A Rare Case of Autoimmune Polyglandular Syndrome (APS) Type 3

[1]Fariha Zerin, [1]Md. Sunny Anam Chowdhury, [1]Md. Nazmul Hossain, [1]Sujon Mahmud, [1]Yeasmin Akter, [1]Bahalul Hasan, [2]Tanvir Ahmad

[1]Institute of Nuclear Medicine & Allied Sciences (INMAS), Kushtia
[2]Medical Officer, National Heart Foundation Hospital & Research Institute

Correspondence Address : Dr. Fariha Zerin, Medical Officer, INMAS, Kushtia, Kushtia Medical College & Hospital Campus, Kushtia
Email: farihazerinpinki@gmail.com Contact: 01721255616

ABSTRACT

Background: Autoimmune Polyglandular Syndrome Type 3 is a rare condition where patients are diagnosed with more than one autoimmune disease having similarity in pathogenesis. Antibody detection with various imaging modalities, including nuclear medicine techniques, is crucial to confirm the diseases.

Case Report: A 61-year-old elderly postmenopausal woman presented with vitiligo, features of hypothyroidism and systemic lupus erythematosus (SLE). After proper clinical evaluation, the anti-TPO antibody report came out positive, and a cold nodule was found in thyroid scintigraphy, thus confirming the diagnosis of autoimmune thyroiditis.

Conclusion: Autoimmune thyroiditis associated with vitiligo is more common in female individuals under APS Type 3, so screening is recommended for clinically manifested pathology.

Keywords: Autoimmune thyroiditis, Vitiligo, APS Type 3, Scintigraphy

Bangladesh J. Nucl. Med. Vol. 28 No. 1 January 2025

DOI: https://doi.org/10.3329/bjnm.v28i1.79554

INTRODUCTION

Autoimmune Polyglandular Syndrome (APS) is a spectrum of diseases involving autoimmune invasion and destruction of two or more endocrine glands. Autoimmune inflammation leading to dysfunction of non-endocrine systems is also included in subtypes of APS. Among the four subtypes of APS, Type 3 is the commonest one, with a wide variety of organs being related (1).

Vitiligo is a dermatological condition of gradual discoloration of skin, hair, and oral mucosa characterized by autoimmune destruction of melanocytes in the epidermis, affecting 1-2% of the population worldwide (2). It can affect any age group and variable ethnicities. Unilateral distribution of macules is common in segmental vitiligo (SV) compared to non-segmental vitiligo (NSV), which exhibits bilateral symmetrical depigmented patches (3).

Among all the causes of primary hypothyroidism with autoimmune origin, Hashimoto's Thyroiditis is the most significant one where chronic lymphocytic destruction of the thyroid gland occurs. Consecutive studies showed a strong association between vitiligo and chronic autoimmune thyroid disorders, specifically Hashimoto's' thyroiditis, as both diseases share some similar pathophysiological pathways, thus falling under Autoimmune Polyglandular Syndrome Type 3 (2, 4).

Apart from hormone profile and high-resolution ultrasonography of the thyroid gland, evaluation of anti-thyroid peroxidase antibody (anti-TPO ab) titer with 99mTc pertechnetate Thyroid scintigraphy can play a valuable role in the detection of Hashimoto's thyroiditis. Thyroid scan generally shows heterogeneous patchy radionuclide uptake, though in rare cases unilateral uptake mimicking a nodule can also be observed (5). The overall knowledge regarding the association between diseases, their immunological basis of pathogenesis, and correlating with investigations aids in avoiding any dilemma and prompt confirmation of diagnosis.

CASE REPORT

A post-menopausal woman of 61 years, visited thyroid clinic and scintigraphy division of Institute of Nuclear Medicine and Allied Sciences (INMAS), Kushtia with the complaints of weight gain, fatigue, occasional constipation and feeling of unwell being. Previous medical history revealed hypothyroidism for 1 year and vitiligo for 10 years. She was on Levothyroxine 50 mcg orally. Recently she noticed recurrent oral ulcerations and severe pain and stiffness in multiple small joints, which persisted after waking up and improved after daily

activities. Sunlight exposure caused facial redness and flushing. Patient was normotensive, non-diabetic, had no history of surgery, trauma or radiation exposure. Her family history was unremarkable as well.

