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A long-standing undiagnosed case of vitamin B12 deficiency: a case report

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Abstract

Background Pernicious anemia, an autoimmune disease, presents with gradual, nonspecific symptoms, often leading to delayed diagnosis owing to its overlap with other conditions and variability in laboratory findings, such as neurological symptoms without anemia or macrocytosis.

Case presentation This case describes a 40-year-old Iranian woman with a decade-long history of nonspecific symptoms, including fatigue, widespread musculoskeletal pain, paresthesia, cognitive disturbances, and optic neuritis; misattributed to conditions such as fibromyalgia, hypothyroidism, and autoimmune diseases. Despite annual monitoring for normocytic anemia, her critically low vitamin B12 levels (< 150 pg/mL) and a diagnosis of pernicious anemia were identified only after persistent symptoms prompted further evaluation, revealing atrophic gastritis as the underlying cause. Neurologic improvement with parenteral B12 therapy, alongside management of fibromyalgia, emphasizes the importance of considering vitamin B12 deficiency even in the absence of classic hematologic findings.

Conclusion This case highlights the diagnostic challenges of pernicious anemia, where nonspecific symptoms and overlapping comorbidities obscure diagnosis, underscoring the need for a systematic, multidisciplinary approach and timely recognition of vitamin B12 deficiency to prevent irreversible complications.

Keywords Misdiagnosis, Nutrient deficiency, Electric shock-like sensations, Case report, Optic neuropathy, Forgetfulness, Mental slowing

Introduction

The gradual onset and nonspecific symptoms of pernicious anemia, which overlap with other diseases, often delay its timely diagnosis [1]. In addition, variability in laboratory findings can further complicate the diagnostic process. Approximately a quarter of patients with pernicious anemia exhibit neurological symptoms without anemia or macrocytosis. Furthermore, comorbid iron deficiency anemia in about 20% of patients with pernicious anemia can obscure the diagnosis of B12 deficiency, as the blood film may reveal normocytic or even microcytic anemia [1]. Here, we describe a long-standing, undiagnosed case of pernicious anemia in which the patient's symptoms and signs were misattributed to several other conditions—including multiple sclerosis (MS), hypothyroidism, systemic lupus erythematosus (SLE), and fibromyalgia—for approximately 10 years, resulting in a missed diagnosis and a failure to recognize the larger clinical picture.

Case presentation

A 40-year-old Iranian woman presented to a primary care office complaining of electric shock-like sensations in her head that had started 2 days earlier. These sensations were exacerbated by neck flexion. The patient described previous self-resolving episodes of similar, though less severe, symptoms. She reported no other symptoms. Her

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physical exam, including neurological assessments such as visual field, position sense, vibration, and Romberg's sign, was normal. Her medical history included hypothyroidism, fibromyalgia, and iron deficiency anemia. She was taking levothyroxine 100 μg orally once daily, duloxetine 30 mg orally once daily, and ferrous glycine sulfate 400 mg daily [equivalent to 80 mg Fe(II)] orally.

While investigating her current complaints, a review of the patient's medical history revealed a longstanding pattern of symptoms dating back to 2014. During the initial visit, a series of targeted questions were asked to rule out potential causes. These included assessing consistent use of duloxetine (to evaluate for serotonin–norepinephrine reuptake inhibitor withdrawal), a history of cervical disc disease, and the presence of numbness or tingling sensations in the limbs. The patient denied all these factors. Given that paresthesia is a common symptom in fibromyalgia, reassurance was provided regarding the likelihood of spontaneous improvement.

On the basis of the patient's history and medical records, it appears that she began experiencing symptoms and signs in 2014, which led to her subsequent diagnoses. According to the patient, the initial manifestations included multiple chronic oral ulcers and widespread musculoskeletal pain, prompting a thorough evaluation by a rheumatologist. On the basis of positive initial test results—currently unavailable—the patient was prescribed prednisolone, azathioprine, and hydroxychloroquine. However, according to the patient, the results of subsequent tests were negative, and the rheumatologist discontinued the medications. Although the patient's oral ulcers improved after a few months, the widespread musculoskeletal pain persisted. Moreover, because the rheumatological tests were normal, a rheumatological diagnosis was not made. During this time, the patient also received psychiatric treatment for major depressive disorder (MDD), with sertraline prescribed for mood stabilization.

By 2021, the patient's symptoms evolved further, culminating in a significant episode of optic neuritis in the left eye. This presented as an acute unilateral decreased vision and severe eye pain, particularly with eye movement. The condition responded well to methylprednisolone treatment. Magnetic resonance imaging (MRI) scans of the brain, orbits, cervical spine, and brain magnetic resonance venography (MRV) imaging showed no significant findings; however, scattered tiny unidentified bright objects (UBOs) ($n=4–5$) were noted in the subcortical white matter on T2-weighted fluid-attenuated inversion recovery (FLAIR) images. Visual field tests revealed significant abnormalities, with the left eye showing field defects in the upper and lower quadrants, and moderate-to-severe MD (mean deviation) loss, while the right eye exhibited peripheral vision loss and an abnormal pattern deviation (Fig. 1). Despite these findings, high-definition optical coherence tomography (OCT) scans demonstrated intact retinal layers, normal macular thickness, and no structural optic nerve damage (Fig. 2). Laboratory tests revealed a positive antinuclear antibody (ANA, 1:160, fine speckled pattern) but negative extractable nuclear antigen (ENA), anti-dsDNA, neuromyelitis optica (NMO), and myelin oligodendrocyte glycoprotein (MOG) antibodies; effectively ruling out systemic autoimmune or demyelinating diseases such as neuromyelitis optica. Notably, a low-normal vitamin B12 level (232 pg/mL) was identified, which could have contributed to the patient's neurological symptoms but was overlooked at the time.

