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SEVERE ANEMIA AS AN INITIAL MANIFESTATION OF TYPE III B AUTOIMMUNE POLYGLANDULAR SYNDROME: CASE REPORT

ANEMIA GRAVE COMO MANIFESTAÇÃO INICIAL DA SÍNDROME POLIGLANDULAR AUTOIMUNE TIPO III B: RELATO DE CASO

ANEMIA GRAVE COMO MANIFESTACIÓN INICIAL DEL SÍNDROME POLIGLANDULAR AUTOINMUNE TIPO III B: CASO CLÍNICO

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ABSTRACT

Introduction: Autoimmune polyglandular syndromes (APS) are the association of two or more autoimmune endocrine diseases. The development of these conditions depends on both genetic and environmental factors. They are classified as type I, known as juvenile-onset PAS, and adult-onset PAS, which can be subdivided into types II to IV. These conditions are underdiagnosed, with a higher prevalence of adult-onset PAS in females and a peak diagnosis between the 2nd and 5th decades of life. Clinical manifestations depend on the association between the autoimmune endocrinopathies, and treatment consists of correction of endocrine dysfunctions, hormone replacement therapy when indicated, symptomatic control, and management of potential complications. Objective: To report a case of type III polyglandular autoimmune syndrome, with severe acute anemia as the initial manifestation. Report: A 58-year-old, previously healthy female patient presented with asthenia, dizziness, weight loss (approximately 10 kg in 2 years), and chronic pain in the lower limbs. She was

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admitted for management of severe anemia, with evidence of hemoglobin of 4.6 g/dL. During the investigation, tests showed thyroid alterations compatible with primary hypothyroidism (TSH: 12.5 µIU/mL; free T4: 0.82 ng/dL), in addition to significant hypovitaminosis B12. Following the investigation, atrophic gastritis and significant elevation of anti-TPO (>1300 IU/mL) were identified, allowing for the diagnosis of Polyglandular Syndrome type IIIB, due to autoimmune thyroiditis and pernicious anemia. The patient subsequently continued outpatient follow-up, with a good response to management of hormonal disorders. She also underwent further investigation to determine the possibility of new autoimmune disorders over the years. Conclusion: Autoimmune polyglandular syndrome type III is a condition with low incidence due to underdiagnosis. Early diagnosis and appropriate management are essential due to the impact on morbidity and mortality of the underlying conditions.

Keywords: Autoimmunity. Hypothyroidism. Atrophic Gastritis.

RESUMO

Introdução: As síndromes poliglandulares autoimunes (SPA) correspondem à associação de duas ou mais doenças endócrinas autoimunes. O desenvolvimento dessas condições depende tanto de fatores genéticos quanto ambientais. Classificam-se em SPA tipo I, sendo conhecida como juvenil, e SPA do adulto, a qual pode ser subdividida de II a IV. Ocorre um subdiagnóstico de tais condições, com uma maior prevalência da SPA do adulto no sexo feminino e pico de diagnóstico entre a 2ª e 5ª décadas de vida. As manifestações clínicas dependem da associação entre as endocrinopatias autoimunes, e o tratamento consiste na correção das disfunções endócrinas, reposição hormonal quando indicada, além de controle sintomático e manejo de potenciais complicações. Objetivo: Relatar um caso de síndrome autoimune poliglandular tipo III, tendo como manifestação inicial a anemia aguda grave. Relato: Paciente do sexo feminino, 58 anos, previamente hígida, apresentou astenia, tontura, perda ponderal (aproximadamente 10 kg em 2 anos) e dor crônica em membros inferiores. Foi internada para manejo de anemia grave, com evidência de hemoglobina de 4,6g/dL. Durante investigação, exames evidenciaram alterações tireoidianas compatíveis com hipotireoidismo primário (TSH: 12,5 µUI/mL; T4 livre: 0,82 ng/dL), além de importante hipovitaminose B12. Seguindo a linha investigativa, foi identificada gastrite atrófica e significativa elevação do anti-TPO (>1300 UI/mL), oportunizando o diagnóstico de Síndrome Poliglandular tipo III B, pela tireoidite autoimune e anemia perniciosa. Logo, a paciente seguiu em acompanhamento ambulatorial, com boa resposta ao manejo das desordens hormonais, como, também, em acompanhamento investigativo pela possibilidade diagnóstica de novos acometimentos autoimunes ao longo dos anos. Conclusão: A síndrome poliglandular autoimune tipo III é uma condição de baixa incidência devido ao subdiagnóstico, sendo indispensável o diagnóstico precoce e o manejo adequado pelo impacto na morbimortalidade das patologias envolvidas.

