TPM Vol. 32, No. S3, 2025
ISSN: 1972-6325
https://www.tpmap.org/

Open Access

# PERNICIOUS ANAEMIA WITH HASHIMOTO'S THYROIDITIS IN A YOUNG MALE—A RARE AUTOIMMUNE DYAD FROM SOUTHERN INDIA

[1].DR.YOHIDHA BALAMURUGAN, [2].DR.SUBASH MOHAN, [3].DR.JIBIN SIMON, [4].DR.ANANTHAKUMAR.P.K, [5] DR.K.GNANA SHANMUGHAM

1.CORRESPONDING AUTHOR: DR.YOHIDHA BALAMURUGAN, POSTGRADUATE, DEPARTMENT OF GENERAL MEDICINE, SAVEETHA MEDICAL COLLEGE AND HOSPITALS, SAVEETHA INSTITUTE OF MEDICAL AND TECHNICAL SCIENCES, SAVEETHA UNIVERSITY, CHENNAI, TAMIL NADU, INDIA, 602105,
2.DR.SUBASH MOHAN, POSTGRADUATE, DEPARTMENT OF GENERAL MEDICINE, SAVEETHA MEDICAL COLLEGE AND HOSPITALS, SAVEETHA INSTITUTE OF MEDICAL AND TECHNICAL SCIENCES, SAVEETHA UNIVERSITY, CHENNAI, TAMIL NADU, INDIA, 602105.
3.DR.ANANTHAKUMAR.P.K, PROFESSOR, DEPARTMENT OF GENERAL MEDICINE, SAVEETHA MEDICAL COLLEGE AND HOSPITALS, SAVEETHA INSTITUTE OF MEDICAL AND TECHNICAL SCIENCES, SAVEETHA UNIVERSITY, CHENNAI, TAMIL NADU, INDIA, 602105.
5 DR.K.GNANA SHANMUGHAM, PROFESSOR, DEPARTMENT OF ORTHODONTICS & DENTOFACIAL ORTHOPEDICS, SREE BALAJI DENTAL COLLEGE & HOSPITAL, CHENNAI, INDIA

**Abstract:**

Background: Autoimmune pernicious anaemia (PA) is uncommon in India, where most vitamin-B12 deficiency is nutritional. Co-existence with Hashimoto's thyroiditis (HT) is even rarer and seldom causes full-blown sub-acute combined degeneration (SCD) in young adults. Case: A 25-year-old South-Indian man presented with acral hyper-pigmentation, spastic paraparesis, proprioceptive ataxia and distal sensory loss. Laboratory evaluation showed pancytopenia, macrocytosis, serum B12 < 159 pg $mL^{-1}$ and strongly positive intrinsic-factor and parietal-cell antibodies. Thyroid profile revealed raised TSH (10.54 mU $mL^{-1}$) and anti-TPO titres (366.9 IU $mL^{-1}$). MRI spine was normal. He was diagnosed with SCD secondary to PA, coexisting with HT.
Management & Outcome: Intramuscular cyanocobalamin (1 mg daily × 7, weekly × 4, monthly × 6) plus levothyroxine produced marked neurological improvement within two weeks. Fewer than a dozen Indian cases of the PA–HT dyad have been published. Early recognition and parenteral B12 therapy are essential to prevent irreversible myelopathy in such patients.

**Keywords: Pernicious anaemia(PA), Hashimotos thyroiditis (HT), Subacute Combined Degeneration(SCD), Macrocytosis, Cyanocobalamin**