The findings strongly suggest optic neuritis, likely as part of a clinically isolated syndrome (CIS), raising concern for a future risk of multiple sclerosis (MS). The episode's clinical presentation and nonspecific UBOs in the brain align with early demyelinating disease, although progression to MS is not definitive at this stage. Recommendations included close neurological monitoring with repeat brain and spinal MRIs in 6–12 months, and cerebrospinal fluid (CSF) analysis if new symptoms occurred. However, the patient did not follow through with these recommendations, and no follow-up imaging or tests were conducted to monitor for disease progression.

Throughout all these years, the patient's chief complaints were persistent; widespread musculoskeletal pain and fatigue, which had never been attributed to a specific diagnosis by any physician. Finally, in 2022, the patient was referred to a psychiatrist for these complaints. The psychiatrist diagnosed fibromyalgia and prescribed duloxetine 30 mg daily, which significantly alleviated her symptoms.

Approximately 1 week later, the patient returned for a follow-up visit, reporting a worsening of her initial symptoms. She also described new complaints, including increased widespread musculoskeletal pain and cognitive disturbances such as forgetfulness, decreased attention, and slowed thinking. A mini-mental state examination (MMSE) was performed, which yielded normal results. Laboratory tests were ordered to investigate potential causes. Gabapentin 300 mg at night was prescribed to alleviate paresthesia. The evaluation focused on possible thyroid hormone imbalances, worsening anemia, and vitamin B12 deficiency as potential contributors to the neurological symptoms.

Four days later, at the third follow-up visit, the patient reported improvement in the electric shock-like sensations but continued to struggle with persistent mental slowness and forgetfulness. Laboratory testing revealed normocytic normochromic anemia, with a hemoglobin

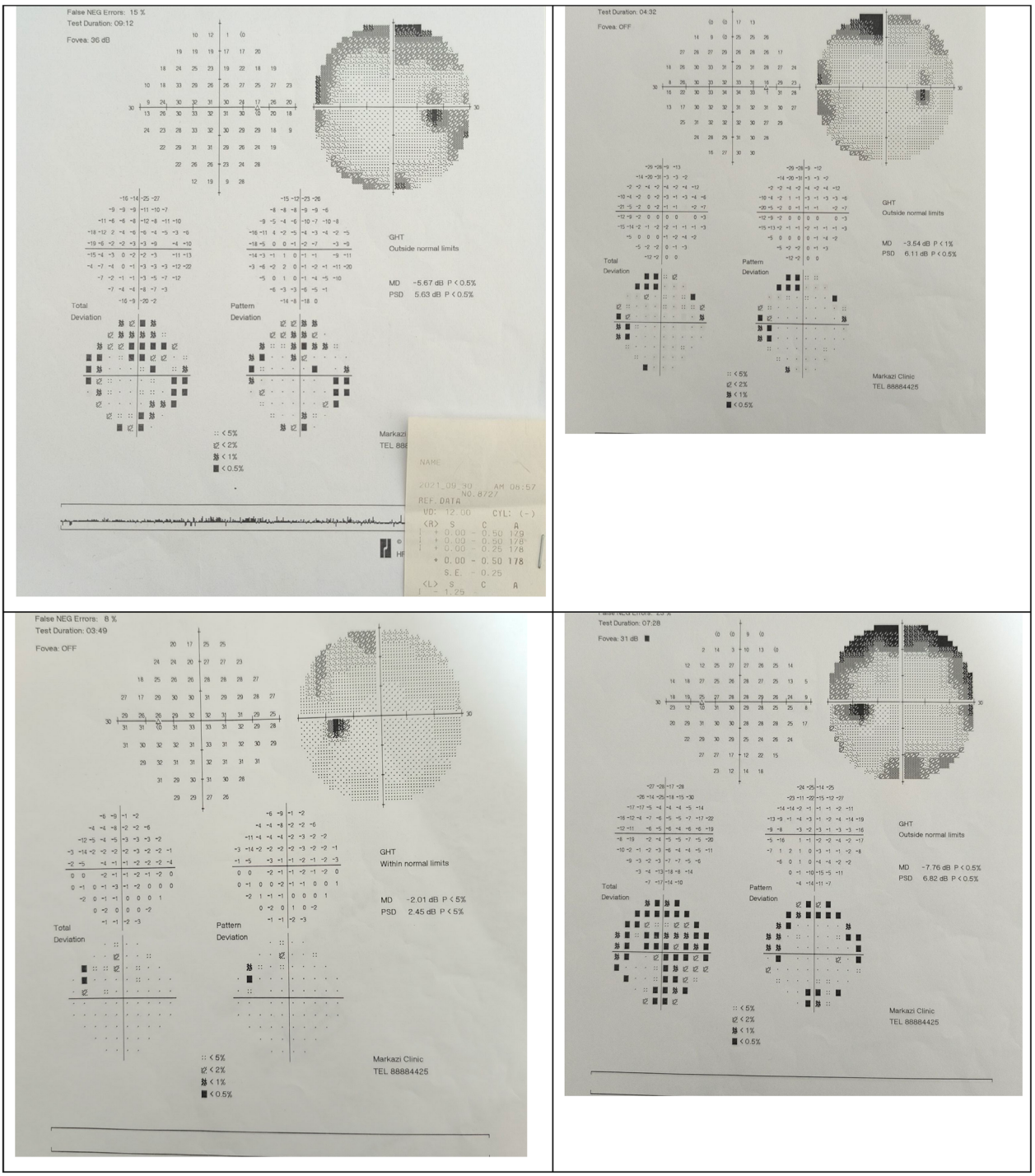

Fig. 1 Visual field test. (**A**) Visual field map. (**B**) Glaucoma hemifield test. (**C**) Deviation maps. (**D**) Statistics

level of 10.9 g/dL, a mean corpuscular volume (MCV) of 81.2 fL, and a mean corpuscular hemoglobin concentration (MCHC) of 33 g/dL, both near the lower limit of normal. Ferritin levels were adequate at 57 ng/mL; however, the patient's vitamin B12 level was critically low at < 150 pg/mL, well below the normal range. Thyroid function was assessed, and thyroid-stimulating hormone (TSH) level was normal at 1.4 mIU/L, ruling out thyroid dysfunction as a contributing factor.

