

Case Report

Multiple Autoimmune Syndrome: Hashimoto's Thyroiditis, Coeliac Disease and Systemic Lupus Erythematosus (SLE)

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Abstract

Various autoimmune diseases have association with each other but it is very rare to see multiple autoimmune diseases in one patient. Presence of more than two autoimmune diseases in one patient is known as multiple autoimmune syndrome (MAS).¹ We report the case of an 11 years old girl who presented with history of swelling in front of the neck along with constipation, anorexia, weight gain and increasing pallor over a period of six months. Additionally she had an episodic history of joint pains and abdominal pain with no specific relation to diet, time, other gastrointestinal or genitourinary symptom. Hypothyroid goiter (Autoimmune thyroiditis, Hashimoto's thyroiditis) was diagnosed by raised thyroid stimulating hormone (TSH), low T4 and presence of thyroid specific antibodies in blood. Patient was discharged on tablet Levothyroxine to which she responded well with reduction in size of the swelling and relief of the symptoms except for the joint pains and abdominal pain. To evaluate the persistent symptoms she was investigated further for other autoimmune diseases and was diagnosed to be having systemic lupus erythematosus (SLE) and Coeliac disease also. The final diagnosis was multiple autoimmune syndrome (Hashimoto's thyroiditis, Coeliac disease and SLE).

Introduction

The combination of at least three autoimmune diseases in one patient has been defined as multiple autoimmune syndrome.¹ The definition of multiple autoimmune diseases is based on 91 reported cases of such associations in the literature.² The exact pathogenesis of multiple autoimmune syndrome is not known but environmental triggers in genetically susceptible individuals are believed to cause the disorder of immune regulation.² We report a case of multiple autoimmune syndrome in an 11 year old girl who was diagnosed to be suffering from Hashimoto's thyroiditis, Coeliac disease and SLE. To the best of our knowledge no case of multiple autoimmune syndrome has ever been reported from Pakistan.

Case Report

An 11 year old girl was admitted in the paediatric

ward; with complaints of progressively increasing swelling in front of the neck over a period of 6 months. Associated symptoms were constipation, decreased dietary intake, weight gain, progressive pallor and lethargy. Besides this she also complained of pains in large joints i.e. knees and ankles, and generalized abdominal pain not related to diet, time or other gastrointestinal or genito urinary symptoms. Her physical activity was significantly reduced in the past six months. Drug history and family history were unremarkable. On examination she was found to be a young girl looking obese and pale, with average height and well oriented in time, place and person. Her weight was 41 kg (75th centile) and height was 141cm (25th centile). She had a firm, smooth non tender goiterous swelling, measuring about 5x8cm in front of her neck. Musculoskeletal and abdominal examinations were unremarkable. Our clinical diagnosis was hypothyroid goiter which was later confirmed by laboratory investigations. Her Haemoglobin was 5.6gm/dl (N=10-11.5gm/dl), peripheral blood film showed microcytic hypochromic anaemia, serum ferritin was decreased to 4.92ng/ml (N=20-200ng/ml). Thyroid profile showed increased Thyroid stimulating hormone (TSH) 13.82units/ml (N=0.17-4.05units/ml), low T4 0.72 g/100 ml (N=0.89-1.79 g/100 ml) and normal T3 3.60 ng/ml (N=1.62-3.77 ng/ml). Both serum thyroglobulin antibodies and antiperoxidase antibodies were positive. Values were 1:160 (1:10 titer), and 1:400 (1:100) respectively. Ultra sound scan showed diffuse non toxic goiter. Based on clinical and laboratory findings diagnosis of autoimmune thyroiditis (Hashimoto's thyroiditis) was made and the patient was discharged on tablet Levothyroxine 100µgm (2µgm/kg) OD. The dose was tapered to 50µgm in three months in the out patient clinic. The future plan was to discontinue levothyroxine on next visit after 3 months if the TSH remained in the normal range. On the six weeks follow up, the swelling had almost subsided with marked improvement in dietary intake and bowel habits. But the joint pains increased and she had episodic generalized abdominal pain, dull in nature with no aggravating and relieving factors. Considering the association of Hashimoto's thyroiditis with other autoimmune diseases, she was readmitted for evaluation of other autoimmune diseases. Being a young adolescent girl with arthritis, we investigated her for SLE. Both Antinuclear antibodies (ANA) and Anti double standard