Palavras-chave: Autoimunidade. Hipotireoidismo. Gastrite Atrófica.

RESUMEN

Introducción: Los síndromes poliglandulares autoinmunes (SAP) son la asociación de dos o más enfermedades endocrinas autoinmunes. El desarrollo de estas afecciones depende de factores genéticos y ambientales. Se clasifican en tipo I, conocido como SAP de inicio juvenil, y SAP de inicio adulto, que puede subdividirse en tipos II a IV. Estas afecciones están infradiagnosticadas, con una mayor prevalencia de SAP de inicio adulto en mujeres y un pico de diagnóstico entre la segunda y la quinta décadas de la vida. Las manifestaciones clínicas

dependen de la asociación entre las endocrinopatías autoinmunes, y el tratamiento consiste en la corrección de las disfunciones endocrinas, terapia hormonal sustitutiva cuando esté indicada, control sintomático y manejo de las posibles complicaciones. Objetivo: Reportar un caso de síndrome autoinmune poliglandular tipo III, con anemia aguda severa como manifestación inicial. Informe: Paciente femenina de 58 años, previamente sana, que presentó astenia, mareos, pérdida de peso (aproximadamente 10 kg en 2 años) y dolor crónico en miembros inferiores. Ingresó para tratamiento de anemia severa, con evidencia de hemoglobina de 4,6 g/dL. Durante la investigación, las pruebas mostraron alteraciones tiroideas compatibles con hipotiroidismo primario (TSH: 12,5 µUI/mL; T4 libre: 0,82 ng/dL), además de hipovitaminosis B12 significativa. Después de la investigación, se identificó gastritis atrófica y elevación significativa de anti-TPO (>1300 UI/mL), lo que permitió el diagnóstico de Síndrome Poliglandular tipo IIIB, debido a tiroiditis autoinmune y anemia perniciosa. Posteriormente, la paciente continuó con seguimiento ambulatorio, con buena respuesta al tratamiento de los trastornos hormonales. También se sometió a investigación adicional para determinar la posibilidad de nuevos trastornos autoinmunes a lo largo de los años. Conclusión: El síndrome poliglandular autoinmune tipo III es una afección con baja incidencia debido al infradiagnóstico. El diagnóstico temprano y el tratamiento adecuado son esenciales debido al impacto en la morbilidad y la mortalidad de las afecciones subyacentes.

Palabras clave: Autoinmunidad. Hipotiroidismo. Gastritis Atrófica.

1 INTRODUCTION

According to Kahaly & Frommer (2018), the concomitant presence of at least two autoimmune endocrinopathies characterizes autoimmune polyglandular syndromes (APS), which present significant clinical heterogeneity. According to Eira et al. (2017), these syndromes can manifest with prolonged intervals between the first and second glandular autoimmune involvement. In addition, it is possible to associate it with non-endocrine systemic autoimmune diseases (DAIS). The first report of this association dates back to 1855, involving vitiligo, pernicious anemia, and adrenal insufficiency (Cutolo, 2013). However, the etiology of these conditions remains elusive (Kahaly & Frommer, 2018). It is known, however, that there is T lymphocyte infiltration directed at target organs, with the influence of genetic and environmental factors, such as infections, hormonal changes, and smoking (Apolinario et al., 2022).

It is important to highlight that PASs differ in terms of age of onset, which is the basis for their classification into two major subtypes: the juvenile form, also called type I, and the adult form, which covers types II to IV (Eira et al., 2017). The first categorization into four types was proposed by Neufeld & Blizzard in 1980, based on the different clinical combinations of associated autoimmune diseases (Tincani et al., 2008).