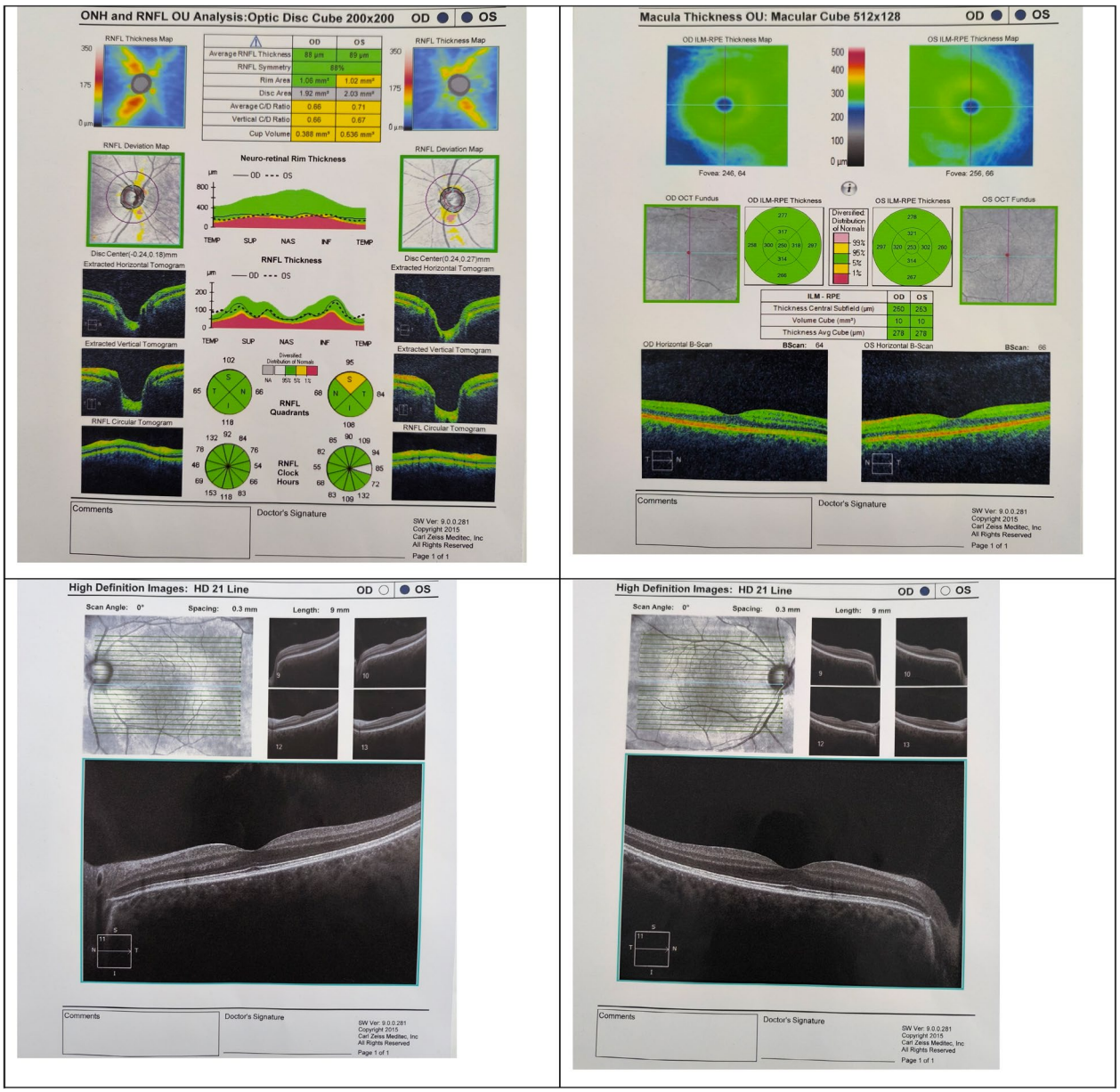

Fig. 2 High-definition optical coherence tomography scans. (**A**) Optic nerve head and retinal nerve fiber layer analysis for both eyes. (**B**) Macula thickness analysis. (**C**) High-definition images. (**D**) High-definition images (alternate view)

A review of medical records revealed that the patient underwent an upper endoscopy in 2016 for chronic dyspepsia, which confirmed the presence of severe chronic gastritis with intestinal and pancreatic metaplasia (Fig. 3). The patient's previous records also showed the following laboratory findings: positive anti-thyroid peroxidase (TPO) and normocytic normochromic anemia, and a ferritin level below 15 ng/mL.

The patient was prescribed parenteral vitamin B12 (hydroxocobalamin) at 1000 µg intramuscularly three times per week for the first week, followed by 1000 µg once weekly for 4 weeks. She was also referred to a hematologist, neurologist, and gastroenterologist for further evaluation.

