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Late Presentation of Neglected Autoimmune Polyglandular Syndrome

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

A 60-year-old male patient, weighing 40 kg, having a BMI of 13, who was also a known case of Diabetes Mellitus Type II was shifted to the Orthopaedic Ward last month due to a fall, which led him to develop an intertrochanteric fracture in the femur. While the treatment of the patient was in an ongoing status for his fracture, his Diabetes was seen to be poorly controlled, with his blood glucose levels being constantly evaluated to be in a state of severe hypoglycaemia to slightly increased levels of blood glucose. On examination, the patient showed clear signs of being malnourished. He was in a bad and dishevelled state, he had creases on the palmar aspects of his hands and hyperpigmentation on his buccal mucosa. Furthermore, his lab reports revealed abnormalities in nearly every lab test ordered. Not only did he have elevated ACTH levels, but there was also a failure of Cortisol stimulation. His DEXA Scan showed that he was predisposed to develop severe osteoporosis and his malnourished condition was supportive of promoting that condition even more. The patient was diagnosed to be suffering from Autoimmune Polyglandular Syndrome, Type II. This is a rare condition of one of its kind where there is a pre-existence of autoimmune adrenal insufficiency along with either autoimmune thyroid disease or autoimmune

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diabetes mellitus. Since this condition is rare, it tends to often get overlooked upon diagnosis, leading to misdiagnosis because almost all of the presenting features or the symptoms of the prevalent endocrinological disorders present in this condition mimic either hypothyroidism, or diabetes, or adrenal insufficiency alone, and thus lead to further consequences when the condition does not resolve despite persistent treatment, such as the case in this patient. This paper reviews the background of the patient and the causes that possibly could have made him reach this advanced stage of the disease. The paper also reflects upon the disease, Autoimmune Polyglandular Syndrome Type II, as a whole and elaborates on the symptoms and signs which the patient tens to confuse with other endocrinological diseases. Lastly, this paper shall also review the appropriate management plan for the patient to ease his symptoms and accelerate his recovery process.

Keywords: Adrenal insufficiency; Addison's disease; adrenal crisis; autoimmune polyglandular syndrome type 2; LADA (latent Autoimmune Diabetes in Adults).

ABBREVIATIONS

APS II : Autoimmune Polyglandular Syndrome type II

1. INTRODUCTION

Some diseases that patients develop might appear to present acutely in a patient, but the truth is that they have been developing form a long time inside the body through disrupted mechanisms and malfunctioning of the body. One such disease is discussed below, where the presentation might be late in a patient is Autoimmune Polyglandular Syndrome Type II.

This disease mimics the presentation off many diseases all at once and so, often tends to get misdiagnosed in a patient. However, there are several distinct and characteristic features that make it possible for doctor to diagnose it within time to start the appropriate management.

The Autoimmune Polyglandular Syndrome Type II is a rare, uncommon disorder that affects people in their middle ages [1]. It comprises a combination of autoimmune adrenal insufficiency mainly with superimposed autoimmune thyroid disease or autoimmune diabetes mellitus or both, depending on the condition and presentation of the patient.

The incidence of this disease was found to be 5 in every 100,000 patients in the United States. In Europe, the incidence of this disease is not that prevalent but the disease seems to get diagnosed in more and more patients with passing time [2].

As far as the cause related to APS Type II is concerned, it is said to occur due to genetic conditions, and that too, with a positive history of autoimmune conditions among the relatives of the affected patients. This proves that the condition runs mostly in the families of those people who have had a positive family history of autoimmune disorders. Before this evidence was found, tuberculosis was thought to be the major cause behind the occurrence of APS Type II [3].

Although people from any age could get affected, APS Type II was found to be more prevalent among people above 30-50 years, and women were seen to be more commonly affected than males.

As far as the major symptoms that lead to the diagnosis of this condition were concerned, primary adrenocortical insufficiency was found to be the initial factor or the primary condition that arises in these patients [4].