DNA (Anti ds DNA) antibodies, which are considered highly specific for SLE, were found to be positive. C3, C4 and urine DR were normal. Since the patient had abdominal pain and was already suffering from two autoimmune diseases, the possibility of the third one was also considered and the diagnosis of coeliac disease was entertained. Anti-tissue transglutaminase IgA antibody (TtGA-IgA) 21.1U/ml (N=0-7) was positive for coeliac disease. The jejunal biopsy revealed heavy chronic inflammatory infiltrates in lamina propria with several plasma cells and occasional eosinophils. The appearance was of subtotal villous atrophy and chronic inflammation. Positive results of TtGA-IgA along with histopathological findings on jejunal biopsy confirmed the diagnosis of Coeliac disease. With the addition of two more autoimmune diseases i.e. coeliac disease and SLE to our initial diagnosis of autoimmune thyroiditis the final diagnosis made was multiple autoimmune syndrome. NSAIDS with short course of corticosteroids were given for SLE, and gluten free diet was advised for coeliac disease. Patient responded positively to this treatment and is following up regularly in our paediatric O.P.D.

Discussion

Autoimmune diseases encompass a wide spectrum of diseases from organ specific Hashimoto's thyroiditis to systemic diseases such as systemic lupus erythematosus. These diseases are characterized by inflammation and production of wide range of autoantibodies detected against multiple autoantigens. Although the etiology is still poorly understood, genetic, immunological, hormonal and environmental factors are the major predisposing and triggering factors.³ A patient suffering from one autoimmune disease has 25% chances of acquiring another autoimmune disease.² Our patient presented with autoimmune thyroiditis but the persistent joint pains and abdominal pain raised the suspicion of the other associated diseases. Multiple autoimmune syndrome (MAS) can be classified into three groups according to the prevalence of their associations with one another. Type 1 MAS comprises myasthenia gravis, thymoma, polymyositis and giant cell myocarditis. Type 2 includes Sjögren's syndrome, rheumatoid arthritis, primary biliary cirrhosis, scleroderma and autoimmune thyroid disease. Type 3 groups together autoimmune thyroid disease, myasthenia gravis and/or thymoma, Sjögren's syndrome, pernicious anaemia, idiopathic thrombocytopenic purpura (ITP), Addison's disease, insulin-dependent diabetes, vitiligo, autoimmune haemolytic anaemia, systemic lupus erythematosus (SLE) and dermatitis herpetiformis.² With the presence of Hashimoto's thyroiditis and SLE, our patient seems to qualify, but only partially with MAS type 3. Coeliac disease, though an immune mediated disorder, is not included in the classification of MAS in the literature. Literature search

did not reveal any case report with these three conditions occurring in a single patient as yet although there have been reports of variable association between any two of these autoimmune diseases.

Hashimoto's thyroiditis is the most common cause of thyroid disease in children and adolescents accounting for many of the enlarged thyroids. Positive antithyroid antibodies are observed in 1-2% of younger school aged children and 4-6% of adolescents which is an evidence of autoimmune thyroid disease. Thyroid antiperoxidase antibodies (TPO Abs), formerly called antimicrosomal antibodies and antithyroglobulin antibodies are demonstrable in the sera of 90% children with Hashimoto's thyroiditis. When both tests are used, approximately 95% of patients with thyroid autoimmunity are detected.⁴ In our patient both types of antibodies were present which along with the suggestive signs and symptoms, confirmed the diagnosis of Hashimoto's thyroiditis.