The gastroenterologist confirmed diagnoses of pernicious anemia and atrophic gastritis. To rule out Crohn's disease and celiac disease, laboratory tests were ordered, all of which returned normal. An upper endoscopy was performed to assess the patient's condition and exclude potential malignancies, with histopathological analysis

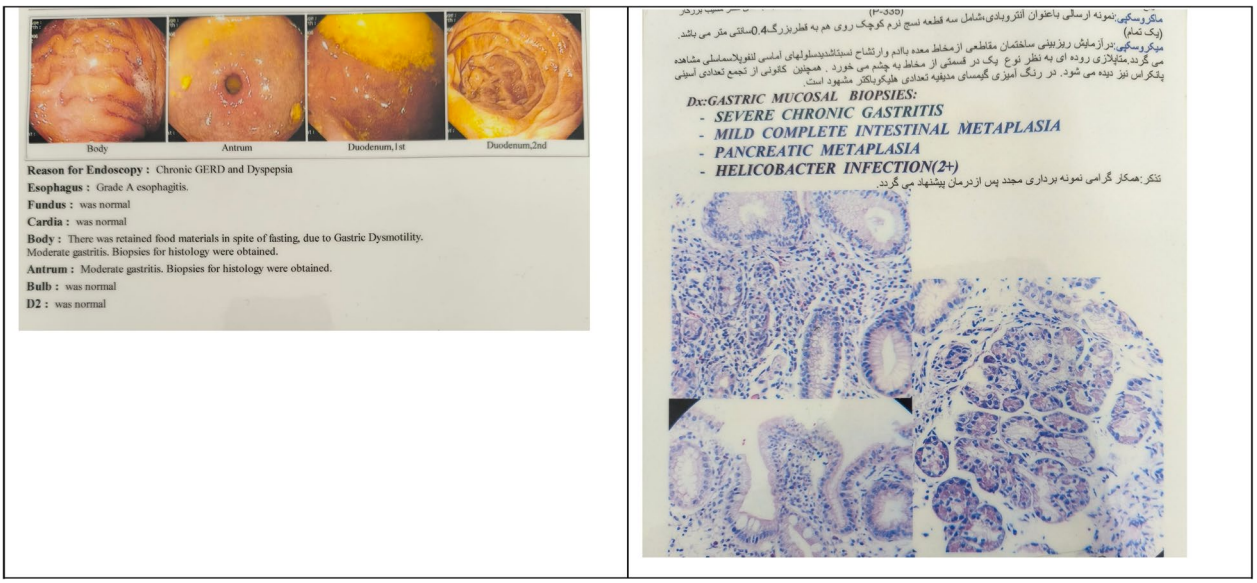

Fig. 3 **A** Endoscopic examination report. (**B**) Gastric mucosal biopsies and pathological report

confirming atrophic metaplastic gastritis. The gastroenterologist recommended repeating an upper endoscopy every 3 years and referred the patient to a hematologist for further management.

The hematologist supported the diagnosis and proposed a treatment plan of weekly intramuscular injections of parenteral vitamin B12 (hydroxocobalamin) at 1000 μg for 3 months, followed by injections every 2 months, depending on the patient's symptoms and laboratory results. A complete blood count and vitamin B12 level test were scheduled 4 weeks after starting treatment. At the follow-up, the patient's vitamin B12 level had increased to 587 pg/mL, and hemoglobin improved to 11.1 g/dL. The hematologist emphasized that, owing to the irreversible nature of atrophic gastritis, lifelong treatment is necessary, which may include injections or oral supplementation, along with iron supplementation. The next follow-up was scheduled for 6 months later to reassess symptoms and laboratory results.

The neurologist requested a follow-up MRI of the brain and cervical spine. The brain MRI showed a few stable unidentified bright objects (UBOs) in the frontal subcortical and deep white matter, consistent with the previous MRI, with no interval changes or new abnormalities. Their nonspecific nature and lack of progression reduced the likelihood of an active demyelinating disease. The cervical spine MRI revealed cervical hypolordosis, with no significant abnormalities in the vertebrae, intervertebral discs, spinal cord, or surrounding soft tissues. On the basis of these findings, physical therapy was recommended to address the cervical spine condition. In addition, a referral to a rheumatologist was suggested for further evaluation and management on the basis of the patient's clinical presentation.

After reviewing the patient's test results, the rheumatologist determined that systemic lupus erythematosus (SLE) was unlikely and attributed the positive ANA test to coexisting Hashimoto's thyroiditis. They concluded that vitamin B12 deficiency alone could not account for the full spectrum of the patient's symptoms. A diagnosis of fibromyalgia was made, and treatment with duloxetine 60 mg once daily and pregabalin 50 mg once daily was recommended. Furthermore, a referral to a psychiatrist specializing in psychosomatic medicine was advised to ensure comprehensive care.

The patient's condition approximately 4 months after diagnosis and the initiation of treatment

The patient has not yet consulted a psychiatrist. While there has been a noticeable improvement in symptoms, particularly cognitive disturbances and fatigue, the patient continues to experience widespread musculoskeletal pain and intermittent electric shock-like sensations in the head. However, the frequency of these sensations has significantly decreased. As previously noted, the patient's vitamin B12 level increased to 587 pg/mL, and their hemoglobin level improved to 11.1 g/dL.

Patient's timeline

2014	Symptoms onset: chronic oral ulcers and widespread musculoskeletal pain Rheumatology: treated with prednisolone, azathioprine, and hydroxychloroquine, later discontinued owing to negative tests. No definitive diagnosis Psychiatric treatment: diagnosed with major depressive disorder (MDD), prescribed sertraline		
2016	Upper endoscopy: severe chronic gastritis with intestinal and pancreatic metaplasia diagnosed		
2021	Optic neuritis: acute vision loss in the left eye treated with methylprednisolone MRI findings: subcortical UBOs (4–5) without active demyelination Laboratory tests: positive ANA (1:160), low-normal vitamin B12 (232 pg/mL), negative for systemic autoimmune or demyelinating diseases Diagnosis: suspected clinically isolated syndrome (CIS) with risk of MS. Recommended follow-up imaging, not completed		
2022	Fibromyalgia diagnosis: treated with duloxetine 30 mg daily, improving symptoms		
2024	Primary care visits	First visit	Symptoms: electric shock-like sensations in the head, worsened by neck flexion, with no other complaints. History of self-resolving similar episodes Exam/assessment: normal neurological exam; suspected paresthesia related to fibromyalgia Plan: reassurance of likely spontaneous improvement
		Second visit (1 week later)	Symptoms: worsened sensations, new widespread musculoskeletal pain, forgetfulness, decreased attention, and slowed thinking Tests/plan: normal MMSE. Laboratory tests ordered for thyroid function, anemia, and B12 deficiency. Gabapentin 300 mg prescribed for paresthesia
		Third visit (4 days later)	Symptoms: improvement in head sensations but ongoing cognitive issues Laboratory results: normocytic anemia, normal ferritin, low vitamin B12 (< 150 pg/mL), and normal TSH Plan: managed anemia and vitamin B12 deficiency
	Specialty care visits	Gastroenterologist: pernicious anemia and atrophic gastritis confirmed. Recommended follow-up endoscopy every 3 years Hematologist: lifelong vitamin B12 supplementation prescribed; laboratory tests showed improved B12 (587 pg/mL) and hemoglobin (11.1 g/dL) Neurologist: stable MRI findings; cervical hypolordosis diagnosed, physical therapy recommended Rheumatologist: SLE ruled out. Fibromyalgia confirmed; treatment adjusted to duloxetine 60 mg and pregabalin 50 mg daily	
	Follow-up	Improved cognitive symptoms and fatigue Reduced electric shock sensations but persistent musculoskeletal pain	

