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Polyendocrine deficiency as a diagnostic challenge - A retrospective clinical study

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ABSTRACT

Polyglandular polyendocrine syndromes (PSs) are an assorted collection of infrequent ailments considered by autoimmune motion contrary to more than one endocrine organ, though non-endocrine organs can be affected. The deficiency of parathyroid is quite rare without surgery. This article summarises clinical, epidemiological, and serological, data of patients with PSs. Multifaceted diagnostic difficulties and treatment choices required that the patient be admitted to the hospital for a rather long period, namely for six weeks. Three diabetic patients with various thyroid disorders such as lymphocytic thyroiditis involving parathyroid glands manifesting with severe hypothyroid and hypo-parathyroid status were studied with an occurrence of dengue viral aetiology as a precipitating factor. Further, the patients were investigated for the determination of antibodies against thyroglobulin and microsomal antigens by chemiluminescent microparticle immunoassay. They were also tested for Parathyroid Hormone and 25-hydroxy vitamin D. After three months, all the three hormonal status were brought to normal with substitution and maintenance therapy, and patients were reviewed after six months were found to maintain with the dose. To conclude, thyroiditis may progress during the progression of dengue fever and should be counted as a manifestation of expanded dengue syndrome.

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INTRODUCTION

Deficiency of any one of the endocrine gland in the body without any obvious aetiology is a diagnostic challenge. The heterogeneous cluster of uncommon conditions identified by more than one endocrine organ is a poly-endocrine deficiency; it can even involve non-endocrine organs in specific instances (Betterle and Zanchetta, 2003). It is characterised into two discrete ailments, based on the foreword of Polyendocrine deficiency syndrome (Cutolo, 2014). The first one described the consequence of the primary adrenal insufficiency

hypoparathyroidism. The second is the occurrence of thyroid deficiency, primary adrenal insufficiency and insulin-dependent diabetes mellitus at an older age level (Lindh *et al.*, 2013). Hypothyroidism, particularly its subclinical form, is most frequently occurring endocrinopathies (Ee *et al.*, 2016). In this situation, encountering patients with multiple endocrine deficiencies, trying to find out the exact aetiology which precipitated the case, to manage these patients and to achieve disease control is the real challenge (Kleerekoper *et al.*, 1974). It distresses women 7-10 times more often than men, and its degree upsurges with age. In post-menopausal women, the treatment of hypothyroidism will be determined by numerous circumstances: the existence of symptoms, rigorousness of hypothyroidism, simultaneous risks, and patient's age. In obvious hypothyroidism, dealing with L-thyroxine is continuously recommended (Wilkins and Lewis, 2009).

Infection must be considered as one of the factors that could cause a parathyroid problem, for instance, dengue virus infection. Dengue fever is generally a rare condition that may induce or worsen illnesses or thyroid disorders (Beall and Solomon, 1973). Just two cases of dengue fever were recorded in Pakistan in 2012 and India in 2013 in the presence of thyroiditis (Singh *et al.*, 2018). The clinician reports on the case to increase consciousness, and to spread information on what causes are causing and how to handle a case of polyendocrine disorder during viral aetiology. We report a retro prospective study on polyendocrine deficiency with dengue syndrome (Obermayer-Straub *et al.*, 2000).

The way and rare suspicion of other endocrine deficiency like parathyroid, which is closely situated with thyroid and also associated with diabetic islets cells deficiency manifesting are sometimes challenging and worth publishing.

MATERIALS AND METHODS

A prospective study was done over three patients with thyroid disorders. Informed consent was obtained in all cases, and the institutional Ethical Committee permitted the proposed work. All cases included in this study were followed up to 6 months, and the tests were repeated. For these examinations, the blood was obtained in collecting tubes, and centrifugation removed the cells from the serum. The investigation took place within 24 hours of the processing of the sample.

Estimation of Microsomal Antibody

Chemiluminescent microparticle immunoassay was adapted to estimate the amount of TPO antibody.

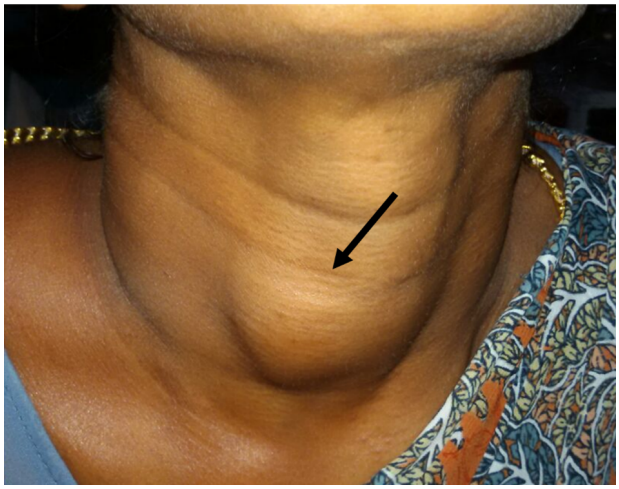

Figure 1: Patient with a thyromegaly indicated with the arrow

The experiment was performed according to the kit's instructions provided. The test was repeated after a six months interval.

Detection of Thyroglobulin Antibody (ATG) in Serum

Estimation of Thyroglobulin Antibody performed in serum with a fully automated 2-step immune-chemiluminometric assay (ATGICMA) with the use of monoclonal antibodies.