From this point forth, either the patient's conditions or symptoms exacerbated further or were found to stay the same, thus leading to the diagnosis getting delayed or stopped beyond this very point. A delay in the diagnosis or misinterpretation of the lab results, combined with the confusing nature of the disease itself has led to delays in treatment and management.

This is the classic presentation of APS, Type II. Now, the next best step is to step forward and decided the appropriate management plan for the patient while also considering his underlying symptoms.

2. CASE REPORT

A 60-year-old male patient, weighing 40 kg, having a BMI of 13, who was also a known case of Diabetes Mellitus Type II at age of 40 he

received oral anti diabetic medications Glibenclamide and Metformin but his Blood glucose level remained fluctuating, after that added basal insulin glargine to his oral medications but still blood glucose remaining high and most of the time his HbA1C above 9%.

After that he noticed significant decrease in his weight and altered bowel habits.

He was recently admitted to the Orthopedic Ward for the operation of his intertrochanteric fracture that he had suffered from a while ago. But before the proper course of action could be prepared for the patient, several complications had arisen and the decision for carrying out his corrective surgery was almost impossible.

The problem was initially with his Diabetes. The patient had poorly controlled diabetes. This was evaluated after looking at his recurrent hypoglycemia. These imbalances in blood glucose levels were highly fluctuant ranging from being as low as 1.1.5 mmol to going up to 15 mmol. He was earlier taking oral medications to control his blood glucose levels but to no avail. Later on, he was shifted to Insulin (8 units of Glargine and 4 units of Lispro, TID). His lab supported the diagnosis of LADA which showed high GAD antibodies.

Moreover, it was also found that this patient had Celiac Disease for which he has been on a gluten-free diet, but this too was useless as failure to alleviate the symptoms were still being seen.

The patient was also severely underweight, having a weight of only 40 kgs and a BMI of 13, which was extremely concerning and also a pointer towards a possible failure to thrive for the patient. On appearance, the patient appeared to be severely malnourished, he had visible signs of hyperpigmentation in his buccal mucosa and also the presence of palmar creases. Muscle wasting was also evident.

Because of these reasons, his full lab workup was ordered. His electrolytes and other lab workups (consisting of Na, K, Ca, ACTH, Vitamin D, PTH) came up with positive findings of Primary Hypoaldosteronism. Furthermore, his Short Synacthen test was ordered which showed a failure of stimulation of cortisol levels.

The DEXA Scan showed that he was suffering from very severe osteoporosis, which clearly suggested his increased tendency to suffer from fractures.

3. DIAGNOSIS

The patient was found to suffer from a myriad of conditions that included latent autoimmune diabetes in adults (LADA), Celiac Disease, Primary Hypoaldosteronism, Secondary Hyperparathyroidism, and an increased risk of severe fractures.

To summarize, Vitamin D levels were below the normal range, whereas Calcium was found to be on the borderline. Serum Albumin was markedly decreased and in contrast, serum PTH levels were markedly increased. This pointing towards the obvious scenario that the patient was suffering from hyperparathyroidism. Addison disease, or primary adrenal insufficiency, is diagnosed after confirming an elevated ACTH level and an inability to stimulate cortisol levels with a cosyntropin stimulation test. This was clearly evident from the lab investigations gathered.

All of these findings were found based on symptoms and the simultaneous lab results that also revealed findings in favor of these diseases. The findings obtained in this patient have been summarized as under.

4. MANAGEMENT PLAN

Looking at the condition of the patient, he was admitted to the ICU and his operation for fracture management was delayed for the time being.

The patient was started on TPN for 7 days straight. He was also concurrently receiving blood transfusions as his Hemoglobin had dropped dangerously to 7.

Apart from this, supportive management of the other underlying conditions was as follows: Vitamin D 300,000 units IM route, a basal-bolus of insulin regimen, Hydrocortisone stress dose 50 mg/6 hourly.

This regimen proved to work for the patient and his condition improved to the point that his operation was carried out successfully and without complications as well. The patient was stable and in good health status following his surgery, but was still malnourished, for which he has been advised a good discharge plan after looking at his condition and then finally

discharged from the hospital with follow-up plans in the coming days.