MRI, magnetic resonance imaging; UBOs, unidentified bright objects; ANA, antinuclear antibody; CIS, clinically isolated syndrome; MMSE, mini-mental state examination; SLE, systemic lupus erythematosus

Patient's symptoms in the past 10 years

- Widespread musculoskeletal pain
- Fatigue
- Symmetric distal paresthesia
- Electric shock-like sensations in the head
- Cognitive disturbances eg, forgetfulness, and cognitive slowing
- Depression
- Visual disturbances, associated with optic neuritis
- Tinnitus
- Somnolence

Discussion

Vitamin B12 deficiency is defined by suboptimal serum or plasma concentrations below 200 or 250 pg/mL (148 or 185 pmol/L) [2]. Patients with vitamin B12 and/or folate deficiency frequently present with anemia, often accompanied by nonspecific symptoms such as fatigue, which is common in anemia of various etiologies. While mild anemia may be incidentally detected in routine complete blood counts (CBC), more advanced or untreated cases of vitamin B12 deficiency typically manifest with characteristic hematologic and neurologic abnormalities [1].

The classic manifestations of vitamin B12 and folate deficiencies encompass worsening macrocytic anemia, jaundice resulting from a combination of anemia and bilirubin elevation, and variable neurologic abnormalities, which are more pronounced in vitamin B12 deficiency and include cognitive slowing and neuropathy [3]. Although these findings were more common in the early twentieth century, neurologic abnormalities remain a critical feature in modern clinical practice.

The most common neurologic findings in vitamin B12 deficiency include symmetric paresthesias, numbness, and gait disturbances [4, 5]. In more advanced cases, subacute combined degeneration of the spinal cord due to demyelination may develop, resulting in progressive weakness, ataxia, paresthesias, spasticity, and paraplegia [6, 7]. Other neurologic findings include impaired proprioception and vibration sense, Lhermitte sign (a shock-like sensation radiating to the lower extremities during neck flexion), ataxia, a positive Romberg test, abnormal deep tendon reflexes, extrapyramidal signs (for example, dystonia, dysarthria, and rigidity), restless legs syndrome, peripheral sensory deficits, and visual disturbances (including optic atrophy). In addition to neurologic findings, vitamin B12 deficiency frequently presents with psychiatric symptoms, including depression, mood disturbances, irritability, insomnia, cognitive slowing, forgetfulness, dementia, and psychosis [8, 9].

Fatigue is often an initial symptom, even in the absence of anemia, and may be associated with cognitive or

mood impairments [8, 9]. Vitamin B12 levels should be evaluated in patients with unexplained neuropsychiatric symptoms or fatigue; however, supplementation should only be initiated upon confirmation of deficiency. Understanding the diverse clinical manifestations of vitamin B12 deficiency is critical for identifying its underlying causes, which include both dietary and absorption-related factors.

Vitamin B12 deficiency arises from a variety of factors, broadly categorized into decreased intake, impaired absorption, and interference from medications. Reduced intake is often seen in individuals consuming insufficient animal-derived products, such as strict vegans, or in infants breastfed by a vitamin B12-deficient mother. Impaired absorption may result from surgical procedures (for example, gastrectomy, bariatric surgery, or terminal ileum resection) or gastrointestinal conditions, including pernicious anemia (due to autoantibodies to intrinsic factor or gastric parietal cells), autoimmune metaplastic atrophic gastritis, Crohn's disease, celiac disease, pancreatic insufficiency, bacterial overgrowth, fish tapeworm infection, and age-related gastric atrophy [1, 10].

Certain medications can also disrupt vitamin B12 absorption or stability, including metformin, histamine receptor antagonists, proton pump inhibitors, and nitrous oxide [1, 10]. These factors collectively contribute to the multifaceted etiology of vitamin B12 deficiency, emphasizing the importance of thorough clinical evaluation when deficiencies are suspected. Despite these diverse causes, the body's significant hepatic storage of B12 delays the onset of symptoms, often by 1–2 years after intake or absorption ceases [11].

Metaplastic (chronic) atrophic gastritis, also referred to as gastric atrophy, is used to describe a form of chronic gastritis that, in addition to inflammation, is associated with mucosal thinning, loss of specialized cells in gastric glands, and changes in epithelial cell types (that is, metaplasia). Metaplastic (chronic) atrophic gastritis includes two main subtypes, autoimmune and environmental metaplastic atrophic gastritis (AMAG and EMAG). AMAG is a subtype that primarily affects the gastric corpus, where the normal oxyntic mucosa is replaced by atrophic and metaplastic mucosa. This leads to corpus-predominant atrophic gastritis, resulting in reduced or absent production of acid, pepsin, and intrinsic factor. Over time, these changes impair vitamin B12 absorption and may progress to pernicious anemia (PA), a severe form of vitamin B12 deficiency anemia characterized by advanced neurological and hematological manifestations [12].