Physical examination revealed anemia. There were universal depigmented patches covering her face, trunk, and extremities with symmetrical hyperpigmented areas around both eyes and temporal regions alongside several hyperpigmented patches over her forearms (Figure 1). The patches were painless and non-blanching. No remarkable joint swelling or deformity was observed. Thyroid gland appeared normal during palpation. Per abdominal examination revealed no abnormalities. Previous Thyroid hormone profile revealed high TSH (9.69 uIU/mL) and Low FT4 level, corresponding primary hypothyroidism. Laboratory investigations showed decreased Hb% (10 g/dL) with low MCV and MCH, suggesting microcytic hypochromic anemia with raised ESR (22 mm in 1st hour). Anti-Nuclear antibody and Anti Ds DNA antibody reports were positive.

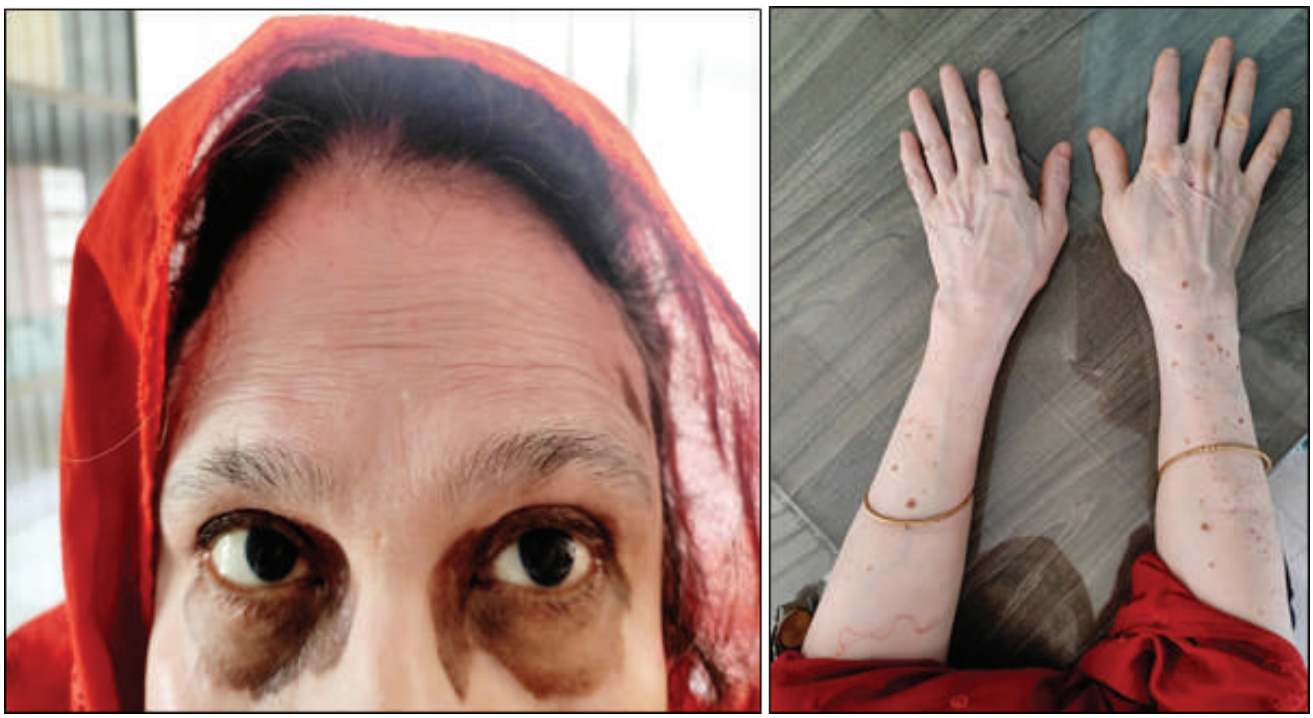

Figure 1: Image of a 61-year-old woman having diffuse depigmentation of the face and forearms with hyperpigmented macules and patches scattered. Patient was diagnosed with Autoimmune Polyglandular Syndrome Type 3

