The hypo-hyper syndrome

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The coexistence of thyroid and parathyroid diseases is not rare. In the review of the recent literature, 25% of the patients with primary hyperparathyroidism (PHPT) had significant associated thyroid diseases including carcinoma in an Australian series.[1] Regal et al,[2] reported a high prevalence of unsuspected varieties of thyroid disease occurring mainly in postmenopausal women in patients with PHPT in another series from Spain.[2] Reciprocally, parathyroid pathology has been described in patients with primary thyroid disease. Sinaesi et al,[3] carried out the results of a recent Italian series of 221 thyroidectomies showed that 29 patients (13%) had a preoperative subclinical PHPT out of which 19 turned out to be due to parathyroid adenoma or hyperplasia.[3] In this communication, we described a rare association of hypothyroidism as part of a polyglandular autoimmune syndrome (PAS) in a patient who in addition, found to have asymptomatic PHPT.

A 56-year-old Omani female and a mother of 10 children was attending the medical clinic for last few years for hypertension and hyperlipidemia. She was noticed to have developed several patches of vitiligo and had also complained of alopecia. She required a combination of atenolol, amlodipine, prazosin, indapamide, and losartan to control her hypertension. The patient had a hysterectomy in 1997, and a laparoscopic cholecystectomy in 2002. At a later point, she began to complain of bilateral pain and tingling in both hands, which turned out to be due to the carpal tunnel syndrome (CTS). Positive nerve conduction studies confirmed the diagnosis. That finding prompted further investigations for a possible underlying thyroid disease. Her serum free thyroxine (FT4) was low (6.07 pmol/l; normal = 9-19) with a high level of thyroid-stimulating hormone (TSH) (7.02 uIU/ml, normal = 0.35-4.94) and markedly elevated thyroid antibodies (antithyroglobulin levels of 546 U/ml, normal = 0-15 and anti-peroxidase antibodies levels of 350 U/l, normal = 0-32) were consistent with hypothyroidism due to autoimmune thyroid disease. Other investigations including the hemogram, blood chemistry, other endocrine workup, electrocardiogram, and relevant radiography were initially within normal limits or values. Serum B12 and folate were also within normal ranges. According to Betterle et al[4] classification, the diagnosis of PAS type 3 on the basis of hypothyroidism secondary to autoimmune thyroiditis, vitiligo, and alopecia areata. There was no family history of similar illness. Antibodies for liver kidney microsomal, adrenal gland, gastric parietal cell, intrinsic factor, and acetylcholine receptor antibodies were negative. Facilities for tyrosinase and tyrosine hydroxylase antibodies were not available to our laboratory. The human leukocyte antigen typing revealed A2, A26, B8, B18, DR (17) 3, DR 52, and DQ 2. This haplotype is different from those commonly associated with type 1 PAS (A3 and A28) or type 2 (DR3/DQB1 or DR4/DQB1).[4] We gradually commenced the L-thyroxine in increasing doses with noticeable improvement of the CTS symptoms on subsequent visits. We also achieved good suppression of TSH and normalization of serum thyroxine.

In further follow-up, we discovered that she has asymptomatic hypercalcemia due to PHPT following repeated routine assays of serum calcium and phosphorous. The calcium reached 12.7 and 12.9 mg/dl (normal = 8.5-10.5) along with marginally reduced level of phosphorous of 2.2 mg/dl (normal = 2.5-4 mg/dl) and repeatedly, markedly raised serum parathyroid hormone of 293 and 312 pg/ml (normal = 11-62 pg/ml). The urinary calcium excretion was 285 mg/day (normal = 100-300 mg/day). The radioisotope scan of the parathyroid glands (Tc 99m-sestamibi), and neck ultrasound examination both confirmed the presence of right inferior parathyroid adenoma. The clinical setting of hyperparathyroid adenoma in a hypertensive patient warranted further work-up to exclude multiple endocrine neoplasia (MEN) syndrome type I or type II A. Assays for serum prolactin, follicle stimulating hormone, luteinizing hormone, insulin, growth hormone, insulin-like growth factor, cortisol, adrenocorticotropic hormone, calcitonin, and 24 hours urine for vanillylmandelic acid (VMA) were within normal values. Serum gastrin was moderately elevated at 67 pmol (normal = 0-43); but not sufficiently high to diagnose pancreatic gastrinoma. Nonetheless, the Indium 111-Octreotide scan was negative for neuroendocrine tumor in pancreas or elsewhere in the abdominal cavity. The findings of the pituitary CT were negative for pituitary tumor and the iodine-131 metaiodobenzylguanidine (MIBG) scans were negative for pheochromocytoma. Subsequently, she underwent successful excision of the parathyroid adenoma resulting in normalization of her serum calcium and phosphorous. The histopathology confirmed a well capsulated parathyroid adenoma with a wedge thyroid tissue showing focal lymphocytic thyroiditis. Polyglandular autoimmune syndrome 3 has been classified into 3 subcategories A, B and C. The latter is characterized by autoimmune thyroiditis with vitiligo and alopecia, or both and other organ