The association of Hashimoto's thyroiditis with a number of other autoimmune disorders is already well established. The association of the Thyroid gland with SLE has been reported by Eberhard et al in adults in the range of 7.5% to 8.9%.⁵ Paediatric data suggests the incidence of SLE with onset before 19 years is between 6-18.9 cases per 100,000 in white females and higher (20-30 per 100,000) in blacks.⁶ The hallmark of SLE is production of Autoantibodies. ANA are seen in 100% of patients and anti-DNA auto antibodies are seen in 60-70% of cases.⁷ Since our patient showed positive results of both ANA and Anti ds DNA with worsening of joint pains over time, she was labeled as a case of Hashimoto's thyroiditis with SLE.

In addition to SLE, a higher incidence of thyroid autoimmune disorder is found in coeliac disease also.⁸ The increased prevalence of coeliac disease in the context of autoimmune thyroid disease is 5.4%.⁹ Collin et al in their study on 62 patients, demonstrated that 2-5% with more than one autoimmune diseases also had coeliac disease.⁹ This increased prevalence of autoimmune thyroiditis with coeliac disease is explained by the sharing of a common genetic predisposition namely the DQ2 allele by the two disorders.⁸ Coeliac disease, an inflammatory condition of the gut with a known autoimmune pathogenesis, is estimated to have a prevalence of 3-13/1000 children in paediatric population.¹⁰ The availability of specific and sensitive serologic tests, particularly anti-endomysial and tissue transglutaminase antibodies have facilitated widespread screening although small bowel biopsy is indicated before establishing a final diagnosis.¹¹ The strong association of coeliac disease with Hashimoto's thyroiditis led to the diagnosis of Coeliac disease. This particular patient was finally proven to have the diagnoses of Hashimoto's Thyroiditis, SLE, and Coeliac disease, not only on the basis of the symptomatology and

investigations but also by response to the treatment. According to definition the combination of three autoimmune diseases in our patient qualifies for the diagnosis of MAS but as already mentioned the literature search did not reveal this particular set of disorders in one single patient although a combination of any two of them have been reported.

Conclusion

In conclusion, the presence of one autoimmune disease should be an indicator for the possibility of another one. The occurrence of multiple autoimmune phenomena in this case shows the need for continued surveillance for the detection of new multiple autoimmune syndromes in predisposed patients.

References

1. Humbert P, Dupond JL. The multiple autoimmune syndrome (MAS). *Br J Dermatol* 1997; 136: 468-9.
 2. Mohan MP, Ramesh TC. Multiple autoimmune syndrome. *Indian J Dermatol Venereol Leprol* 2003; 69: 298-9.
 3. Szyper-Kravitz M, Marai I, Shoenfeld Y. Coexistence of thyroid autoimmunity with other autoimmune diseases: friend or foe? Additional aspects on the mosaic of autoimmunity. *Autoimmunity* 2005; 38: 247-55.
 4. Stephen I. Disorders of thyroid gland. In: Behrman RE, Kliegman RM. *Nelson textbook of paediatrics* 18th ed. Philadelphia: WB Saunders 2008; pp2327-9.
 5. Eberhard BA, Laser RM, Eddy AA, Silverman ED. Presence of thyroid abnormalities in child with systemic lupus erythematosus. *J Pediatr* 1991; 119: 277-9.
 6. Siegel M, Lee SL. The epidemiology of systemic lupus erythematosus. *Semin Arthritis Rheum* 1973; 3: 1-54.
 7. Benseler SM, Silverman ED. Systemic lupus erythematosus. *Pediatr Clin N Am* 2005; 52: 443-67.
 8. Kumar V, Rajadhyaksha M, Wortsman J. Celiac disease associated with other endocrinopathies. *Clinical and diagnostic laboratory immunology* 2001; 8: 678-85.
 9. Kaukinen K, Collin P, Mykkanen AH, Partanen J, Maki M, Salmi J. Celiac disease and autoimmune endocrinologic disorders. *Dig Dis Sci* 1999; 44: 1428-33.
 10. O'leary C, Walsh CH, Wieneke P, Buckley B, O'halloran DJ, Ferriss JB, et al. Coeliac disease and autoimmune Addison's disease. A clinical pit fall. *Q J Med* 2002; 95: 79-82.
 11. Farrell RJ, Kelly CP. Celiac sprue. *N Eng J Med* 2002; 346: 180-8.
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