High resolution ultrasound (HRUS) of thyroid gland revealed decreased vascularity and a mixed echoic (having solid and cystic components) nodule with internal macrocalcifications (TIRADS-3) located in between isthmus and lower pole of left lobe of thyroid gland measuring about 21.5 X 10.2 mm (Figure 2). Thyroid scan with 99mTc-pertechnetate reported focal area of reduced radioisotope accumulation near isthmus suggesting a cold nodule (Figure 3).

Anti TPO antibody was found to be elevated (890 U/mL) from reference range, thus confirming autoimmune thyroiditis with co-existing vitiligo.

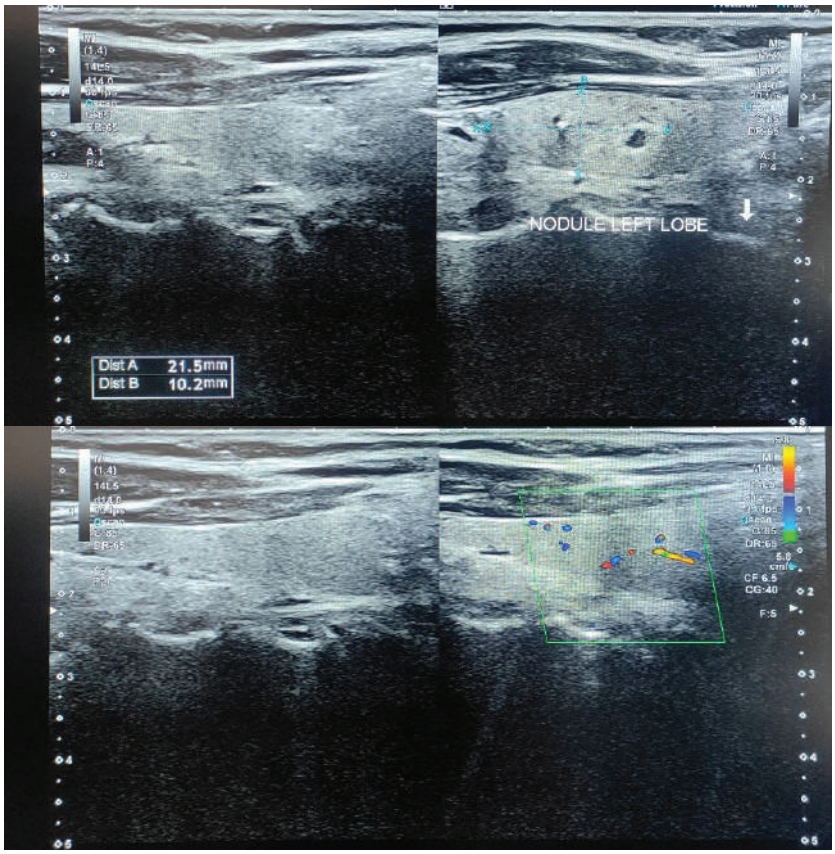

Figure 2 : HRUS image of thyroid gland showing decreased vascularity with a mixed echoic nodule in left lobe and isthmus area.