Specifically with regard to Autoimmune Polyglandular Syndrome type III, it is an autosomal dominant inherited condition of polygenic nature (Tavares et al., 2023). This form is subdivided into subtypes III A, III B, III C, and III D, with the mandatory criterion being the presence of an autoimmune thyroid disease — such as Hashimoto's thyroiditis, idiopathic myxedema, asymptomatic thyroiditis, or Graves' disease — associated with at least one other autoimmune disease, as long as there is no adrenal insufficiency (Addison's disease), which differentiates it from the type II form.

The classification into subtypes is based on the organ systems additionally affected: subtype III A involves other endocrine diseases, such as type 1 diabetes mellitus; III B is characterized by autoimmune gastrointestinal manifestations, such as atrophic gastritis or pernicious anemia; subtype III C is defined by cutaneous, hematological, or neurological involvement, which is the most prevalent among the subtypes of type III; finally, type III D is associated with connective tissue diseases or vasculitis, including rheumatologic manifestations, such as systemic lupus erythematosus.

Despite the recognized global underdiagnosis of PAS, it is estimated that the type III form corresponds to approximately 40% of cases, making it the most frequent subtype, often associated with non-glandular autoimmune diseases (Chaparro et al., 2014).

It is admitted that complex interactions between genetic, epigenetic, and environmental factors contribute to the development of PAS, whose early detection is essential, given their high morbidity and mortality (Tavares et al., 2023). Regarding polygenic inheritance, genes located on chromosome 6, especially those of the major histocompatibility complex (MHC), play a predominant role (Kahaly & Frommer, 2018).

From an epidemiological point of view, underdiagnosis still represents a challenge for the precise determination of the prevalence of the different clinical forms of APS (Chaparro et al., 2014). An annual incidence of 1:100,000 inhabitants is estimated for the type I form. For the other subtypes, the prevalence is 1:20,000, with an annual incidence ranging from 1 to 2 per 100,000 population. Incomplete clinical presentation can reach a prevalence of up to 150 per 100,000 people (Betterle & Zanchetta, 2003). There is also a predominance of females, representing about 75% of cases (Apolinario et al., 2022). The diagnosis of the adult form, in turn, usually occurs after the second decade of life, with a peak of clinical manifestations between the fourth and fifth decades, depending on the combinations of DAIS present (Vilar; Hansen; Kahaly, 2025).

Given the relevance of a condition that is still largely underdiagnosed (Pham-Dobor et al., 2020), the present study aims to report the case of a female patient diagnosed with type III B PAS, established from the clinical investigation of severe acute anemia.

2 OBJECTIVE

OBJECTIVE: To report a case of Autoimmune Polyglandular Syndrome type III B, whose initial manifestation was severe acute anemia, with emphasis on diagnostic workup, the importance of early identification and appropriate therapeutic management.

3 CASE DESCRIPTION

A 58-year-old female patient from Recife, Pernambuco, Brazil, worked as a gym receptionist, who was previously healthy. The patient presented asthenia, dizziness, unintentional weight loss of approximately 10 kg over two years, and chronic pain in the lower limbs, associated with slowly progressing paresthesia, with more than four months of

evolution. He also reported a previous diagnosis of anemia about one year earlier, treated with ferric oxide saccharate parenterally, with only partial clinical improvement of symptoms.

The patient sought care at an emergency unit, where initial laboratory tests revealed severe acute anemia, with hemoglobin (Hb) of 4.6 g/dL, maintaining a white blood cell count and platelet count within the reference limits. Hormone measurements were requested, which demonstrated primary hypothyroidism (TSH: 12.5 µIU/mL; Free T4: 0.82 ng/dL; T3: 0.6 ng/dL) and significant hypovitaminosis B12 (serum level: 50 pg/mL; reference value > 210 pg/mL), with folate within the normal range. Red blood cell concentrate was transfused and hormone replacement therapy with levothyroxine (75 µg/day) was instituted, in addition to vitamin supplementation. The patient was then referred to a referral service in internal medicine for diagnostic investigation and specialized clinical management.

