

Systemic lupus erythematosus, Celiac and Hypothyroidism complicating type 1 diabetes: a rare tetrad.

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease involving multiple organs and is often associated with other autoimmune conditions, diabetes mellitus being one of them. Type 2 diabetes complicating SLE has been reported in adults, higher anti-insulin antibodies, chronic inflammation and chronic use of steroids been associated with hyperinsulinemia and insulin resistance leading to diabetes [1,2].

However type 1 diabetes mellitus (T1DM) developing in SLE is very rare and there is not much data to report the incidence of the same. There are very few of these cases reported in literature and the occurrence in children is even lesser [1,3].

Genetic predisposition, autoimmunity and viral infections are the main etiopathological factors implicated in the pathogenesis of type 1 diabetes mellitus and an association between T1DM and Celiac disease (CD) has a high incidence. This is probably due to the human leukocyte antigen (HLA) DR3-DQ2 and DR4-DQ8 that is common to both the diseases [4].

But the association of the T1DM and CD subsequently developing SLE has only been reported once prior in a child to the best of our knowledge [5].

This would be the first case to report the tetrad of T1DM, CD, autoimmune hypothyroidism and SLE in the same child.

CASE REPORT

A 9 year-old girl, was diagnosed with T1DM with HbA1c of 9.3, she was started on Insulin degludec and glulisine and was maintaining normal sugars. Her IgA anti-tissue transglutaminase antibodies (AtTG) was positive – 101 RU/ML, which was followed up with a duodenal biopsy showing villus atrophy and increased intra-epithelial cells, confirming the diagnosis of CD and was advised a gluten free diet. Her anti thyroid peroxidase (TPO) was > 573 IU/ml (positive) but her TSH and Free T4 were within normal limits and hence were regularly followed for her thyroid functions.

Her hemoglobin at the time was 12.9 gm/dl and rests of the hematological parameters were within normal limits.

She continued to be followed up regularly for the next three years. She then developed high-grade fever and macular rashes on her hand, legs (including palms and sole) and face. This was presumed to be a viral exanthem initially and managed symptomatically. However the fever continued to be of high grade and persisted for three weeks not responding to oral anti-pyretic and antibiotics, for which she was admitted and evaluated. She continued to have high grade remitting fever, her throat swab was positive for hemophilus influenza and was treated with ceftriaxone according to sensitivity. She also had pancytopenia, which continued to persist despite the antibiotic treatment.

The thyroid function tests, anti TPO and anti thyroglobulin were repeated which came back strongly positive and low free T4 and high TSH, she was started on tab thyroxine 25ug once a day.

Her blood and urine cultures came back with no pathogenic growth. Due to her persisting fever and rash, and co existing positive autoimmune conditions, anti-nuclear antibodies (ANA), anti double stranded DNA (ds DNA) were sent, the reports for which came back strongly positive.

Conflict of Interest: The authors have no real or perceived conflicts of interest in any matters, including financial issues, relating to this work.

DISCUSSION

Genetically predisposed patients are known to have associated autoimmune conditions manifesting together. It has been reported that as high as 30% of patients with SLE may develop two, three or sometimes even four autoimmune disorders, but even though diabetes mellitus is a very rare association [6].

In an Indian study by Kota et al, 260 children and adolescents with T1DM were enrolled and their co existing conditions evaluated. They reported 7% incidence of CD in this population of diabetic children but only 3 children with SLE were reported, where one child died due to SLE flare up. The etiology and duration of diabetes and SLE was not mentioned. But there were no cases with T1DM, SLE and CD all together in a single child [3].

The only other study to have reported all the three conditions together was by Hela Zeglaoui in a 15yr old girl with T1DM since the age of 6yrs, who developed SLE and systemic scleroderma. Even though she tested positive for anti-TPO, TSH was normal. She also tested positive for IgA and IgG anti gliadin (AGA), IgA antiendomysial (AEA), IgA anti reticulin (ARA) and IgA anti-tissue transglutaminase antibodies (AtTG), and was biopsy confirmed for CD [5].

Though the association of T1DM and SLE is very rare, children with T1DM have anti-insulin antibodies (IAA) and anti islet cell antibodies (ICA) may be at a higher risk of developing SLE due to non-organ specific autoantibodies (ANA, anti-dsDNA) [7].

In a study by Harrop, they evaluated the presence of IAA in patients with other autoimmune diseases. In this study 10 patients with SLE were positive for IAA, however the follow up of these was not mentioned, whether any of the antibody positive patients developed T1DM [8].

The number of cases with T1DM and SLE are very few. There have been only four cases of this association reported in children, and of these only one case had additional autoimmune disorders other than T1DM and SLE.

There needs to be an awareness about the co existence of 2 or more autoimmune conditions in the same patient or even progressive development.

CONCLUSION

- T1DM and SLE are both autoimmune processes, but their association together is rare.
- However it should be borne in mind as both together can result in organ damage.
- The autoimmune diseases known to occur together should always be screened for, as they can develop it later.

References:

1. Cortes, S., Chambers, S., Jerónimo, A. & Isenberg, D. Diabetes mellitus complicating systemic lupus erythematosus—analysis of the UCL lupus cohort and review of the literature. *Lupus* **17**, **2008**; 977–980.
2. Lidar, M. et al. Anti-insulin antibodies and the natural autoimmune response in systemic lupus erythematosus. *Lupus* **10**, 2001; 81–86
3. Kota SK, Meher LK, Jammula S, Kota SK, Modi KD (2012) Clinical profile of coexisting conditions in type 1 diabetes mellitus patients. *Diabetes Metab Syndr* **6**: 70-76.
4. Redondo MJ, Eisenbarth GS. Genetic control of autoimmunity in type 1 diabetes and associated disorders. *Diabetologia* **2002**; **45**: 605–22.
5. Zeglaoui H, Landolsi H, Mankai A, Ghedira I, Bouajina E. Type 1 diabetes mellitus, celiac disease, systemic lupus erythematosus and systemic scleroderma in a 15-year-old girl. *Rheumatol Int* (2010) **30**: 793–795
6. Chambers, S, Charman, SC, Rahman, A, Isenberg, DA. Development of additional autoimmune diseases in a multiethnic cohort of patients with reference to damage and mortality. *Ann Rheum Dis* **2007**; **66**: 1123–1127.
7. Heras P, Mantziros M, Mendrinis D, Heras V, Hatzopoulos A, et al. (2010) Autoantibodies in type 1 diabetes. *Diabetes Res Clin Pract* **90**: e40-42.
8. Harrop M, Caudwell J, Stojanovski C, Colman PG (1992) Insulin autoantibodies in patients with autoimmune diseases. *Diabetes Res Clin Pract* **18**: 107-112.

