European Journal of Clinical Pharmacy
Print ISSN: 2385-409X **Online ISSN**: 3105-0409
Website: https://farmclin.com/

Case Report

Unmasking Schmidt Syndrome: A Hidden Threat in Rural Pakistan" -A Case Report

Article History:

Name of Author:
Fawad Khalid[1*], Irshad Ali[2], Javairia Riaz Masood[3], Attiq Ur Rehman[4] and Muhammad Kashif Habib[5]

Affiliation: *[1]Resident Physician, Saidu Group of Teaching Hospital Swat, Pakistan*
[2]Redesignated Assistant Professor Medicine, Saidu Group of Teaching Hospital Swat Pakistan
[3]Resident surgeon (Surgical A), Saidu Group of Teaching Hospitals, Swat, Pakistan
[4]MBBS, Saidu Medical College, Mingora Swat, Pakistan
[5]Resident Physician, Saidu Group of Hospital Teaching Swat, Pakistan.
Corresponding Author:
Fawad Khalid
(fawadkhalid004@gmail.com)

Received: 28-12-2025
Revised: *18*-01-2026
Accepted: 05-02-2026
Published: 20-02-2026

Abstract: Autoimmune polyendocrine syndrome type 2 (APS-2, Schmidt syndrome) is defined by the combination of autoimmune Addison's disease and autoimmune thyroiditis. A 45-year-old woman from rural Pakistan presented with fatigue, substantial weight loss, generalized hyperpigmentation, and orthostatic hypotension. Laboratory evaluation revealed hyponatremia, hyperkalemia, low morning cortisol with elevated ACTH, and high TSH with low free T4, confirming autoimmune Addison's disease and primary hypothyroidism. She received glucocorticoid/ mineralocorticoid replacement and levothyroxine, leading to rapid clinical improvement and full symptom resolution. This case underscores the critical need for early recognition of APS-2 in resource-limited settings, as delayed diagnosis of adrenal insufficiency can be life-threatening. There is a very little literature related to Schmidt syndrome we hope this case report can add to research world. Words count: 902 words (Not including Title page, Abstract and references) Source of funding; None Conflict of interest: The corresponding author affirm that there is no conflict of interest on behalf of the author

Keywords Addison's disease; autoimmune; autoimmune hypothyroidism; Schmidt's syndrome; type 1 diabetes.

INTRODUCTION

Autoimmune poly endocrine syndrome type 2, also known as Schmidt syndrome, is a rare polygenetic disorder characterized by primary adrenal insufficiency (Addison disease) along with autoimmune thyroid disease or type 1 diabetes mellitus. By definition, APS 2 requires at least two of these components, commonly adrenal insufficiency along with hypothyroidism(6) The syndrome is life-threatening if not diagnosed and treated early due to the risk of adrenal crisis. Epidemiologically, Schmidt syndrome affects adults at their peak (30-50 years) and is 3 to 4 times more frequent in women. The reported prevalence is on the order of 1 to 4 per 100,000, reflecting its rarity.(1)

The pathophysiology involves autoimmune lymphocytic destruction of endocrine glands. Major histocompatibility genes, especially HLA-DR3 AND DR4 haplotypes, and other autoimmune regulatory genes(CTLA-4, PTPN22, IL2RA) have been implicated in genetic susceptibility(2)

In APS-2, the adrenal cortex is infiltrated by auto-reactive lymphocytes, leading to cortisol and aldosterone insufficiency, while the thyroid gland is similarly targeted in Hashimoto thyroiditis. This leads to a combined endocrine failure.

The common presentation of Schmidt syndrome is fatigue, hypotension, gastrointestinal upset, and

hyperpigmentation (due to increased ACTH stimulating melanogenesis). Oral and mucosal hyperpigmentation of the tongue and lips is characteristic of adrenal involvement.(3)

CASE PRESENTATION

After the initial consent history was taken. Shaheen Bibi, a 45-year-old female from a rural area of Pakistan, was presented to the endocrine clinic with unintentional weight loss over the past months. She reported fatigue, anorexia, and an initial history of constipation followed by a recent episode of loose stools. The patient was hypotensive with a blood pressure of 75/40 mm of Hg and had severe tachycardia. The patient had a past medical history significant of hypothyroidism and adrenal insufficiency. Physical examination revealed generalized hyperpigmentation; a diffusely darkened(black) tongue and brown blue discoloration of the vermilion lips and palmar creases. There was no goiter or exophthalmos [Figure 1-3]

Figure 1: A 45-year-old female with diffuse yperpigmentation seen over face, mouth and lips.