## INTRODUCTION:

Vitamin $B_{12}$ (cobalamin) is a water-soluble cofactor that drives the reactions catalysed by methionine synthase and methyl-malonyl-CoA mutase; adequate tissue reserves are therefore critical for DNA replication, red-blood-cell production and upkeep of the myelin sheath.Pernicious anaemia (PA) develops when autoimmune injury to gastric parietal cells or the formation of Intrinsic Factor(IF)-neutralising antibodies disrupts vitamin-B12 metabolism pathway, leading to severe cobalamin malabsorption, megaloblastic anaemia and—if uncorrected—subacute combined degeneration of the spinal cord. In Western nations PA represents the predominant cause of marked vitamin $B_{12}$ deficiency, affecting roughly 1–2 % of individuals older than 60 years.[1] Data from India depict a different pattern: most $B_{12}$ deficiency arises from dietary insufficiency, and classical PA appears only sporadically. This discrepancy implies that PA is both genuinely uncommon and frequently overlooked in the Indian setting.[2] We herein describe a 25-year-old South-Indian man presenting with the full neurological

spectrum of PA complicated by concurrent Hashimoto's thyroiditis, highlighting diagnostic challenges and the importance of prompt recognition and treatment.

**Case report:**

A 25-year-old gentleman with no prior co-morbidities presented with a one-year history of progressive hyper-pigmentation of the dorsum of his feet (extending above the ankles) and hands, followed six months later by gradually worsening lower-limb weakness (difficulty rising from a chair, squatting, climbing stairs, and knee buckling) and gait unsteadiness, especially in darkness and while washing face. Two months before presentation he noted unaware slippage of slippers and distal numbness in both feet. He denies alcohol use, or drug exposure. Occupational history revealed two years of work in car-painting. His mother had vitiligo; he consumed an ovo-lacto-vegetarian diet.

On examination he was conscious, oriented, pale, with early greying of hair and symmetrical acral hyper-pigmentation.

**Figure:1 showing hyperpigmentation in feet extending above ankle joint**

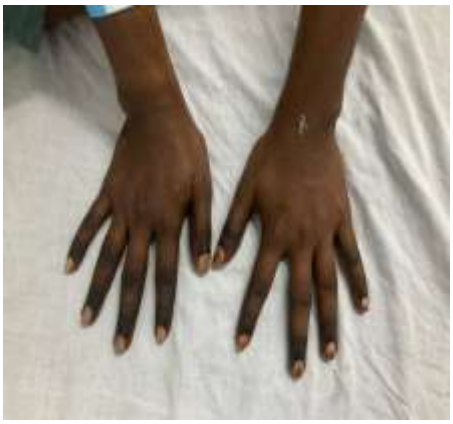

**Figure:2 Showing acral hyperpigmentation**

**Figure:3 showing early greying of hair.**

Cardiovascular, respiratory, and abdominal examinations were normal. Neurologically, cranial nerves and upper-limb tone, power, and reflexes were normal; lower-limb tone was increased, power was 4/5 at hips and knees, 3/5 at ankles and toes, and plantar responses were extensor bilaterally. Knee and ankle jerks were exaggerated(3+). Distal vibration, proprioception, and fine touch were impaired upto knee joint in lower limb and limited to hands in upper limb, while pain and temperature sensation were preserved.

Laboratory tests showed pancytopenia with macrocytosis and hyper-segmented neutrophils. Serum vitamin-B12 was <159 pg/mL; folate was normal.With no history of nutritional deficiency, there was a strong suspicion of

autoimmune pathology for his given age. Both Parietal-cell and intrinsic-factor antibodies were strongly positive. Upper GI endoscopy revealed only a lax lower esophageal sphincter; duodenal biopsy showed non-specific duodenitis. MRI spine was normal.Thyroid tests demonstrated elevated TSH (10.54 mU/mL) with normal fT3/fT4 and markedly raised anti-TPO antibodies (366.9 IU/mL); neck ultrasonography showed a homogeneous thyroid.