specific disease excluding Addison's disease.[5] Obviously, the features of our patient were consistent with this subcategory. The PAS 3 is also known to be associated with other organ-specific and non-specific disorders such as sarcoidosis, celiac disease, myasthenia gravis, rheumatoid arthritis, and Sjogren's syndrome. An associated gastric carcinoid syndrome was also reported. Autoimmunity, environmental, and genetic factors are the 3 major components of the pathophysiology of PAS. The presence of circulating organ-specific and cellular autoimmunity in patients with PAS 3 provides the strong evidence for the autoimmune pathogenesis of the disorder. Environmental precipitator/s such as viral infection, for example may exaggerate an ongoing immune response and precipitate glandular failure. In this regard, the links between congenital rubella infection and type 1 diabetes mellitus, and hypothyroidism is well known. Polyglandular autoimmune syndrome is often observed in subjects of the same family and suggested an autosomal dominant trait with variable penetrance. Certain genetic markers have been found to confer susceptibility to PAS 3, and the frequently described haplotypes include DR-B*04/ DQA 1*0301/DQB1*0302, HLA-DR B1*13, DRB1*1104, and DRB1*0401.[5] A significantly higher frequency of DR3 and DR4 antigens were also detected in patients with PAS 2 and 3 compared with controls in a recent study. Our patient exhibited A26, B8 and DR3 on tissue typing. It is of interest to note that the combination of A26 and B8 has recently been found to be an autoimmune favoring haplotype in Indians.

Evidently, this is an interesting combination of glandular hypo and hyper-function producing constellation of features of PAS type 3, and PHPT in the same patient. Although, the latter was the only apparent manifestation of the endocrine hyper-function, the patient was adequately investigated for a possibility of an associating or evolving MEN syndrome. However, a regular monitoring of the initially elevated serum gastrin would certainly remain imperative in the future management. Unfortunately, the patient lost to follow-up in the last 6 months, and relatives refused to be evaluated. Finally, the association of MEN and PAS is rarely reported in the English literature. We only managed to trace a single case report in which PAS was characterized by mucocutaneous candidiasis, vitiligo and macroglossia, and occurred together with Cushing's disease and PHPT (MEN type I).

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Actinomyces meyeri isolation from synovial fluid of a patient with metastatic squamous cell lung carcinoma

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The genus actinomycetes consists of several species of gram-positive, non-spore forming bacteria, which grow as obligate or facultative anaerobes. *Actinomyces* organisms are important constituents of the normal flora of mucous membranes. These organisms may produce infection after local trauma, surgery, or aspiration. The main forms of actinomycosis are cervicofacial, thoracic, and abdominal; most cases are due to *Actinomyces israelii,* whereas Garduno et al[1] report occasional implication of other *Actinomyces species*.

We rarely isolate *Actinomyces meyeri* (*A. meyeri*) in cases of actinomycosis. However, an increasing number of cases recognize its potential pathogenicity. In contrast to other species of *Actinomyces, A. meyeri* often causes pulmonary infection and shows a tendency for hematogenous dissemination. Involvement can include any organ of the human body so that a wide range of symptoms may be present. Although, multiple organs are involved, the outcome for these patients is excellent when we administer penicillin for several months and perform surgical procedures when necessary. As actinomycetes are rarely opportunistic agents in immunocompromised patients, the disease deserves special attention in those patients.[2] Here, we report a case of actinomycosis with an uncommon localization that was due to *A. meyeri* in a patient with metastatic squamous cell lung carcinoma.