The insulin doses were adjusted to counter hypoglycemia. Ibandronate (150 mg) was advised for a month for his osteoporosis and prednisolone replacement therapy was continued from then onwards.

Calcium and vitamin D supplements were also advised for a better health outcome.

Table 1. Diagnosis test results of patient

Test Name	Values
Na	128mmol/lit (135-145)
K	3.8 mmol/lit (3.6 -5.1)
Ca	1.7 mmol/lit (2.1 -2.6)
Corrected Ca	2 mmol/lit (2.1-2.6)
Albumin	24 g/L (35-50)
Mg	0.45 (0.7-1.05)
Anti-GAD antibody	Positive (98 IU/ml)
PTH	19pmol/lit(1.6 - 6.9)
Vitamin D	31 nmol/lit (50-200)
ACTH	90.6(1.6- 13.9)
Serum Cortisol	206 nmol/lit (138-635)
C peptide	0.01nmol/l(0.37 – 1.4)
Fasting insulin	< 2mIU/mL(2.6- 24.9)
HbA1C	8.58 %
DEXA Scan T - scores	
Lumbar area -6	
Hip -4.4	
Calculated FRAX (Abu Dhabi version):	
Major osteoporotic risk 87%	
Total Hip 74%	
Severe Osteoporosis with very high risk of fractures	
Short Synacthen Test - Failure of stimulation of cortisol level	
Basal Cortisol	250
30 min after 250 mcg of IM tetracosactide	274
After 1 hour	305

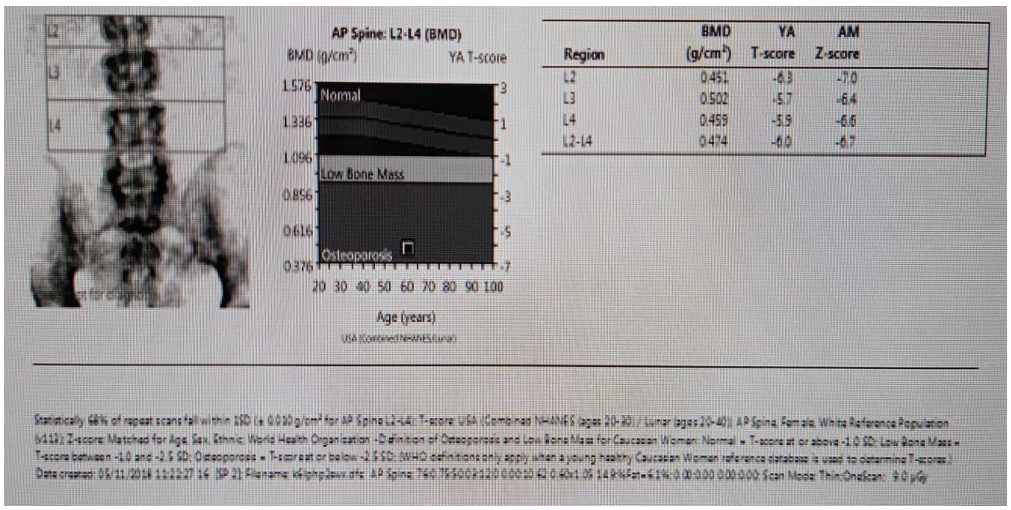

Fig. 1. (Dexa scan on AP Spine)