Pernicious anemia, the clinical end-stage of AMAG, is caused by autoantibodies that disrupt vitamin B12 absorption by targeting intrinsic factor or gastric parietal cells [1]. The condition develops gradually, with a range of nonspecific symptoms—including fatigue, cognitive impairment, and neuropathy—that can complicate timely diagnosis. While pernicious anemia arises from the autoimmune destruction of intrinsic factor and parietal cells, it is underpinned by the same pathological processes of AMAG, underscoring its role as the severe hematologic manifestation of this chronic gastric condition [1].

One of the diagnostic challenges in this case was the atypical presentation of anemia due to vitamin B12 deficiency. Despite annual complete blood counts (CBC) to monitor anemia, the patient consistently exhibited normocytic, normochromic anemia with low ferritin and transferrin saturation levels, as well as a high Mentzer index. While iron deficiency anemia typically presents as microcytic, hypochromic anemia, this patient's blood tests revealed an atypical pattern. This discordance should prompt clinicians to consider alternative etiologies for anemia, particularly when additional indices, such as elevated mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC), do not align with classical iron deficiency anemia. In this case, hypothyroidism could have been considered as a contributing factor. Thus, physicians must remain vigilant for concurrent conditions that might explain the anemia's atypical features.

Despite iron supplementation and subsequent improvements in ferritin levels and transferrin saturation, the patient's anemia indices remained abnormal. This lack of improvement served as a second clue to pursue a more comprehensive anemia workup or to consider referral to an internist or hematologist. When anemia persists despite adequate iron repletion and normalized iron studies, it is crucial for clinicians to explore alternative diagnoses, such as vitamin B12 deficiency or other concurrent conditions, that could be contributing to the abnormal blood test results.

Another diagnostic challenge in this case was the complex clinical presentation, marked by nonspecific symptoms overlapping with various medical conditions, complicating the diagnostic process. The patient presented with electric shock-like sensations in her head exacerbated by neck flexion, alongside fatigue, widespread musculoskeletal pain, oral ulcers, paresthesia, depression, cognitive disturbances, and a history of optic neuritis. These symptoms collectively suggested a broad differential diagnosis spanning autoimmune, neurologic, infectious, endocrine, metabolic, and psychiatric conditions, requiring a systematic evaluation to determine the underlying cause.

Autoimmune diseases such as systemic lupus erythematosus (SLE), Behçet's disease, and Sjogren's syndrome were initially considered owing to the patient's fatigue,

oral ulcers, musculoskeletal pain, and paresthesia [13–15]. However, laboratory findings did not support these diagnoses. The ANA titer was positive at 1:180 with a speckled pattern, but this is a nonspecific finding and does not confirm an autoimmune disease. Anti-dsDNA, anti-Smith (anti-Sm), and extractable nuclear antigen (ENA) antibodies were negative, ruling out active SLE. In addition, complement levels (C3: 120 mg/dL; C4: 20.8 mg/dL) were within normal limits, making complement-mediated autoimmune diseases such as SLE or vasculitis unlikely.

Sjögren's syndrome was also considered given the patient's fatigue, but anti-SS-A/Ro and anti-SS-B/La antibodies were negative, ruling out primary Sjögren's. Behçet's disease remained a possibility owing to oral ulcers, but the absence of genital ulcers, ocular inflammation, or major vascular involvement made it unlikely. The presence of ANA positivity without definitive autoimmune markers raised the possibility of Hashimoto's thyroiditis, which was confirmed by significantly elevated anti-TPO antibodies (> 1000 IU/mL) [16]. Chronic inflammatory states, including atrophic gastritis and pernicious anemia, may contribute to ANA positivity in the absence of a definitive autoimmune disease [17, 18].

Given the patient's long-standing history of Hashimoto's thyroiditis, it is important to consider the possibility of coexisting autoimmune conditions. Pernicious anemia, which occurs in 10% of patients with hypothyroidism caused by chronic autoimmune thyroiditis, often presents alongside other autoimmune disorders such as vitiligo [1]. Therefore, physicians should be vigilant in screening for additional autoimmune conditions in patients with Hashimoto's thyroiditis. The patient's antinuclear antibody (ANA) test was positive using both solid-phase assays and indirect immunofluorescence (IIF). Given the negative results of other laboratory tests, Hashimoto's thyroiditis, a primary organ-specific autoimmune disease associated with positive ANA, may be the underlying cause of the patient's positive ANA test.

Given the history of optic neuritis, electric shock-like sensations, and paresthesia; multiple sclerosis (MS) was initially suspected [19, 20]. However, brain and cervical spine MRIs were unremarkable, showing only a few stable unidentified bright objects (UBOs) in the subcortical white matter, without evidence of active demyelination. CSF analysis for oligoclonal bands was not available, but given the normal MRI findings, it was unlikely to change the diagnosis. Peripheral neuropathy was better explained by critically low vitamin B12 levels (< 150 pg/mL), which accounted for paresthesia and cognitive slowing. Fibromyalgia was ultimately confirmed owing to the presence of widespread musculoskeletal pain and fatigue, without systemic inflammation or structural abnormalities [21].

Infectious causes, including brucellosis, HIV/AIDS, and chronic hepatitis, were also considered [22–24]. Brucellosis was a relevant differential owing to regional endemicity, but the absence of livestock exposure, unpasteurized dairy consumption, or fever made it unlikely. Brucella serology was not available, but testing may be warranted in high-risk individuals. HIV/AIDS and hepatitis C could not be definitively ruled out, as no serology or polymerase chain reaction (PCR) testing was documented in the available records. However, the patient lacked significant risk factors for HIV, such as intravenous drug use, high-risk sexual behavior, or history of blood transfusions; and no clinical signs such as lymphadenopathy, chronic infections, or wasting syndrome were present. Similarly, hepatitis C was not tested, but the patient had no history of intravenous drug use or unexplained liver enzyme abnormalities. If clinical suspicion remains, targeted HIV enzyme-linked immunosorbent assay (ELISA) and hepatitis C serology (HCV Ab, HCV RNA) could be considered.