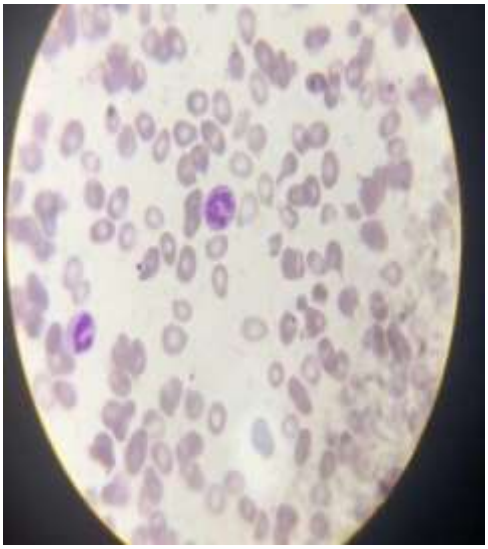

**Figure:4 Peripheral smear of the patient showing macrocytes. The red arrow points to hypersegmented neutrophil**

| | VALUE | REFERENCE |
|---|---|---|
| HAEMOGLOBIN | 6.6gm/dl | 13-17gm/dl |
| MCV | 128.4fl | 83-101 fl |
| MCH | 40.7pg | 27-32pg |
| TLC | 2420cells/cu.mm | 4000-11000cells/cu.mm |
| PLATELET | 1.07 lakhs | 1.5-4 lakhs |

| | | |
|---|---|---|
| RETICULOCYTE COUNT | 0.3% | 0.5-2.5% |
| VITAMIN-B12 | <159pg/ml | 190-950pg/ml |
| HOMOCYSTEINE | >50micromoles/liter | 5-15micromoles/liter |
| PARIETAL CELL ANTIBODY | 109.3RU/ml | >20 positive |
| INTRINSIC FACTOR ANTIBODY | 143.2 RU/ml | >20 positive |

**Table.1 showing laboratory values of complete blood count, reticulocyte count, vitami-B12, homocysteine, parietal cell and intrinsic factor antibody**

A diagnosis of subacute combined degeneration with large-fibre axonal neuropathy secondary to pernicious anaemia, coexisting with Hashimoto's thyroiditis, was made. Treatment comprised intramuscular cyanocobalamin 1000 µg daily for one week, weekly for one month, then monthly for six months, alongside oral folic acid, pregabalin, and levothyroxine. At two-week follow-up his lower-limb strength and sensory symptoms had improved markedly. Lifelong vitamin-B12 and thyroid-hormone replacement with regular follow-up was advised.

## DISCUSSION:

Pernicious anaemia is an organ-specific autoimmune gastritis marked by autoantibodies against gastric parietal cells and intrinsic factor, resulting in cobalamin malabsorption and megaloblastic anaemia. Epidemiologically, PA affects approximately 0.1–1% of the general population, rising to ~2% in individuals over 60 years in Western cohorts[3]. Pernicious anaemia arises from a chronic, organ-specific autoimmune gastritis in which autoreactive $CD4^+$ T lymphocytes attack the $H^+/K^+$-ATPase proton pumps on gastric parietal cells, leading to their progressive loss and resulting corpus–fundus atrophy. Concurrently, patients develop two types of intrinsic-factor autoantibodies: "blocking" antibodies that inhibit cobalamin binding to intrinsic factor and "binding" antibodies that hasten its removal, together effectively abolishing intrinsic-factor activity. These immunological events, possibly exacerbated by shifts in the gastric microbiome that perpetuate mucosal inflammation, culminate in achlorhydria and severe impairment of vitamin $B_{12}$ absorption despite normal dietary intake[3].

Aggarwal et al. reported that, among 1,026 anaemic adults evaluated at a North-Indian tertiary centre, PA was diagnosed in 1.1% of cases and accounted for approximately 6% of those with biochemical $B_{12}$ deficiency, underscoring its rarity relative to nutritional causes.[4]

Cobalamin deficiency can affect the haematopoietic, gastrointestinal and nervous systems.Neurologically, patients exhibits features of subacute combined degeneration of the spinal cord, including paresthesia, sensory loss (especially of vibration and joint position sense), gait ataxia, distal limb weakness, spasticity, and occasionally cognitive or psychiatric symptoms such as confusion, depression, or irritability. Hematological findings included severe macrocytic anemia, hypersegmented neutrophils, thrombocytopenia, and low reticulocyte counts. Gastrointestinal evaluation often reveals antral gastritis, and many patients tested positive for parietal cell antibodies, suggesting an autoimmune basis. These findings highlight the critical need for early

diagnosis and treatment to prevent irreversible neurological damage. [5]In our case, patient had hematological as well as severe neurological manifestations.

