

## CASE REPORT

# DOWN's syndrome with Systemic Lupus Erythematosis: Never turn a blind eye

Saera Suhail Kidwai\*<sup>1</sup>, Hoori Shehwar<sup>2</sup>

<sup>1</sup>Department of Internal Medicine, Fazaiya Ruth Pfau Medical College, Karachi, Pakistan

<sup>2</sup>Neurospinal and Medical Institute, Karachi, Pakistan

**Received:** March 11, 2020

**Accepted:** May 22, 2020

**Online Published:** June 3, 2020

**DOI:** 10.5430/dcc.v6n4p17

**URL:** <https://doi.org/10.5430/dcc.v6n4p17>

## ABSTRACT

Down's syndrome (DS, Trisomy 21) with a prevalence of 1:8,000 live births is considered the most common genetic chromosomal disorder, with an extra full or partial copy of chromosome 21. In addition to physical and mental developmental delays and disabilities being a challenge to this disorder, vulnerability of DS patients to a variety of autoimmune diseases like diabetes, thyroid disorders and celiac disease is also well established suggesting impaired immune response especially cell mediated immunity. In the last 3 decades, a few cases of Systemic Lupus Erythematosis (SLE) have been identified and reported internationally, this case report adds to this rare association and also endorses the need to carefully evaluate and investigate the DS individuals for the presence of connective tissue disorders especially if there is already an existing autoimmune disorder like diabetes, celiac or thyroid disorder.

**Key Words:** Down's syndrome, Systemic Lupus Erythematosis, Diabetes mellitus

## 1. INTRODUCTION

Down's syndrome (DS) is the most common identified cause of intellectual disabilities, with an average prevalence of 1 per 1,000 registered births.<sup>[1]</sup> Patients with DS have an increased prevalence of autoimmune disorders affecting both endocrine and non-endocrine organs including coeliac disease, diabetes mellitus, hypo- and hyperthyroidism. DS associated with connective tissue disorders is hypothesized but is still rare.

## 2. CASE REPORT

We reported a case of 14-year-old female of DS who presented in the outpatient department having low set ears, knocked knees and typical facies, her milestones were delayed but she was able to communicate in short simple sentences. Although the patient was phenotypically and geno-

typically DS but with a milder mosaic type, there was no family history of DS in the pedigree known. Her past history was remarkable as she started experiencing gross tremors of extremities 2 years ago and was advised MRI Brain and EEG in 2013 which were Normal, however, in 2015, she was again advised for an MRI Brain which showed subcentral hyperintense signal intensity in parietal cortex, bilaterally near high vertex suggestive of small ischemic infarcts.

Three months prior to this visit, our patient experienced a rash on chest, abdomen and right arm which persisted and low grade fever which was ignored, she got anorexic and lethargic and complained of joint pains frequently. One month before presentation, she had pedal edema which gradually increased, developed a malar rash with recurrent

\*Correspondence: Dr. Saera Suhail Kidwai, Prof.; Email: saerakhan@hotmail.com; Address: Department of Internal Medicine, Fazaiya Ruth Pfau Medical College, Karachi, Pakistan.

episodes of high grade fever and burning micturition. On examination, she was toxic with a B.P 110/70 mmHg, Pulse 104/min, Temp 100 °F, having gross tremors, oral ulcers and a malar rash. Pedal edema was present with dry skin. She had a pleomorphic non blanching rash on her chest, abdomen and left upper arm, in addition typical vasculitic lesions on palms and soles were also present.

Investigations done showed Hb 9.4g/dl , TLC 10.9/mm<sup>3</sup>, Platelets 98,000×10<sup>9</sup>/cmm with an ESR of 68. Urea 47 mg/dl with creatinine 1.7 mg/dl and Serum Potassium of 5.1 mEq/L. LFT's shows an SGPT of 67 mg/dl. Serum ferritin was 4 four times normal 655. TSH was 6 times normal that was 23 IU. Immunoserological testing was done ANA ++ homogenous, Anti Double stranded DNA was 1.84 (twice normal) however complement levels were normal.

Echocardiogram showed an ejection fraction of 60%. Patient was fulfilling 6 of the 11 criterias of Systemic Lupus Erythematosus (SLE) so she was treated as a case of SLE flare with hypothyroidism. She was given prednisolone 40 mg, azathioprine 50 mg, Hydroxychloroquine 200 mg, folic acid 5 mg, and an antibiotic to cover the UTI. She was also started on thyroxine 50 µg. Patient showed significant clinical improvement in one week with a resolving rash, her infection subsided and she went afebrile. Her steroids were gradually weaned off after 3 months.

Patient is on regular follow up since a year, now with mild flares twice during the year which were managed with a course of steroids, she is currently on azathioprine 50 mg and hydroxychloroquine 200 mg running a stable course. Her serial thyroid profile is within normal range along with the baseline laboratory tests.

### 3. DISCUSSION

The prevalence of SLE in DS is explored in the literature and it was found only occasional with this report as the fifth in line in the last 36 years.

The first case was reported by Flanklin et al.<sup>[2]</sup> in the year 1985 when a 20-year-old female presented with fever, polyarthritis and rash along with hematological involvement, her ANA, Ds DNA and LE cells were positive but she was controlled on NSAID's as the disease severity was low.