On hospital admission, he reported a recent episode of viral syndrome with fever, myalgia, and impairment of the general condition, raising the hypothesis of antecedent arbovirus. She denied dietary changes, recent travel, use of alcohol, smoking or other drugs, as well as previous surgeries or hospitalizations. She reported a remote history of childhood asthma and allergy to dipyrone. There was no family history of relevant comorbidities, autoimmune diseases, neoplasms, or consanguinity.

On physical examination, the patient presented evident weight loss, pale mucous membranes, and lower limb edema (1+/4+), with no other significant alterations in the cardiovascular, respiratory, abdominal, or neurological systems. Empirical treatment for intestinal parasitosis, parenteral supplementation with B-complex on alternate days, and maintenance of levothyroxine were initiated.

In the continuation of the investigation, complementary tests revealed an increase in lactate dehydrogenase (LDH: 985 U/L), with bilirubins, haptoglobin and reticulocytes normal. Serology for hepatitis B and C, HIV, and syphilis was negative, with evidence of vaccine immunity for hepatitis B. Thyroid profile was repeated after six weeks of replacement and antithyroid peroxidase antibody (anti-TPO) was requested to be rescued in outpatient follow-up.

Ultrasound of the total abdomen showed only hepatic hemangioma with no clinical repercussions. In view of the vitamin B12 deficiency and anemia, the hypothesis of pernicious anemia was suggested, although the anti-intrinsic factor antibody was not available at the service. Upper gastrointestinal endoscopy revealed moderate enanthematous pangastritis,

with pale mucosa and visualization of the submucosal vascular network, suggestive of atrophic gastritis, and biopsy was performed for histopathological confirmation.

During hospitalization, he received a new transfusion of packed red blood cells, reaching post-transfusion hemoglobin levels of 10 g/dL and hematocrit of 29.4%, with mild anisocytosis, maintaining normal leukocyte and platelet counts. The patient had preserved renal and hepatic function, with no hydroelectrolyte disturbances. In view of the clinical improvement and hemodynamic stability, he was discharged from the hospital, with guidance on alarm signs and early return to the outpatient clinic for the rescue of pending tests and diagnostic conclusion. The prescription of levothyroxine and B complex was maintained, with guidance for outpatient follow-up.

At the outpatient follow-up, three months after discharge, she was asymptomatic and reported complete resolution of symptoms. The new tests showed a high anti-TPO titer (>1300 IU/mL), confirming autoimmune thyroidopathy. Thyroid function was normalized (TSH: 1.080 μIU/mL) and anemia was resolved, with hemoglobin of 13.8 g/dL and hematocrit of 42.2%, in a normocytic and normochromic pattern. Leukocyte, platelets, lipid and glycemic profile remained within the reference parameters, ruling out diabetes mellitus or dyslipidemia. Vitamin B12, however, remained below the reference value (189 pg/mL), which justified the continuation of monthly intramuscular replacement (5,000 μg).

The result of the histopathological study of the gastric biopsy, retrieved late, showed moderate chronic erosive gastritis in the antral mucosa, with mild atrophy, absence of intestinal dysplasia or metaplasia, and positivity for Helicobacter pylori by Giemsa staining. In view of the patient's absence at the time of obtaining the report, it was decided to return again to the outpatient clinic to prescribe eradication treatment.

Thus, the diagnosis of Autoimmune Polyglandular Syndrome type IIIB was concluded, characterized by the presence of pernicious anemia associated with atrophic gastritis and autoimmune hypothyroidism, with a recommendation for regular clinical follow-up to monitor comorbidities and surveillance for the possible manifestation of other autoimmune diseases associated with the syndrome.

4 DISCUSSION

The evident clinical manifestation of an endocrine autoimmune disease often raises the suspicion of other associated insufficiencies (Marui, 2016). This association stems from the natural course of Systemic Endocrine Autoimmune Diseases (ISAD), in which the

progression from latent and subclinical stages to clinical conditions is common, often associated with the presence of circulating specific autoantibodies (Betterle et al., 2023). In this context, autoimmune polyglandular syndromes (APS) are complex and heterogeneous clinical entities, with a wide variability of clinical manifestations (Tavares et al., 2023).