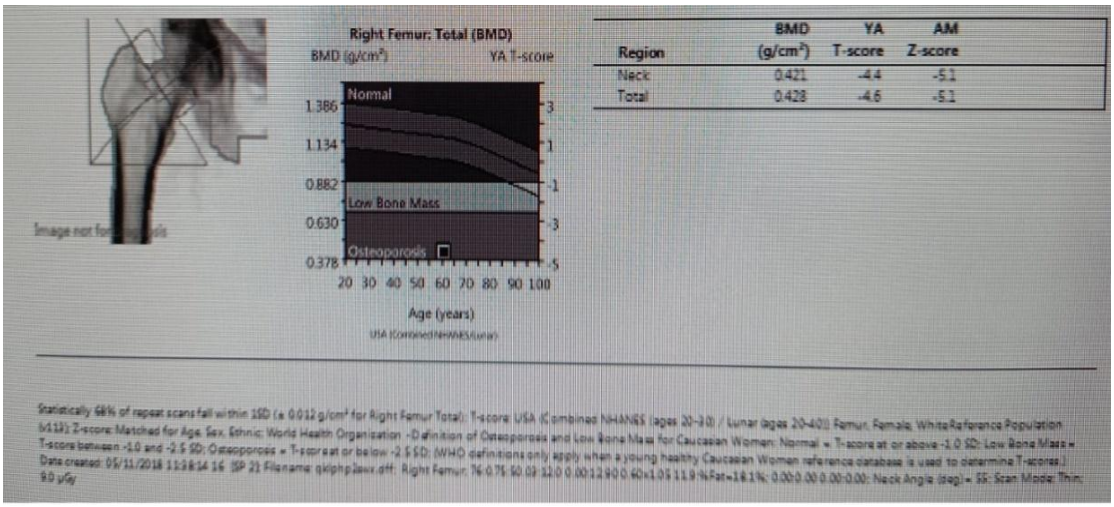

Fig. 2 (Dexa scan on Right Femur)

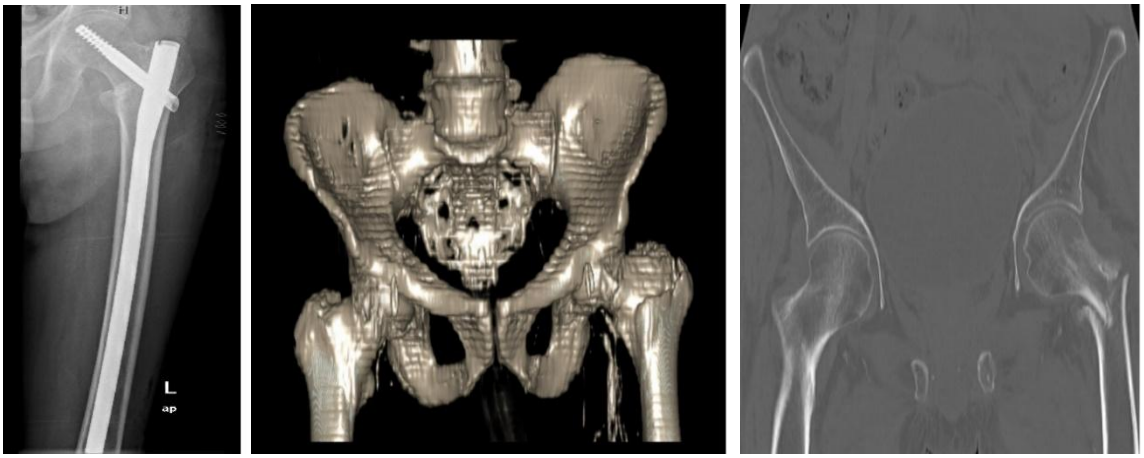

Fig. 3. (Fracture left femur)