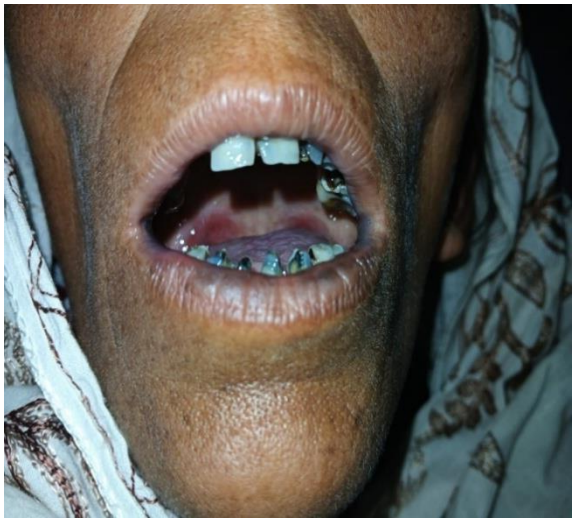

Figure 1: A diffused darkened black tongue and brown-blue discoloration of lips and teeth.

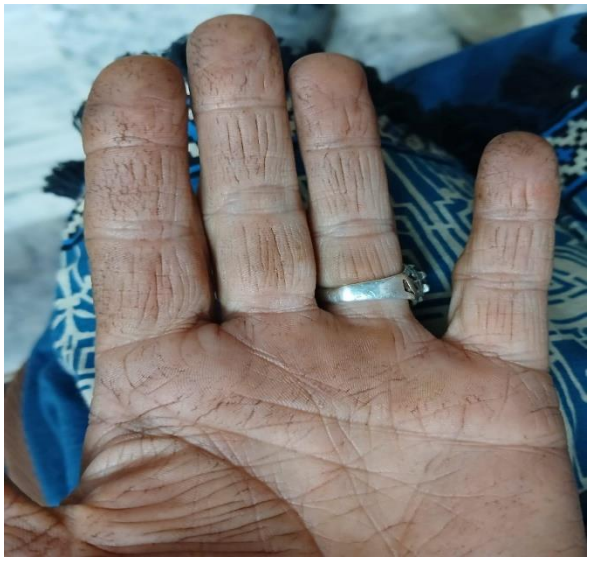

Figure 3: Accentuation of pigmentation over palmar creases.

Laboratory studies demonstrated primary hypothyroidism and adrenal insufficiency. Thyroid-stimulating hormone (TSH) was markedly elevated at 26.2mIU/L (normal 0.3-4.2), with correspondingly low free thyroxine (FT4, which was not done) consistent with long-standing Hashimoto thyroiditis. Morning serum cortisol was profoundly low (13.6nmol/L; normal 140-690), confirming primary adrenal failure. Complete blood count (CBC) report showed that inflammatory markers were modestly raised: white blood cell count was 13.14 into 10^3/uL (normal 4 – 11 × 10^3/ 10^3/uL), indicating mild leukocytosis. Erythrocyte sedimentation rate (ESR) was 40mm/ hour (elevated). No serum electrolytes were done.

Abdominal ultrasound showed normal appearing liver, spleen, kidney, and adrenals, but showed intestinal helminths (round worms) within the bowel lumen.

Taken together, these findings indicated Schmidt syndrome (APS-2). The patient had documented Hashimoto thyroiditis (from her past hypothyroidism) and now demonstrated primary adrenal insufficiency. Importantly, her adrenal imaging was unremarkable with no adrenal enlargement or calcification, supporting an autoimmune etiology. She was therefore diagnosed with Schmidt syndrome and was treated accordingly.

The patient was initially treated with hydrocortisone to reverse adrenal crisis along with levothyroxine tablets for the management of hypothyroidism. These were found to have a good effect on the overall health of the patients and also improved the patient condition.

DISCUSSION

This case illustrates classic laboratory and clinical hallmarks of Schmidt syndrome. The markedly elevated TSH and low FT4 confirm primary hypothyroidism, while an extremely low cortisol level establishes Addison's disease. The co-existence of these two autoimmune endocrinopathies defines APS-2. Notably, her white blood cell count and ESR were elevated. Mild leukocytosis can occur in adrenal insufficiency (due to stress de margination and lack of cortisol), and elevated ESR reflects chronic inflammation, possibly autoimmune adrenalitis. Hemoglobin was normal, which is typical in acute Addison's disease. Cutaneous and mucosal hyperpigmentation were striking in this patient; the black tongue and deeply pigmented lips and palms are pathognomic of high ACTH levels in primary adrenal failure. Hyperpigmentation may precede other symptoms and may be the earliest clue to Addison's disease. Indeed, Addison pigmentation involves the vermilion border of the lips and oral mucosa,(5) as seen in this case.

