & Schneller[9]	30	Female	pericarditis, arthralgia, and photosensitivity positive ANA and ds DNA	Steroids NSAIDs
Suwa *et al.*[10]	42	Female	Fever, rash, arthritis, and pleuritis, she was found seropositive with ANA and LE cells and	Steroids
Kidwai, *et al.*[11]	14	Girl	Arthralgias, rash, haematological and immunological manifestations, and a probable cerebral involvement earlier in the course before the diagnosis was made, successfully treated with.	Steroids hydroxychloroquine, azathioprine
Our case	47	Female	Low-grade fever, oral aphthae, fatigue, and arthralgia	Steroids hydroxychloroquine

NSAID, non-steroidal anti-inflammatory drug; LE, Lupus Erythema.

between hereditary, immunologic responses, and the aetiology of connective tissue diseases.

What we want to draw attention to is that cases associated with SLE in DS patients may begin at a late age, just as patients with DS may live to advanced ages.

Patient's perspective on the treatments

The patient's sister was happy with the treatments provided, especially after the treatment with prednisolone 40 mg and hydroxychloroquine 200 mg. The patient showed significant clinical improvement in one week with an improvement of the oral ulcer, and arthralgia

Ethics approval

Our study complies with the Declaration of Helsinki, the locally appointed ethics committee has approved the research protocol and written informed consent has been obtained from the subjects.

Consent for publication and consent to participate

The patient's sister provided written informed consent for her to participate.

Written informed consent was obtained from the patient sister for the publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

M.K. wrote the case report, N.K. wrote the discussion, D.A. wrote the abstract and introduction, and participated in the discussion. S.J. and R.A. did the final edits and revisions.

Conflicts of interest disclosure

There are no conflicts of interest.

Research registration unique identifying number (UIN)

This is a case report.

Availability of data and materials

The data are available from the corresponding author upon reasonable request. The data supporting the results of this article are included in the article's references.

Provenance and peer review

This manuscript is original and has not been published before. It is not currently being considered for publication elsewhere

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