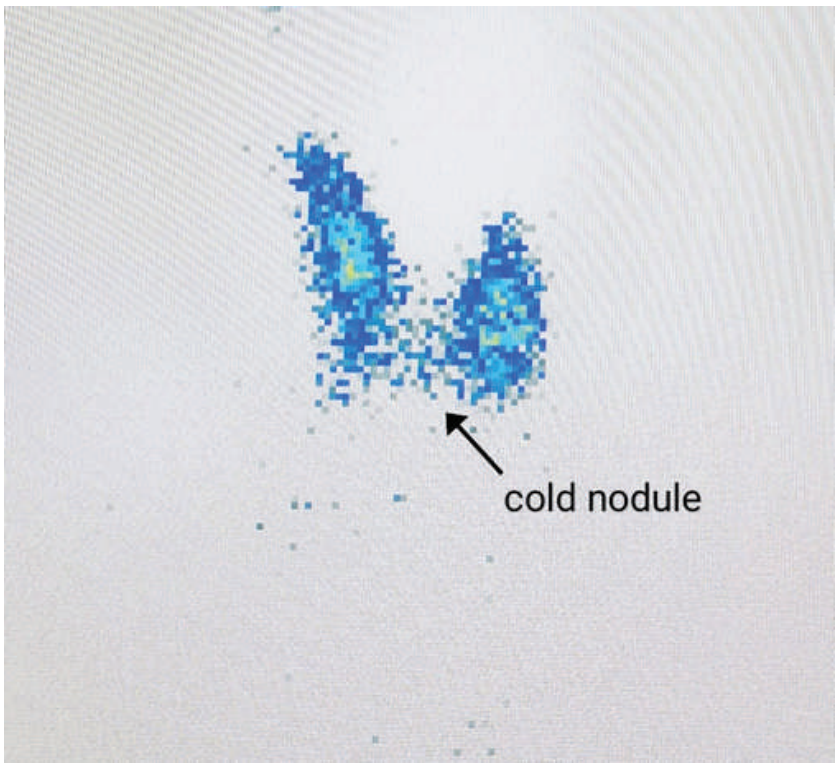

Figure 3: 99mTc Pertechnetate Thyroid Scan showing area of reduced radiotracer accumulation suggesting presence of cold nodule.

DISCUSSION

Autoimmune polyglandular syndrome was first described by Schmidt during 1926. (1) Among all the types of APS, Type 3 is the commonest one, including autoimmune thyroid disorders (Graves' disease or Hashimoto's' thyroiditis), with any of the following—vitiligo, type 1 diabetes mellitus, autoimmune thrombocytopenia, pernicious anemia, celiac disease, Sjogren's syndrome, SLE, alopecia areata, and many more. (6)

Vitiligo is an autoimmune disease characterized by progressive destruction of melanocytes, causing discoloration of skin. Disease susceptibility is carried by more than 50 genes (2,4). The most common involving site is the face, whereas hand depigmentation is highly suggestive of associated thyroid disorder. Autoimmune pathogenesis of vitiligo involves various biomarkers, staining CD4+, CD8+ T lymphocytes as key activators of melanocytes, as well as interleukins, interferon gamma, reactive oxygen species (ROS), and TGF-beta with human leukocyte antigen (HLA) association. The pathogenesis of Hashimoto's Thyroiditis also revolves around CD4+, CD8+ T cell, and antibody-mediated thyrocyte destruction with HLA predisposition (4, 7).

Higher prevalence of vitiligo with autoimmune Hashimoto's Thyroiditis was observed among female patients, having 34% positive thyroid autoantibodies. Atrophic autoimmune myxedema was also found in elderly patients with reduction of size of the gland. Non-segmental vitiligo is more frequent with higher anti-thyroid peroxidase antibody (TPOAb) titers. The diseases share common pathogenesis, such as oxidative stress-induced destruction of melanocytes and thyrocytes, as both cells secreting melanin and thyroxine have a common precursor origin: tyrosine. Other hypotheses say mutations of Forkhead transcription factor D3 (FOX D3) are linked to positive thyroid antibodies and vitiligo. (2,4)

Reported case was previously diagnosed with vitiligo alongside symptoms and biochemical findings suggestive of hypothyroidism, so it was important to detect and rule out other autoimmune pathologies under the spectrum of autoimmune polyglandular syndrome, especially Hashimoto's Thyroiditis.