In the present case, the patient initially presented with severe acute anemia, which served as a starting point for a broader diagnostic investigation, since multiple etiologies may be involved. Faced with normocytic and normochromic anemia, with iron parameters within the normal range, it was necessary to search for underlying endocrine causes (Betterle et al., 2023). Hypothyroidism was identified as a plausible cause, and the diagnosis was confirmed by laboratory tests, given the low specificity of typical clinical manifestations (Means et al., 2024). Laboratory findings of total T4, reduced free T4, and T3, associated with increased TSH, confirmed hormone deficiency (Jonklaas et al., 2014). The etiological investigation revealed high titers of anti-TPO, a classic serological marker of autoimmune thyroiditis, which reinforces the autoimmune etiology of hypothyroidism.

In addition, the patient had unintentional weight loss greater than 5% of usual body weight in an interval of 6 to 12 months, with no reported change in appetite or bowel habit (Gupta et al., 2024). Considering that non-malignant causes are the most prevalent in individuals over the fifth decade of life (Gaddey & Holder, 2014), the investigation was expanded, and hypovitaminosis B12 was found with normal serum levels of folic acid. B12 deficiency can explain several symptoms of the patient, including asthenia, weight loss, muscle weakness, sensory changes, and neuropsychiatric symptoms, such as depression, delusions, and postural hypotension (Means et al., 2024).

Vitamin B12 is an essential cofactor in methylation processes, which are fundamental for DNA integrity and cell metabolism. Its deficiency results in biochemical disruptions with significant clinical consequences (Hunt; Harrington; Rodinson, 2014). In this case, B12 deficiency contributed significantly to the neurological symptoms observed. In the face of suggestive clinical signs, replacement is indicated empirically, even if laboratory tests are not conclusive (Means et al., 2024).

Autoimmune metaplastic atrophic gastritis, often associated with vitamin B12 deficiency, was also diagnosed. Although intrinsic factor measurement has not been performed, the clinical and laboratory combinations allow the diagnosis of pernicious anemia. This condition has a genetic predisposition and can be triggered by environmental factors, and is often associated with other autoimmune diseases, such as vitiligo, type 1 diabetes

mellitus, and thyroid diseases (Souto et al., 2020). In the case under analysis, the patient also had Helicobacter pylori infection and predominantly bodily gastric atrophy, which contributes to hypochlorhydria, loss of pepsin and intrinsic factor, culminating in vitamin B12 malabsorption and development of pernicious anemia (Jansen; Lamont; Meyer, 2024). Autoimmune atrophic gastritis is more prevalent in women and can coexist with autoimmune thyroid disease in up to one-third of cases (Rodriguez et al., 2015).

Autoimmune thyroid diseases are the most prevalent among DAIS, and up to one-third of patients with these conditions develop other autoimmune diseases throughout their lives (Eira et al., 2017). The diagnosis of thyroid autoimmune involvement can be delayed, and is often established after exclusion of other syndromes. It is important to emphasize that ISDs are chronic conditions, requiring continuous follow-up (Vilar; Hansen; Kahaly, 2025).

In this context, the clinical case is compatible with Autoimmune Polyglandular Syndrome type III, subtype B, characterized by the association of thyroid disease with gastrointestinal autoimmune disease, such as atrophic gastritis, celiac disease, autoimmune hepatitis, or primary biliary cirrhosis (Navarrete-Tapia, 2013). The absence of adrenal gland involvement rules out the diagnosis of type II PAS (Vilar; Hansen; Kahaly, 2025). Thus, comprehensive autoimmune evaluation, including regular monitoring of autoantibodies and hormonal parameters, is essential (Subtil et al., 2024).