The second case was reported 22 years ago in the year 1994 by Bakkaloglu et al.<sup>[3]</sup> when an 8-year-old DS (mosaic) patient previously diagnosed as having SLE in 1987<sup>[2]</sup> presented with acute flare, he had all the characteristic stigmata of DS with mild mental retardation. He presented with oral lesions, cutaneous findings, Coombs (+) hemolytic anemia, + ANA titer and high anti-DNA levels. Over the course

of 5 years, he repeatedly had flares of SLE with involvement of kidneys and hypocomplementemia (low C4 levels), it was postulated that a low C4 level may have resulted in development of SLE at a young age. Later on he had a resistant course of disease with CT examination demonstrating bilateral calcifications of the basal ganglia, which were interpreted to be secondary to cerebral vasculitis only controlled when cyclophosphamide was started with steroids. Unfortunately, he could not survive the progressive disease with pulmonary involvement, pancytopenia, and low C3 and C4 levels. Despite prompt treatment, the child died due to failure of the respiratory system.

Another case reported in 1998 by Feingold & Schneller,<sup>[4]</sup> presented with a 30-year-old female DS (trisomy 21) with chest pain and pericardial effusion which was followed by arthralgia and a photosensitive rash, further investigations revealed chronic persistent hepatitis with a positive serology for ANA (1:320) and Ds DNA (10.3 u/ml) and normal complement levels. The disease went into remission with oral steroids and NSAIDS with discontinuation of therapy one year later.

The fourth case was reported in 1999 by Suwa et al.<sup>[5]</sup> when a 42-year-old Japanese female with DS (Mosaic) presented with fever, rash, polyarthritis and pleuritis, she was found seropositive with ANA and LE cells and responded well to low dose prednisone 20 mg.

Unlike the earlier case reports, our patient presented with arthralgias, vasculitic rash, hematological and immunological manifestations and a probable cerebral involvement earlier in the course before the diagnosis was made, the disease however, is successfully controlled on medications (steroids, hydroxychloroquine and imuran), and she is on regular follow up.

Among all the five case reports, only one male presented at a very early age with severe disease activity and end organ involvement of CNS, renal, haematological and immunological system including a low complement level. Unfortunately, the child succumbed to death even though he was treated aggressively with steroids and pulse cyclophosphamide.

Abnormalities of cell-mediated, humoral, and phagocytic functions has been linked to patients with DS,<sup>[6]</sup> resulting in qualitative and quantitative defects in lymphocytes, these immunological aberrations may predispose DS patients to autoimmune disease. This is suggested previously by Ivarsson et al.,<sup>[7]</sup> who also suggested the possibility of presence of additional genes on chromosomes which along with precipitation of environmental factors can result in susceptibility to SLE.

Scarcity of such data may be deceptive and probably a lot of other undiagnosed cases of SLE and connective tissue disorders are ignored because of the coexistence with other mimicking diseases like hypothyroidism, infections, fibromyalgia, psychiatric and mental disorders, only to be discovered later at a more advanced and sometimes irreversible stage. Clinicians often get biased because of the existing condition in DS and the inability of the patient to correctly explain their complaints adds up to this ignorance. Another reason of missed diagnosis is the short life expectancy of patients with DS whereas the peak age of appearance of most SLE features is in adulthood.

#### 4. CONCLUSION

DS is associated with a predisposition to develop autoimmune disorders which include diabetes, thyroid dysfunctions

and celiac disease. SLE is another severe systemic disease to be considered carefully especially in females with already having an autoimmune disorder. To date, there are only 4 case reports documented in this respect, unfortunately, patients were not diagnosed in all 4 cases until later with a flare because of the cognitive defect.

Clinicians should be aware of the possibility of an autoimmune defect in female with DS as they can present with SLE features at a young age. 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 investigated.

#### CONFLICTS OF INTEREST DISCLOSURE

The authors declare they have no conflicts of interest.

---

#### REFERENCES

- [1] Badiu C, Verzea S, Picu M, et al. Autoimmunity puzzle in Down syndrome. *Down Syndrome Research and Practice*. 2010; 12(2): 98-102. PMID:19026279. <https://doi.org/10.3104/updates.2054>
- [2] Franklin CM, Torretti D. Systemic lupus erythematosus and Down's syndrome. *Arth Rheum*. 1984; 27: 929-34.
- [3] Bakkaloglu A, Ozen S, Besbas N, et al. Down syndrome associated with systemic lupus erythematosus: a mere coincidence or a significant association? *Clin Genet*. 1994; 46: 322-323. PMID:7834901. <https://doi.org/10.1111/j.1399-0004.1994.tb04170.x>
- [4] Feingold M, Schneller S. Down syndrome and systemic lupus erythematosus. *Clin Genet*. 1995; 48: 277. PMID:8825610. <https://doi.org/10.1111/j.1399-0004.1995.tb04106.x>
- [5] Suwa A, Hirakata M, Satoh S, et al. Systemic lupus erythematosus associated with Down syndrome. *Clinical and Experimental Rheumatology*. 2000; 18(5): 650-651.
- [6] Lockitch G, Singh VK, Puterman ML, et al. Age-related changes in humoral and cell-mediated immunity in Down syndrome children living at home. *Pediatr Res*. 1987; 22: 536-40. PMID:2960948. <https://doi.org/10.1203/00006450-198711000-00013>
- [7] Ivarsson SA, Ericsson UB, Gustafsson J, et al. The impact of thyroid autoimmunity in children and adolescents with Down syndrome. *Acta Padiatr*. 1997; 86: 1065-7. PMID:9350885. <https://doi.org/10.1111/j.1651-2227.1997.tb14808.x>