Gastrointestinal symptoms in APS2 may be multifactorial. Adrenal insufficiency commonly causes nausea, vomiting, diarrhea, and constipation due to mineralocorticoid loss. Our patient's alternating bowel habits may reflect Addison GI dysmotility compounded by parasitic infection. In fact, helminthiasis (her intestinal worms) can mimic Addison's by causing weight loss and hyperpigmentation to the skin. In one report, strongyloidiasis produced malnutrition and even skin darkening in a patient misdiagnosed with Addison's disease until cortisol proved normal(4). However, in our case, the key distinction was endocrine: cortisol was low and adrenal imaging was normal, confirming true Addison's disease rather than parasitic mimicry. The worms were treated to address potential malabsorption, but were not the primary problem.

The therapeutic approach in APS2 is critical. Glucocorticoid replacement must precede thyroid hormone replacement This is because initiating levothyroxine in untreated adrenal insufficiency can precipitate an adrenal crisis(7)(thyroxine increases cortisol metabolism and clearance, unmasking cortisol deficiency). In our patient, hydrocortisone was begun immediately, followed by levothyroxine. This sequence reflects best practice and is supported in the literature. Her prompt improvement (resolution of hypotension and normalization of electrolytes) confirms this.

Unique aspects of this case include the patient's demographic (middle-aged women, which is typical) and incidental findings of intestinal worms. The black tongue is a dramatic but well-described manifestation of Addison's disease, and can be clearly seen in our case.

CONCLUSION

Schmidt syndrome is a rare but important cause of multi-glandular failure. This case emphasizes the need to evaluate adrenal and thyroid functions together when the symptoms overlap. Early identification of mucocutaneous hyperpigmentation and gastrointestinal symptoms leads to the diagnosis. Hormonal assays (low cortisol with high ACTH and elevated TSH) confirm APS 2. Treatment with glucocorticoids before thyroid therapy yielded rapid clinical recovery. Clinicians should remain vigilant for this syndrome in patients with hypothyroidism who develop hyperpigmentation or unexplained GI symptoms, as prompt management is life-saving.

REFERENCES

1. Abdullah, I., et al. "Atypical Case of Schmidt's Syndrome in a Young Male." *Cureus*, 25 June 2022, www.cureus.com/articles/97229-atypical-case-of-schmidts-syndrome-in-a-young-male. Accessed 8 Aug. 2025.
2. Al-Rifai, A., J. Chbib, and G. Kdouh. "Schmidt's Disease: A Case Report." *Frontiers in Medical Case Reports*, vol. 3, no. 3, 2022, www.jmedicalcasereports.org/uploads/178/13707_pdf.pdf. Accessed 8 Aug. 2025.
3. Verma, D., et al. "Addisonian Pigmentation – The Great Mimicker – A Review." *Indian Journal of Dermatology*, 18 Sept. 2024, journals.lww.com/10.4103/ijd.ijd_234_23. Accessed 8 Aug. 2025.
4. Mudraje, S., et al. "Strongyloidiasis Masquerading as Addison's Disease." *IJEM Case Reports*, vol. 1, no. 4, Oct. 2023, pp. 121–24.
5. Bugălă, N. M., et al. "New Approach to Addison Disease: Oral Manifestations Due to Endocrine Dysfunction and Comorbidity Burden." *Diagnostics*, vol. 12, no. 9, 28 Aug. 2022, p. 2080.
6. "Schmidt Syndrome and Autoimmune Polyendocrine Syndrome Type 2." *Johns Hopkins Diabetes Guide*, Johns Hopkins University, www.hopkinsguides.com/hopkins/view/Johns_Hopkins_Diabetes_Guide/547131/all/Schmidt_Syndrome_and_Autoimmune_Polyendocrine_Syndrome_Type_2. Accessed 8 Aug. 2025.
7. Graves, L., R. M. Klein, and A. D. Walling. "Addisonian Crisis Precipitated by Thyroxine Therapy: A Complication of Type 2 Autoimmune Polyglandular Syndrome." *Southern Medical Journal*, vol. 96, no. 8, 1 Aug. 2003, pp. 824–27.