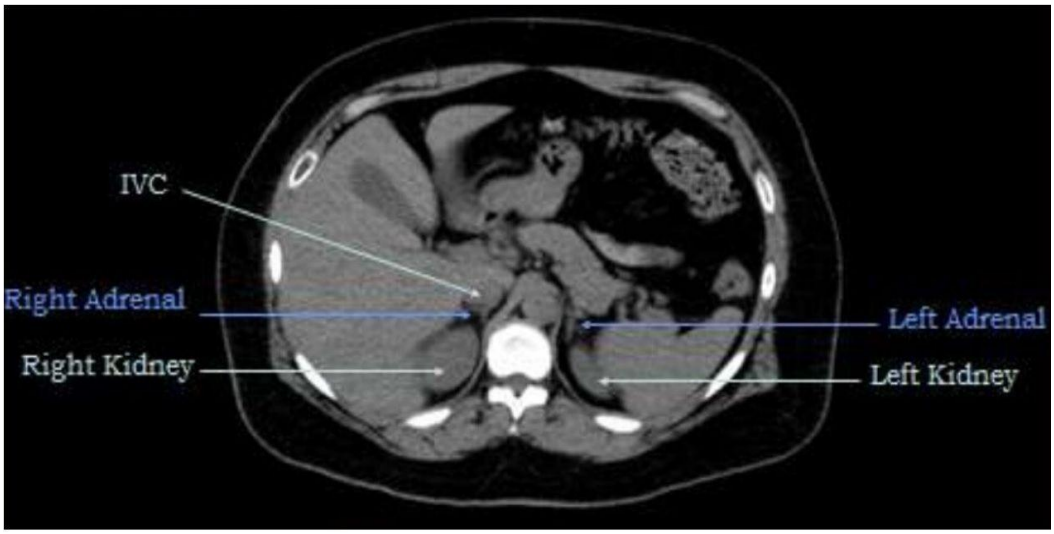

Fig. 4. (Normal CT abdomen)

5. DISCUSSION

The coexistence of at least two or more endocrinological diseases in an individual is given the name of APS or Autoimmune Polyglandular Syndrome Type II [5].

Before the advent of this syndrome, it was recognized through different names. It was called Schmidt Syndrome by Schmidt in 1926 who published two case studies regarding patients who were simultaneously suffering from Addison's disease as well as Chronic Lymphocytic Thyroiditis at the same time [6].

Later on, it was renamed as the 'Carpenter Syndrome', which now consisted of a triad of diseases, namely Addison's disease, Autoimmune Thyroid Disease, and Type I Diabetes Mellitus.

The prevalence of APS Type II has been found to be between 1.4 to 2.0 per 100,000. It was also noted that this disease was more prevalent in the United States as compared to European countries [7].

Women were more affected than men. The presence of at least 2 out of the total 3 diseases of the Carpenter's triad must be present for a person to get labeled as suffering from APS Type II.

The symptoms are usually non-specific and vary from patient to patient. In the initial stages of the disease, the patient might present with a fluctuating picture.

However, some of the major symptoms that are found to occur in this disease include profound or chronic fatigue or weakness, darkening of the skin creases and the buccal mucosa, vitiligo, and other pigmentation-related signs.

Since the earliest presentation is that of Addison's disease, therefore, for diagnosis, a systematic course should have opted too. The primary test is the cosyntropin test which is highly specific and sensitive [8].

Hypoglycemia, hyponatremia may also be present but late. Women may suffer from ovulatory disorders and amenorrhea. The disease keeps on fluctuating its course and also varies in intensity from being manageable in the beginning to progressing eventually towards complications in the latter course [9].

Later on, thyroid function testing and diabetes tests should be carried out to separate which disease it is that is causing the other symptoms in addition to Addison's Disease in the patient.

As far as the management plan is concerned, it is highly dependent on how severe or serious the condition of the patient is when they are brought to the hospital.

The earliest and the most suitable course of action is to correct the underlying electrolyte imbalances and fluid disturbances or pH disturbances if any, for if they are left untreated, they could end up worsening the condition of the patient even more.

IV fluids, IV hydrocortisone, dexamethasone, etc. are some of the popularly used medications for this problem [10]

6. CONCLUSION

The Autoimmune Polyglandular Syndrome Type II is a rather uncommon and therefore, less commonly understood condition that occurs in a smaller number of patients.

However, when it occurs, it is often mistaken to be some other disease and so, the correct diagnosis and then, later on, the appropriate management plan takes longer than necessary to be brought into action, leaving space for complications to ensue in the meantime.

However, with prompt management and patient education regarding the factors that they are supposed to avoid or take care of, this condition could easily be kept at bay and at its minimal course.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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