Neurological sequelae requires prolonged severe deficiency. Sharma et al. reported a mean age of 38 ± 9 years among 15 Indian Subacute Combined Degeneration (SCD) patients, with only two cases <30 years[5]. This finding deviates from the usual profile of SCD—which predominantly affects middle-aged and older adults—and underscores the exceptional rarity of its occurrence in younger populations.Our patient presented at 25 years of age , underlining that profound autoimmune B12 malabsorption can precipitate early SCD.

Autoimmune thyroiditis (AITD) and pernicious anaemia (PA) frequently occur together due to overlapping genetic and immunological factors. Both disorders are linked to shared susceptibility loci—such as HLA-DR3 and DR5—and polymorphisms in immune-regulatory genes like CTLA-4 and PTPN22, which predispose to loss of self-tolerance and organ-specific autoimmunity. An initial immune response targeting thyroid antigens may trigger epitope spreading, exposing gastric $H^+/K^+$-ATPase and leading to autoimmune gastritis, intrinsic factor deficiency, and subsequent PA. The pathogenic process in both conditions involves Th1-driven cytokine release and B-cell–mediated production of organ-specific antibodies (anti-TPO, anti-thyroglobulin, anti-parietal cell, and anti-intrinsic factor)[6]. Moreover, a recent meta-analysis reported that a substantial proportion of PA patients harbour thyroid autoantibodies, underscoring the importance of screening for thyroid dysfunction in this population. Clinically, individuals with AITD should be evaluated for vitamin $B_{12}$ deficiency and gastric autoantibodies, and those with PA merit regular monitoring of thyroid function [7].

Only two individual patients with concomitant pernicious anaemia and Hashimoto's thyroiditis have been documented in the India. Pandit and Shah reported the first such case of autoimmune polyglandular syndrome IIIb(Hashimoto's thyroiditis and pernicious anaemia) in an Indian female in 2012 [8]. Seven years later, Bhatia et al. described a second patient with this uncommon overlap in 2019 [9].

Diagnosis of pernicious anaemia is established by demonstrating megaloblastic anaemia with macrocytosis (mean corpuscular volume >100 fL) and hypersegmented neutrophils on peripheral smear, together with a serum cobalamin level below 148 pmol/L, and the presence of intrinsic factor antibodies (sensitivity 73%, specificity 100%) or anti–parietal cell antibodies as surrogate markers of autoimmune gastritis. Additional supportive findings include elevated fasting gastrin, a decreased pepsinogen I : II ratio, and histological confirmation of atrophic body gastritis on gastric biopsy. In diagnostically uncertain cases, elevated methylmalonic acid and homocysteine levels can further corroborate cobalamin deficiency [10,11].

Intramuscular hydroxocobalamin is the preferred treatment for pernicious anaemia; in those without neurological signs, the regimen is 1 mg IM three times per week for two weeks, then 1 mg IM every two to three months thereafter. The recommended intramuscular cyanocobalamin schedule begins with 1000µg daily (or every other day) for one week, followed by 1000 µg once weekly for four weeks, and then 1000µg monthly for life. Our patient was treated with IM cyanocobalamin regimen.

Assess treatment efficacy by checking the reticulocyte count one week after initiation, repeating a full blood count with MCV by eight weeks, and measuring serum $B_{12}$ at intervals; if results remain equivocal, consider methylmalonic acid or holotranscobalamin assays. Once intrinsic-factor antibody–mediated deficiency is established, patients must continue $B_{12}$ replacement indefinitely [11].

