

SLE and Type 1 Diabetes Mellitus Leading to End Stage Renal Disease: A Case Report and Review of the Literature

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Abstract

Objective: Type I diabetes (T1D) and Systemic lupus erythematosus (SLE) are two autoimmune conditions. When occurring in the same patient, they can lead to deleterious end points if not managed aggressively and adequately. The aim of this report is to alert physicians on the seriousness of this combination by presenting the case of a patient with end stage renal disease secondary to T1D and SLE.

Methods: We present the case of a 32 year-old lady with long standing uncontrolled diabetes and 3 years history of SLE, who presented recurrently to our institution with her last admission for preparation for hemodialysis.

Results: Patient had progressive proteinuria and declining GFR since 2012 (first admission). Kidney biopsy was done twice (3 years apart) showing a mixture of lupus nephritis and diabetic nephropathy.

Conclusion: T1D and SLE share common immunological and molecular basis that can aggravate each other leading to important vascular end points.

Keywords: SLE, Diabetes Type 1, Hemodialysis

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Introduction

Type I diabetes (T1D) is the most common autoimmune disorder in childhood [1]. It is characterized by selective loss of insulin-producing β -cells in the pancreatic islets in genetically susceptible subjects [2]. There are four types of autoantibodies found in patients with type I diabetes: classical islet cell antibodies, insulin autoantibodies, auto-antibodies to the 65 kD isoform of glutamic acid decarboxylase (GADA) and the protein tyrosine phosphatase-related IA-2 molecule (IA-2A) [2]. Moreover, Genetic analyses of T1D have linked the Human leukocyte antigen (HLA) complex, mainly class II alleles, to susceptibility to T1D [3].

Systemic lupus erythematosus (SLE) on the other hand, is a chronic severe systemic autoimmune disease characterized by the production of high titers of autoantibodies directed against native DNA and other cellular constituents [4]. Human leukocyte antigen (HLA) system, whose genes are located on chromosome 6, is a key mediator of inflammatory and immune reactions and HLA- DRB1 was proven to be associated with SLE [5].

It has been established that patients with an organ-specific autoimmune disease have increased risks of developing autoimmune responses against other organs/tissues [6,7].

Illustrating this theory, we present the case of a 32 year old lady with long standing T1D, with superimposed SLE leading to end stage renal disease requiring dialysis. We will also review the literature on the link between T1D and SLE.

Case Presentation

We present the case of a 32 year-old lady with T1D since the age of 9 years (maintained on detemir and insulin aspart), diagnosed with SLE in March 2012 in Egypt because of a one-year history of thrombocytopenia and proteinuria (maintained since then on hydroxychloroquine, prednisolone and mycophenolate mofetil) and hypertension (currently maintained on perindopril/amlodipine combination and bisoprolol). In 2013, she was also diagnosed with hypothyroidism in Egypt and started on Levothyroxine replacement.

She presented first to our institution in June 2012 for kidney biopsy. Results showed mesangial expansion with thickening of the capillary loops and marked glomerular obsolescence, consistent with diabetic nephropathy, focal tubular atrophy, fibrosis and tubulointerstitial chronic inflammation and mild vascular intimal thickening. Mesangioproliferative lupus nephritis could be

excluded. Her estimated GFR (eGFR) was 53. Her urine protein/Creatinine (Cr) ratio was 2071 mg/g Cr and her urine albumin/Cr ratio was 1621.7 mg/g Cr. Her HbA1C was 7.4%. Her hemoglobin was 10.5 g/dl. C3 was 1.4 g/l (within normal) and C4 was 0.53 g/l (normal).

In March 2013, her eGFR was 44. C3 was 1.27 g/l (normal) and C4 was 0.33 g/l (normal). Her hemoglobin was 9.4 g/dl.

In August 2013, she was pregnant and in her second trimester, eGFR was 58, hemoglobin 8.5 g/dl and C3 1.37g/l (normal) and C4 was 0.32 g/l (normal). Her HbA1C was 5.2%. In September 2013, her eGFR was 58, and her hemoglobin 7.2 g/dl.

In December 2013, she was admitted for delivery and underwent Cesarean Section (after failure of induction) at 37 weeks of gestation. Baby's weight was 2630g. Her eGFR was 38, hemoglobin 8.2 g/dl, and reached a nadir of 6.6 g/dl.

In January 2014, her eGFR was 35 and her urine albumin/Cr ratio was 10249.0 mg/g Cr. C4 was normal.

In view of the progression of her kidney disease, a repeat kidney biopsy was performed in Egypt and slides were re-read at our institution as advanced sclerosis, with a background of diabetic nephropathy, collagen deposits and Kimmelstiel-Wilson nodules. She presented to our institution in July 2015 with an eGFR of 5, a urine albumin/Cr ratio of 6569.2 mg/g Cr, C3 0.83 g/l (low) and C4 0.48 g/l (normal). She was started on hemodialysis.

Discussion

Approximately 30% of patients with SLE develop a second, third or fourth autoimmune condition [8]. T1D is one example, though few patients have been reported to have both diabetes and SLE [9]. Kota et al. studied the co-existing autoimmune conditions in patients with T1D [10]. 3 out of 260 patients (1.2%) had associated SLE [10]. Cortes et al. on the other hand looked at the lupus cohort and identified diabetic patients [11]. 3 out of 485 had T1D (0.61%) and 6 out of 485 had type 2 diabetes (0.82%) [11], further proving the rarity of this co-existence.

2 out of those patients had kidney biopsies both of which showed WHO type IV lupus nephritis. Some diabetic features were also seen in the biopsy from one patient [11].

It is quite important to determine the etiology leading to renal failure in those patients since they differ in their pathophysiology and management (lupus nephritis is autoimmune in nature) [11]. Kidney biopsy is therefore a must to guide management.

More-so, some patients with T1D are at higher risk to develop SLE based on their immunologic profile i.e. in those with diabetes caused by insulin resistance due to autoimmunity against insulin receptors, the serum contains non-organ specific autoantibodies (ANA, anti-dsDNA) and there is an increased risk of developing SLE [12]. Harrop et al. showed that 5 out of 27 patients (19%) with SLE had insulin autoantibodies [13].

Interestingly, newly diagnosed T1D patients treated with Rituximab (anti-CD20) had partially preserved beta-cell function at one-year post treatment as evidenced by decrease in loss of C-peptide and less insulin requirements [14]. This improvement was noted through depletion of B cells (the effectors cells in SLE), further strengthening the link between T1D and SLE immune mechanisms.

In 1985, Pottathil et al. made the following observation: Arachidonate content in diabetic and SLE individuals were significantly lower than that of controls, implying possible increase in cardiovascular risks in those patients [15]. 30 years later, Koenig et al. showed in a cross-sectional study (comparing the multicenter Swiss lupus cohort to a diabetes cohort) that patients with SLE are at least as likely to develop cardiovascular diseases as T1D patients further emphasizing the need to screen aggressively those patients [16].

Conclusion

SLE and T1D do not frequently occur together. However, they share some common immunological and molecular basis that can aggravate each other leading to important vascular end points.

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