Thyroid scan with 99mTc-Pertechnetate and anti-TPO antibody play important roles in diagnosing chronic autoimmune thyroiditis in long-standing disease where typical USG features of Hashimoto's thyroiditis are less seen. Scintigraphic finding is highly variable, frequently showing decreased radiotracer uptake, a heterogeneous pattern with both cold and hot areas, or unilateral uptake mimicking a single toxic nodule (6, 8). In our patient we found a focal area of decreased radioisotope accumulation indicating the presence of a hypofunctioning cold nodule.

Our patient had been experiencing gradual skin discoloration for a decade. The acral-facial skin involvement of vitiligo, mostly upper extremities, imposed a strong association with a positive anti-TPO antibody titer, thus confirming the diagnosis (7). As ANA or anti-dsDNA antibody was positive, the patient was subsequently suffering from SLE. Thus, we classified this case under the subtypes of autoimmune polyglandular syndrome. Alongside these, nuclear medicine techniques, including thyroid uptake and scintigraphy, can also play a crucial role in establishing thyroid pathology in autoimmune conditions (9).

CONCLUSION

The case underscores the need for comprehensive evaluation of autoimmune diseases in patients with thyroid disorder and vitiligo, emphasizing the importance of a proactive approach to identify potential autoimmune disorders and manage them effectively. Autoimmune Thyroiditis with Vitiligo is prevalent in women under APS Type 3, necessitating screening and antibody detection through imaging modalities, including nuclear medicine techniques.

CONFLICTS OF INTEREST

Authors have no conflicts of interest regarding this case report. All images were used with informed consent of the patient and these images are not for distribution in the electronic media for further use.

REFERENCES

1. Sun Y, Kan X, Zheng R, Hao L, Mao Z, Jia Y. Hashimoto's thyroiditis, vitiligo, anemia, pituitary hyperplasia, and lupus nephritis—A case report of autoimmune polyglandular syndrome type III C+ D and literature review. Frontiers in Pediatrics. 2023 Mar 29;11:1062505. doi: 10.3389/fped.2023.1062505
2. Chivu AM, Bălășescu E, Pandia LD, Nedelcu RI, Brînzea A, Turcu G, Antohe M, Ion DA. Vitiligo—Thyroid Disease Association: When, in Whom, and Why Should It Be Suspected? A Systematic Review. Journal of Personalized Medicine. 2022 Dec;12(12):2048.
3. Baldini E, Odorisio T, Sorrenti S, Catania A, Tartaglia F, Carbotta G, Pironi D, Rendina R, D'Armiento E, Persechino S, Ulisse S. Vitiligo and autoimmune thyroid disorders. Frontiers in endocrinology. 2017 Oct 27;8:290.
4. Sandru F, Carsote M, Albu SE, Dumitrascu MC, Valea A. Vitiligo and chronic autoimmune thyroiditis. Journal of Medicine and Life. 2021 Mar;14(2):127.
5. Zengi A, Karadeniz M, Demirpolat G, Akgun A, Karakose S, Yilmaz C. Hypothyroid Hashimoto's thyroiditis with scintigraphic and color flow Doppler sonography features mimicking a hot nodule. Internal Medicine. 2009;48(4):231-4.
6. Kahaly GJ. Polyglandular autoimmune syndromes. European journal of endocrinology. 2009 Jul;161(1):11-20.
7. Dourmishev L, Pozharashka J, Miteva L. Probable multiple autoimmune syndrome in a patient with vitiligo, autoimmune thyroiditis, and diabetes mellitus: A case report. Journal of Skin and Stem Cell. 2019 Dec 31;6(4).
8. Yarman S, Mudun A, Alagol F, Tanakol R, Azizlerli H, Oguz H, Cantez S. Scinitigraphic varieties in Hashimoto's thyroditis and comparison with ultrasonography. Nuclear medicine communications. 1997 Oct 1;18(10):951-6.
9. Ovčariček PP, Görges R, Giovanella L. Autoimmune thyroid diseases. InSeminars in nuclear medicine 2024 Mar 1 (Vol. 54, No. 2, pp. 219-236).