Psychiatric conditions, such as major depressive disorder (MDD) and somatic symptom disorder, were evaluated owing to the patient's depression, cognitive disturbances, and persistent musculoskeletal pain [25]. However, the neurological symptoms were better explained by vitamin B12 deficiency, and the musculoskeletal pain was more consistent with fibromyalgia than somatization.

Endocrine disorders, including hypothyroidism and adrenal insufficiency, were considered owing to fatigue, depression, and musculoskeletal pain. Hypothyroidism was ruled out, as TSH levels were normal (1.4 μIU/mL). The presence of elevated anti-TPO confirmed Hashimoto's thyroiditis, but thyroid function remained adequate. Adrenal insufficiency was unlikely, as the patient lacked hyperpigmentation, weight loss, or postural hypotension [26, 27].

Sarcoidosis was also considered owing to fatigue, neurological symptoms, and musculoskeletal complaints, but it could not be definitively ruled out as no chest imaging was available to assess for hilar lymphadenopathy or pulmonary involvement. While normal angiotensin-converting enzyme (ACE) levels (16 U/L) reduced the likelihood of active disease, a chest X-ray or computed tomography (CT) scan would be required for confirmation [28]. Chronic fatigue syndrome (CFS) was deemed unlikely, as fatigue improved with vitamin B12 supplementation and fibromyalgia treatment, indicating a specific etiology rather than idiopathic chronic fatigue. However, as CFS remains a diagnosis of exclusion, further evaluation is warranted if symptoms persist [29].

Cerebral vasculitis and ischemic optic neuropathy were considered owing to the history of optic neuritis and neurological symptoms. However, brain imaging showed no ischemic changes, vascular inflammation, or optic nerve damage. In addition, CH50 levels were normal (71 U/mL), further reducing the suspicion for complement-mediated vasculitis [30, 31].

Another significant diagnostic challenge in this case was the electric shock-like sensation in the head, a symptom that is poorly documented in medical literature and often overlooked in clinical training. The patient's sensations, exacerbated by neck flexion, required a broad differential diagnosis, including multiple sclerosis (MS), subacute combined degeneration (SCD) of the spinal cord, cervical disc disease, radiation myelitis, neck trauma, antidepressant discontinuation (brain zaps), trigeminal neuralgia, and somatosensory hallucinations [20, 32–34]. However, after careful evaluation, the symptoms were ultimately linked to a combination of vitamin B12 deficiency and fibromyalgia, both of which can explain her presentation without the need for more invasive investigations.

Vitamin B12 deficiency is a well-recognized cause of neurological symptoms such as paresthesia, cognitive slowing, and abnormal sensory perceptions, even in the absence of subacute combined degeneration (SCD) of the spinal cord. While SCD typically involves the dorsal columns and lateral corticospinal tracts, not all patients with B12 deficiency develop advanced demyelination detectable on MRI. In this case, the critically low vitamin B12 level (< 150 pg/mL) and the patient's history of atrophic gastritis and pernicious anemia support B12 deficiency as a major contributor to her symptoms. These symptoms are consistent with small fiber neuropathy or early-stage sensory neuropathy, which can manifest as tingling, burning, or shock-like sensations in the absence of significant spinal cord involvement.

The role of fibromyalgia is also critical in understanding the patient's presentation. Paresthesias, including numbness, tingling, burning, or crawling sensations, are commonly reported in fibromyalgia, especially in the arms and legs. These sensations are often unexplained by detailed neurological evaluations or electrophysiologic testing, as they typically reflect small fiber neuropathy or altered pain processing. The patient's widespread musculoskeletal pain and fatigue further support the fibromyalgia diagnosis, which was confirmed clinically. Interestingly, the perception of swelling or edema without visible findings in fibromyalgia could also contribute to her sensory complaints.

The improvement of the electric shock-like sensations with gabapentin 300 mg daily reinforces the neuropathic nature of her symptoms, which aligns with both vitamin B12 deficiency and fibromyalgia as underlying causes [35]. While MS was initially suspected, given the history of optic neuritis and paresthesia, this diagnosis was ruled out on the basis of normal MRI findings and the absence of spinal cord involvement or demyelinating lesions. Similarly, structural causes such as cervical disc disease were not supported by imaging [10].

The patient's history of optic neuritis, characterized by acute unilateral vision loss, severe eye pain with movement, and field defects documented on visual field testing, is a notable clinical feature. While vitamin B12 deficiency is associated with optic neuropathy, its presentation typically involves gradual, painless, bilateral central vision loss due to damage to the optic nerve, and it is rarely associated with the acute, painful onset characteristic of optic neuritis. Furthermore, the patient's response to methylprednisolone treatment and the findings of scattered unidentified bright objects (UBOs) on brain MRI are more suggestive of a demyelinating process than a nutritional deficiency. The absence of structural optic nerve damage on OCT and normal retinal layers further supports the notion that the optic neuritis in this case is likely inflammatory or autoimmune in origin, rather than due to axonal degeneration from vitamin B12 deficiency. In addition, the negative NMO and MOG antibody tests effectively rule out neuromyelitis optica and MOG-associated disorders as alternative causes, leaving the possibility of clinically isolated syndrome (CIS) or an early demyelinating condition, such as multiple sclerosis (MS), as more probable explanations. Although vitamin B12 deficiency plays a significant role in the patient's neurological symptoms, the acute inflammatory nature of the optic neuritis makes it unlikely to be directly related to B12 deficiency [36, 37].

