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A Case Of Polyglandular Autoimmune Syndrome Type -2

Dr.Ishaivanan Dr.V.Padam, Dr.P.C.Sandhya ,Dr.Sathyapriya ,Dr.Chaitanya, Dr.Sharath Nallaperumal , Dr.Heshish , Dr.Sujana, Dr.Rahul Dr.Veeravignesh ,Dr.Sharath Chandra Reddy, Dr.Bhavna

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A 25 year old female came to casuality with complaints breathless , one episode of seizure ,at the time admission Cbg was 700mg/dl ,ABG was done it showed metabolic acidosis saturation was 88% , use abdomen done it showed ectopic right kidney , bilateral hydronephrosis , emphysematous cystitis .urine routine showed albumin 2+, pus cells plenty ,spot urine per done it showed 10000mg/dl.EEG done it showed normal limits.viral serology done it showed negative .Blood culture done it showed klebsiella pneumonia and antibiotics started.usg neck done it showed two well defined heterochoic nodules in the right lobe of thyroid-tirads III. patient is known case of type 1 diabetes mellitus ,on irregular treatment known case of hypothyroidism on irregular treatment ,known case of addison disease.Patient was kept on non invasive ventilation support ,Insulin infusion was started titrate according to capillary blood glucose, iv fluids given.She was previously maintained on daily levothyroxine and daily hydrocortisone supplementation but had been off his medication for 8 days. No history of chest pain or shortness of breath. No history of tremors, easy fatigability, weight gain, hoarseness of voice, or changes in bowel habit. He had no family history of autoimmune disease and review of systems was otherwise unremarkable. His knowledge about his medical condition was limited.On physical examination, she was in no acute distress. He was hypotensive with BP 89/67 and tachycardic with pulse rate of 115 bpm. Other vital signs were normal. Thyromegaly on neck palpation.

Basic metabolic panel revealed hyponatremia with Na 129 meq/L (136–145) and potassium of 4.8 meq/L (3.5–5.1). He was also severely hypocalcemia with ionized calcium of 0.96 mmol/L (1.15–1.33). Fasting blood glucose was normal. Thyroid function test showed elevated thyrotropin level at 5.807 uIU/mL (0.450–5.330) with normal free thyroxine level at 0.94 ng/dL (0.58–1.64). AM cortisol was markedly reduced at <1 mcg/dL (6.7–22.6). ACTH was markedly elevated at 785 pg/mL (7–69) and direct renin was also very elevated at 390 pg/mL (2.5–45.7). Parathyroid hormone was markedly reduced at <6 pg/mL (12–88). Complete blood count was normal, as was coagulation profile.ECG also showed sinus tachycardia with no ischemic changes.The patient was given intravenous saline and double his normal dose of his steroids. His levothyroxine dose was continued at 75 mcg daily while intravenous and oral calcium were given to correct hypocalcemia. His symptoms gradually improved, and he was discharged home on hydrocortisone 20 mg in the morning and 10 mg at night with fludrocortisone 0.1 mg daily and levothyroxine 75 mcg daily.On follow-up in clinic 2 weeks later, patient was noted to be doing well. Patient education regarding medication adherence and stress dosing to avoid potentially life-threatening adrenal crisis and the importance of medic alert bracelets was reinforced. The patient was classified as having APS type 1 because of the presence of hypoparathyroidism, Addison's disease, and chronic muco-cutaneous candidiasis, and promptly referred to the endocrinologist for continuity of care

I. Discussion

Polyglandular autoimmune syndrome is a complex and heterogeneous disorder. The fact that these conditions are so rare and that the number of variations is so high make the use of evidence-based approach difficult . The screening and diagnostic protocol of these patients is a hard task for clinicians . To our knowledge, this is the first meta-analysis in the field of PAS.

In PAS II, AD is present in 100% of the cases, AITDs in 69–82% and T1DM in 30–52% of the patients . No analysis of the other coexisting autoimmune disorders was previously available. The aim of this meta-analysis was to identify the main characteristics of PAS patients according to age, gender and combination of autoimmune disorders to develop relevant diagnostic and screening protocols. PAS II frequently appears later than PAS I, mostly in young adulthood . The mean age of the PAS patients at the time of diagnosis in our work was 34.7 years, which is unexpectedly high . It is well known that PAS are more common in females and this was confirmed by our study as well. As opposed to the common belief, PAS III was more prevalent than PAS II . This is due to the much higher prevalence of AITDs in comparison with AD, which is a diagnostic criteria for PAS II . In fact, AITDs are the most common autoimmune endocrinopathies in combination with other autoimmune conditions .

According to literature data, dual combinations in PAS II are more common than the classical triad of AD, AITDs and T1DM, which appears true only for approximately 10–20% of cases . According to our results, AD occurred in dual combinations in 83.9% of the PAS II patients, while the proportion of the triple combinations was 10.3%. The combination of AD, AITD and T1DM was diagnosed in 7.5% of PAS II patients. More than three autoimmune manifestations are more common in patients who have Addison's disease . Unfortunately, the categorization of the patients suffering from two or more autoimmune disorders in the PAS subgroups is not a clear task for the clinicians . These patients are receiving medications and therapies for their disorders separately and their conditions are not managed as a part of a complex disease. This may be the reason why only 18 articles fulfilled the inclusion criteria in this meta-analysis.

There are some limitations of our meta-analysis. We found case studies in a large number, while case series—studies analyzing larger populations—were found in a limited number. The data found in case studies could not be used for statistical analyses. In the future, the classification of PAS patients suffering from two or more autoimmune disorders is important to better understand the epidemiological data and the possible combinations of autoimmune disorders. The prevalence of autoimmune thyroid diseases is 40–200 times higher than that of Addison's disease in the general population and in association studies, the reference disorder must be the most frequent. Development of consecutive registries for autoimmune thyroid disorders and other autoimmune endocrinopathies seems to be essential to estimate the real prevalence of co-associations.

PAS II and PAS III are both due to polymorphisms in the HLA DQ/DR regions . PAS II has been found to be strongly associated with HLA haplotypes with DR3/DQ2 and DR4/DQ8 and with DRB1*0404 . Identification of the affected regions may be useful to estimate the risk of PAS. Circulating organ- and cell-specific autoantibodies can be detected in patients with the syndrome . However, it is difficult and expensive to search for all these markers during the follow-up period. Based on risk assessment, the screening of high-risk individuals would be possible. The screening process is further complicated by the late manifestation of the second autoimmune disorder; decades may elapse between two autoimmune manifestations . Detailed data are not available in the literature, few reports found that the shortest interval may be between AD and AITD, the longest between T1DM or vitiligo and AITDs . There are some studies about the prevalence of combined autoimmunities among children and adults . Association of autoimmune disorders is more common in adult patients; however, many autoimmune diseases can develop in childhood .

In conclusion, our meta-analysis clearly confirmed that the association of various other forms of autoimmune disorders which are not the obligatory components of PAS is not uncommon. However, AITDs, T1DM and AD are the most frequent combinations occurring in PAS, thus screening for these conditions seems to be reasonable. The development of relevant diagnostic and screening protocols to identify these patients timely is warranted.

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