The therapeutic management of PAS involves hormone replacement, symptomatic relief, and prevention of complications (Vilar; Hansen; Kahaly, 2025). In hypothyroidism, levothyroxine is used at an initial dose of 1.6–1.8 µg/kg/day, adjusted based on TSH levels, assessed every 4 to 6 weeks (Jonklaas et al., 2014). After stabilization, TSH should be monitored annually, or more frequently, as clinically needed (Ross; Cooper; Mulder, 2024).

It is relevant to note that autoimmune gastritis can compromise levothyroxine absorption due to hypochlorhydria and the presence of autoantibodies against parietal cells, which affect the gastric proton pump (Jansen; Lamont; Meyer, 2024). Gastric atrophy associated with achlorhydria interferes with the absorption of B12 and levothyroxine in the small intestine (Hunt; Harrington; Rodinson, 2014).

As for vitamin B12 replacement in cases of pernicious anemia, the parenteral (intramuscular) route is preferred. Although there is no consensus on the optimal regimen, 1,000 µg/week for four weeks is proposed, followed by a monthly maintenance dose (Means & Fairfield, 2024).

Finally, it is noteworthy that recent advances in genetic testing and autoantibody detection have contributed to the early diagnosis and treatment of PAS. The incorporation of genomic approaches may allow the early introduction of immunomodulatory therapies, with the aim of mitigating the autoimmune process before the development of irreversible organic lesions (Sperling; Angelousi; Yau, 2000).

5 CONCLUSION

From the reported case, the diagnostic complexity inherent to Autoimmune Polyglandular Syndrome type III is observed, due to its multifactorial etiology. In the presence of an autoimmune endocrinopathy, it is essential to investigate the possible coexistence of other autoimmune manifestations, considering the underlying genetic potential. Early recognition of these additional manifestations is essential to reduce the diagnostic delay and enable a more effective therapeutic intervention.

The path to definitive diagnosis is, in general, prolonged, mainly due to the subclinical course that often characterizes the initial evolution of the syndrome, favoring underdiagnosis. In this context, the early diagnostic definition, based on the available clinical and laboratory resources, is essential for the timely initiation of treatment. In addition, longitudinal and individualized follow-up, with a biopsychosocial approach, is of great relevance and can positively modify the natural history of the disease.

REFERENCES

Apolinario, M., et al. (2022). Autoimmune polyglandular syndrome type 3: A case report and literature review. Clinical Case Reports, 10(2), e05391. https://doi.org/10.1002/ccr3.5391

Betterle, C., & Zanchetta, R. (2003). Update on autoimmune polyendocrine syndromes (APS). Acta Biomedica, 74(1), 9–33.

Betterle, C., et al. (2023). Type 3 autoimmune polyglandular syndrome (APS-3) or type 3 multiple autoimmune syndrome (MAS-3): An expanding galaxy. Journal of Endocrinological Investigation, 46(4), 643–665. https://doi.org/10.1007/s40618-022-01994-1

Chaparro, J. M. O., et al. (2014). Type III polyglandular autoimmune syndrome: A case report. Revista Española de Geriatría y Gerontología, 49(5), 244–245. https://doi.org/10.1016/j.regg.2014.03.003

Cutolo, M. (2014). Autoimmune polyendocrine syndromes. Autoimmunity Reviews, 13(2), 85–89. https://doi.org/10.1016/j.autrev.2013.07.006

Eira, C., et al. (2017). Caso clínico - Síndrome poliglandular autoimune tipo III. Revista Portuguesa de Endocrinologia, Diabetes e Metabolismo, 12(2), 200–205. https://doi.org/10.1016/j.rpedm.2017.03.005

Gaddey, H. L., & Holder, K. (2014). Unintentional weight loss in older adults. American Family Physician, 89(9), 718–722.