Oral high-dose cyanocobalamin has become a reliable substitute for intramuscular injections in pernicious anaemia. A systematic review of two randomized trials (n=108) demonstrated that daily oral doses of 1–2 mg achieved the same haematological and metabolic improvements by three to four months as traditional intramuscular schedules, yielding equivalent increases in serum $B_{12}$, haemoglobin, and MCV, as well as similar neurological recovery. Consequently, an initial regimen of 1 mg orally each day for four weeks, followed by 1 mg weekly for one month and then 1 mg monthly for maintenance, is recommended to preserve optimal $B_{12}$ levels and clinical stability [12].In a 12-month prospective cohort of 26 patients on 1 mg oral cyanocobalamin daily, 88.5% normalized their biochemical markers within one month—median serum $B_{12}$ rising from 148 to 407 pmol/L ($P < 0.0001$) and homocysteine and methylmalonic acid returning to normal—and these gains were sustained through the study period. The regimen was well tolerated with high adherence, confirming that daily high-dose oral therapy effectively restores and maintains cobalamin status in compliant individuals [13].

One drawback of high-dose oral cyanocobalamin is the absence of proof that it reverses neurologic damage. Snow and Barrett's review excluded patients with clear neurologic involvement and measured only hematologic and metabolic parameters, offering no solid evidence on clinical neurologic improvement. Similarly, Lee et al. showed that daily 1 mg dosing corrects biochemical indices but did not assess neurologic or neuropsychiatric outcomes, so its effect on neuropathic symptoms remains unknown [12,13].

## CONCLUSION:

Autoimmune pernicious anaemia occurring alongside Hashimoto's thyroiditis and presenting as sub-acute combined degeneration in a young Indian adult is exceptionally rare. Recognizing acral hyperpigmentation and spastic paraparesis in a pancytopenic patient should immediately prompt investigation for cobalamin deficiency. Confirming the diagnosis requires comprehensive testing for intrinsic-factor, parietal-cell, and thyroid autoantibodies. Early initiation of intramuscular cyanocobalamin and levothyroxine yielded marked neurological improvement within two weeks. Lifelong parenteral vitamin $B_{12}$ replacement is imperative to prevent irreversible myelopathy. In regions where nutritional $B_{12}$ deficiency predominates, clinicians must remain vigilant for autoimmune aetiologies. Broader reporting will deepen our understanding and inform optimal management of this uncommon dyad.

## REFERENCES:

1. Stabler SP. Vitamin B12 deficiency. *N Engl J Med*. 2013;368(2):149-60.
2. O'Leary F, Samman S. Vitamin B12 in health and disease. *Nutrients*. 2010;2(3):299-316.
3. Carmel R. Pernicious anaemia: new insights. *Blood*. 2021;138(23):1981–9.
4. Aggarwal A, Kumar N, Kankaria R, Singh V, Mishra P. Spectrum of vitamin B12 deficiency in Indian adults presenting to a tertiary centre. *J Assoc Physicians India*. 2021;69(5):11–16
5. Sharma R, et al. Sub-acute combined degeneration of spinal cord in young adults: case series. *Neurol India*. 2018;66(4):1125-8.
6. Iddah MA, Macharia BN. Autoimmune thyroid disorders. *Autoimmune Dis*. 2013;2013:23455.
7. Bora K, et al. Prevalence of thyroid auto-antibodies in pernicious anaemia: a meta-analysis. *Clin Endocrinol (Oxf)*. 2022;97(1):12-20.
8. Pandit RB, Shah MC. Autoimmune polyglandular syndrome type IIIb in an Indian female. *Indian J Endocrinol Metab*. 2012;16(3):486-8.
9. Bhatia P, et al. Pernicious anaemia with autoimmune thyroid disease: an uncommon overlap. *J Clin Diagn Res*. 2019;13(2):OD07-OD08.
10. Lahner E, Annibale B. Pernicious anemia: new insights from a gastroenterological point of view. World J Gastroenterol. 2009;15(41):5121–8.
11. Devalia V, Hamilton MS, Molloy AM; British Committee for Standards in Haematology. Guidelines for the diagnosis and treatment of cobalamin and folate disorders. Br J Haematol. 2014;166(4):496–513.
12. Snow CF, Barrett C. Oral versus parenteral vitamin B12 in pernicious anaemia: a systematic review. *Am J Med*. 2019;132(9):1010-22.
13. Lee SY, et al. High-dose oral cyanocobalamin therapy in patients with pernicious anaemia. *Blood Adv*. 2020;4(7):1394-1400.