Detection of Parathyroid Hormone in serum

Intact PTH has been demonstrated to be labile and is susceptible to fragmentation. It's detected with the help of CMIA, according to the kit instruction and compared with the biological reference.

Quantification of 25-hydroxy vitamin D

The 25-OH vitamin D direct competitive chemiluminescence immunoassay kit was adapted for the quantitative measurement of the total 25-OH vitamin in human serum.

RESULTS AND CASE PRESENTATION

Sixty years aged multiparous myedema known diabetic with diffused thyromegaly well maintained with thyroid substitution, clinically diagnosed as colloid goitres (Figure 1). On further evaluation, the results were found to be positive for Hashimoto's lymphocytic thyroiditis that patient presenting with fever, giddiness, and joint pain. Being a person with diabetes, first suspected to be hyperglycemia, sweating and fever. The evaluation found to be abnormal sugar treated adequately for the same. Simultaneous evaluation for fever and joint pain focussing on dengue, presentation of tetani, and estimation of calcium and phosphorous revealed with dengue pos-

Table 1: Comparison of autoantibodies and PTH, Vit D in patients with thyroid disorders(before and after treatment)

Patient ID	Microsomal (TPO) Antibody Titer, Serum (IU/mL) Detected Value		Thyroglobulin Antibody (ATG), Serum(IU/mL) Detected Value	
	Before Treatment	After Treatment	Before Treatment	After Treatment
No 1.	219.53	68.24	881.83	148.80
No.2	235.16	72.48	753.13	106.20
No 3.	306.48	85.31	828.56	102.32

Table 2: Comparison of autoantibodies and PTH, Vit D in patients with thyroid disorders (before and after treatment)

Patient ID	PTH-(Intact Molecule) (Serum, CMIA)pg/mL Detected Value		25 Hydroxy (OH) Vit D ng/mL (Serum, CLIA) Detected Value	
	Before Treatment	After Treatment	Before Treatment	After Treatment
No 1.	3	9.8	3	9.8
No.2	3.8	10.2	3.8	10.2
No 3.	3.2	10.6	3.2	10.6

itive and hypocalcaemia which prompted the diagnosis of viral aetiology with a hyper parathyroid stage. Since calcium, phosphorous is very low, and the patient is further evaluated with parathormone and vitamin-D, which was significantly low (Table 1, Table 2). Finally confirming these three deficiency statuses manifesting simultaneously due precautions and precise monitoring of all the deficiency of endocrine thyroid, parathyroid and diabetic status corrected. Repeat FNAC of thyroid gland condition showed only lymphocytic thyroiditis parathyroid could not be localised for biopsy. Substitution correction for parathyroid took longer time with calcitonin, nasal spray and oral Vit-D3. After three months, all the three hormonal status were brought to normal with substitution and maintenance therapy, and patients were reviewed after six months found to maintain with the dose which they have to substitute for a lifetime. CT neck and image-guided FNAC of thyroid swelling again revealed the same lymphocytic thyroiditis possibly of viral aetiology. Steroids used in the review of continued status only on two occasions during the crisis.

DISCUSSION

Parathyroid deficiency without any surgical procedure is very rare. And we have come across 3 cases, one due to viral aetiology affecting the patient and other lymphocytic thyroiditis involving parathyroid glands also manifesting with severe hypothyroid and hypo-parathyroid status all the three in diabetic patients in women (Sasso *et al.*, 2003). The cause of which unknown for the bias of female gender and this diabetic status are insulin-dependent and chronic. The patient who presented with fever, joint pain, and giddiness during evaluation revealed dengue positive and clinical examination revealed hypo-parathyroid state which is of tetani prompting us to think of parathyroid (Császár and Patakfalvi, 1992). A further biochemical assessment revealed that hypocalcaemia profound low parathyroid level, and low Vit-D3 grossly elevated TSH, hypothyroid status aggravated by dengue manifestation (Manns and Strassburg, 2001). All three patients showed an elevated level of microsomal antibodies. As the antibodies in patients in serum differ, at least two samples, one with thyroglobulin and one with the microsomal antigen (thyroid peroxidase), are usually expected to be integrated (Wege *et al.*, 2020). Our results indicated that in patients have anti microsomal antibodies (thyroid peroxidase) while thyroglobulin antibodies also observed in all the three cases (Kirino *et al.*, 2020). These findings are in line with the results published previously, which are found in these cases, 80 per cent thyroid peroxidase microsomal antibodies to be effective (Gutch *et al.*, 2014). All three patients managed considerately with replacement therapy and insulin. The diabetic status also controlled, the severity of hypothyroid stage, destruction of parathyroid could not be explained since FNAC of the parathyroid showed severe lymphocytic infiltration, electrolytes and cal-

cium estimation was periodically done during the recovery phase and the treatment phase. Patients have recovered by prompt recognition and appropriate substitution and replacement therapy of the three hormonal status.

CONCLUSION

In conclusion, the cases stated in this article was tough to approach since it required the degree of difference in diagnosis of polyendocrine deficiency in severely ill patients, with manifold organ glitches. In our day-to-day medical practice, this pathological association increases important diagnosis difficulties, typically since the others can conceal the symptomatology of each of these diseases. As a concern, treatment choices are problematic to take and put into practice.

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Conflict of interest

Authors do not have any conflict of interest.

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