Gupta, R., et al. (2024). Approach to the patient with unintentional weight loss. In UpToDate. Retrieved October 2024, from https://www.uptodate.com/contents/approach-to-the-patient-with-unintentional-weight-loss

Hunt, A., Harrington, D., & Robinson, S. (2014). Vitamin B12 deficiency. BMJ, 349, g5226. https://doi.org/10.1136/bmj.g5226

Jansen, P. J., Lamont, J. T., & Meyer, C. (2024). Metaplastic (chronic) atrophic gastritis. In UpToDate. Retrieved September 2024, from https://www.uptodate.com/contents/metaplastic-chronic-atrophic-gastritis

Jonklass, J., et al. (2014). Guidelines for the treatment of hypothyroidism: Prepared by the American Thyroid Association task force on thyroid hormone replacement. Thyroid, 24(12), 1670–1751. https://doi.org/10.1089/thy.2014.0028

Kahaly, G. J., & Frommer, L. (2018). Polyglandular autoimmune syndromes. Journal of Endocrinological Investigation, 41(1), 91–98. https://doi.org/10.1007/s40618-017-0740-9

Marui, S. (2016). Doença poliglandular autoimune. In M. A. Martins et al. (Eds.), Clínica médica, volume 5: Doenças endócrinas e metabólicas, doenças ósseas, doenças reumatológicas (2nd ed., pp. 224–231). Manole.

Means, R. T., et al. (2024). Clinical manifestations and diagnosis of vitamin B12 and folate deficiency. In UpToDate. Retrieved July 2024, from https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-vitamin-b12-and-folate-deficiency

Means, R. T., et al. (2024). Diagnostic approach to anemia in adults. In UpToDate. Retrieved October 2024, from https://www.uptodate.com/contents/diagnostic-approach-to-anemia-in-adults

Means, R. T., & Fairfield, K. M. (2024). Treatment of vitamin B12 and folate deficiencies. In UpToDate. Retrieved June 2024, from https://www.uptodate.com/contents/treatment-of-vitamin-b12-and-folate-deficiencies

Navarrete-Tapia, U. (2013). Síndrome poliglandular autoimune. Revista Médica del Hospital General de México, 76(3), 143–152.

Pham-Dobor, G., et al. (2020). Prevalence of other autoimmune diseases in polyglandular autoimmune syndromes type II and III. Journal of Endocrinological Investigation, 43(1), 1–9. https://doi.org/10.1007/s40618-019-01069-6

Rodriguez, E. S., et al. (2015). Pernicious anemia: From past to present. Revista Clínica Española, 215(5), 276–284. https://doi.org/10.1016/j.rce.2015.02.001

Ross, D., Cooper, D. S., & Mulder, J. E. (2024). Diagnosis of and screening for hypothyroidism in nonpregnant adults. In UpToDate. Retrieved July 2024, from https://www.uptodate.com/contents/diagnosis-of-and-screening-for-hypothyroidism-in-nonpregnant-adults

Souto, J. T. D. F., et al. (2020). Predictive risk factors for autoimmune thyroid diseases in patients with pernicious anemia. Medicina Clínica, 154(9), 344–347. https://doi.org/10.1016/j.medcli.2019.06.022

Sperling, M. A., Angelousi, A., & Yau, M. (2024). Autoimmune polyglandular syndromes. In K. R. Feingold, B. Anawalt, M. R. Blackman, et al. (Eds.), Endotext. MDText.com, Inc. https://www.ncbi.nlm.nih.gov/books/NBK279151/

Subtil, J., et al. (2024). Autoimmune polyglandular syndrome type 3: A case report. Cureus, 16(12), e76152. https://doi.org/10.7759/cureus.76152

Tavares, F. R. S., et al. (2023). Síndromes poliglandulares autoimunes: Uma revisão geral em busca de novas evidências. Arquivos de Ciências da Saúde da UNIPAR, 27(9), 52825300. https://doi.org/10.25110/arqsaude.v27i9.2023-024

Tincani, A., et al. (2008). Autoimmune polyendocrine syndromes. In Y. Shoenfeld, R. Cervera, & M. E. Gershwin (Eds.), Diagnostic criteria in autoimmune diseases (pp. 265–269). Humana Press.

Vilar, L., Hansen, M. P., & Kahaly, G. (2025). Síndromes poliglandulares autoimunes. In L. Vilar et al. (Eds.), Endocrinologia clínica (8th ed., pp. 1139–1144). Guanabara Koogan.