Treatment with intramuscular hydroxocobalamin was initiated promptly after the diagnosis was made, reflecting the importance of timely intervention in cases of vitamin B12 deficiency. This approach not only addresses the immediate deficiency but also helps mitigate potential long-term neurological complications associated with untreated pernicious anemia.

Neuropsychiatric symptoms from vitamin B12 deficiency generally improve gradually with treatment, with noticeable changes beginning around 3 months after initiation and continuing for up to a year. In some cases, neurological symptoms may temporarily worsen before improvement is observed. However, long-standing neurological deficits may become irreversible, especially if treatment is delayed [31].

In the case of this patient, there has been a noticeable improvement in symptoms, particularly cognitive disturbances and fatigue, following vitamin B12 treatment. The patient's electric shock-like sensations in the

head have become less frequent, although they have not fully resolved, and widespread musculoskeletal pain persists. These ongoing symptoms may reflect either the chronicity of the condition prior to treatment or the contribution of a concurrent diagnosis of fibromyalgia. Laboratory findings support the response to therapy, with the patient's vitamin B12 level increasing to 587 pg/mL and hemoglobin improving to 11.1 g/dL. While these improvements are promising, continued monitoring and further symptom management are necessary to address the residual neurological and musculoskeletal complaints.

Other teaching points

- Physicians should recognize that, at times, several concurrent conditions with overlapping symptoms and signs may collectively contribute to the overall clinical picture of the patient, rather than attributing it solely to a single explanatory cause.
- For patients presenting with nonspecific, chronic complaints that cannot be attributed to a specific disease or condition, physicians should request the most relevant and appropriate laboratory and imaging tests on the basis of the patient's history and physical examination to narrow down the differential diagnosis.
- Physicians should consider that vitamin B12 levels between 200 and 300 pg/mL (148 to 221 pmol/L) are considered borderline, suggesting a possible deficiency, and further testing with methylmalonic acid (MMA) and homocysteine may be necessary.
- Physicians should consider ruling out organic causes before making a psychiatric diagnosis.
- Physicians should consider the complex interplay between the mind (psych-) and body (soma) when evaluating patients.
- Physicians should consider reviewing all previous patient records to guide their diagnostic approach and narrow the differential diagnoses.
- Physicians should consider that about 25% of patients with pernicious anemia may present with neurological symptoms without classic signs of anemia or macrocytosis.
- Physicians should consider timely referral to higher levels of care and specialists whenever needed.
- Physicians should have a lower threshold for checking other autoimmune diseases in patients with pernicious anemia.
- Physicians should consider that duloxetine and gabapentin can be effective in managing neuropathy symptoms, regardless of the underlying cause.

Conclusion

This case highlights the diagnostic complexity of pernicious anemia, particularly when overlapping nonspecific symptoms and comorbidities, such as fibromyalgia, hypothyroidism, and autoimmune diseases, obscure the clinical picture and delay recognition. The patient's chronic, nonspecific symptoms—including fatigue, musculoskeletal pain, paresthesia, cognitive disturbances, and optic neuritis—were misattributed to multiple conditions for nearly a decade, with the absence of classic hematologic findings further complicating the diagnosis. Importantly, this case underscores that up to 25% of patients with pernicious anemia may present with neurological symptoms without anemia or macrocytosis, emphasizing the need for heightened clinical suspicion and timely diagnostic testing, even when vitamin B12 levels are borderline. The significant improvement in symptoms with parenteral vitamin B12 treatment reinforces the importance of early recognition to prevent irreversible complications. Furthermore, this case demonstrates the value of a systematic, multidisciplinary approach to evaluating complex presentations, underscoring the importance of considering multiple concurrent conditions, thoroughly reviewing medical history, and conducting a comprehensive diagnostic workup to achieve timely and accurate diagnosis.

Abbreviations

ACE	Angiotensin-converting enzyme
AMAG	Autoimmune metaplastic atrophic gastritis
ANA	Antinuclear antibody
CBC	Complete blood count
CFS	Chronic fatigue syndrome
CH50	Total complement activity
CIS	Clinically isolated syndrome
CSF	Cerebrospinal fluid
CT	Computed tomography
dsDNA	Double-stranded DNA
ENA	Extractable nuclear antigen
EMAG	Environmental metaplastic atrophic gastritis
FLAIR	Fluid-attenuated inversion recovery
HCV	Hepatitis C virus
HIV/AIDS	Human immunodeficiency virus/acquired immunodeficiency syndrome
IIF	Indirect immunofluorescence
IV	Intravenous
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
MDD	Major depressive disorder
MMA	Methylmalonic acid
MMSE	Mini-mental state examination
MOG	Myelin oligodendrocyte glycoprotein
MRI	Magnetic resonance imaging
MRV	Magnetic resonance venography
MS	Multiple sclerosis
NMO	Neuromyelitis optica
OCT	Optical coherence tomography
PA	Pernicious anemia
PCR	Polymerase chain reaction
SCD	Subacute combined degeneration
SLE	Systemic lupus erythematosus
SNRI	Serotonin–norepinephrine reuptake inhibitor
SS-A/Ro	Sjögren's syndrome antibody A

SS-B/La	Sjögren's syndrome antibody B
TPO	Thyroid peroxidase
TSH	Thyroid-stimulating hormone
UBOs	Unidentified bright objects

Supplementary Information

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Supplementary Material 1.

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Author contributions
AM was responsible for conceptualizing the study, curating the data, and drafting the initial manuscript. MR provided critical review and editing of the manuscript. She also supervised the study, providing guidance throughout the writing process and ensuring the manuscript's final form. Both authors read and approved the final manuscript.

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All data are included within the article.

Declarations

Ethics approval and consent to participate
Due to the observational nature of this case report, which does not involve any interventions or experimental procedures, formal ethical approval was not required.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
The authors declare that they have no competing interests.

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