CASE REPORT

From blemishness to pathology: Reflections on a case of alopecia

Valerio Massimo Magro

Echocardiography Unit Department of Internal Medicine and Geriatry, University of Campania "Luigi Vanvitelli", Naples, Italy; International School of Aesthetic Medicine, Isola Tiberina - Gemelli Isola Hospital, Rome, Italy

Abstract. Alopecia areata is an organ-specific autoimmune disorder that targets anagen phase hair follicles. Taking charge of a patient with this problem is a recurring task by both dermatologists and aesthetic physicians. Less frequently, this problem may be brought to the attention of a general practitioner, internist, or endocrinologist. The immune system recognizes autologous constituents of the organism, triggering immunological responses that cause different, even multiple, pathologies in an individual. Alopecia, a complex condition represents a serious imperfection but can sometimes be a sign of autoimmunity. We present a clinical case that has come to our attention, the study of which allows us to underline the potential connection of this disease with many other autoimmune pathologies, as well as serious ones, which in the adult subject must be investigated for the purpose of early diagnosis and prompt intervention, not only aesthetic purposes.

Key words: alopecia areata, anemia, blemishes, polyglandular autoimmune syndromes, thyroiditis

Introduction

Alopecia areata is a clinical problem that is becoming more common in women. Although there are various classifications that have attempted to systematize this imperfection, the presence of alopecia should induce the physician who takes charge of this patient to take charge of the patient more internally than dermatologically, in order not to risk missing clinical signs and symptoms that can be indicative of important pathologies^{1,2}. In fact, the immune system recognizes autologous constituents of the organism, triggering immunological responses that cause different, even multiple, pathologies in an individual. Alopecia, a complex condition, represents a serious imperfection but can sometimes be a sign of autoimmunity. We present a clinical case report.

Case report

A 34-year-old patient with alopecia areata was investigated; the woman, in good general condition and health, had been complaining of the presence of this imperfection for a few months, with natural repercussions on social interactions and relationships. Weight: 50 kg; height: 170 cm (body mass index - BMI - 17.3, indicative of an underweight situation). There was no history of important pathologies. The patient reported a non-specific allergy to dust mites. Vital signs: blood pressure was 100/80 mm Hg, HR 70 heartbeats, rhythmic, 17 breaths per minute, normal peripheral arterial saturation in room air, apyrexia. The patient presented a patch of baldness located on the parietal level; in the absence of any association with hair loss elsewhere on the body. She also had a normal development

of primary and secondary sex organs, and normal skin appendages. Her thyroid neither visible, nor palpable. Her abdomen was tense, swollen, with pain in the mesogastric area on deep palpation. It was decided to deepen the visit with some routine blood tests and a thyroid ultrasound and a normal blood chemistry routine. The normal thyroid structure was characterized by antibody positivity (anti-TPO 249 IU/ml, n.v. <9; anti-Tg 400 IU/ml, n.v. <20) with inhomogeneity on ultrasound, as from Hashimoto's thyroiditis. After 8 months she returned to outpatient control due to asthenia and muscle weakness. New tests showed thyroid axis integrity, mild anemia, MCV 98 fl and positive gastric parietal cell antibodies (Figure 1). Indices of inflammation, ANA, ENA, Anti-Ach-R, LKM, AMA, ASMA, GAD, ICA, serology for herpes viruses and toxoplasma, brain MRI, adrenal study, were performed: all exams demonstrated negative outcomes, excluding an appendicular disease as a cause of abdominal pain.

Discussion

Thyroid hormones are required for the physiological growth and maintenance of hair follicles. Based on the conclusions of several works, including that of Patel D et coll.³ ("routine thyroid function screening should be restricted to alopecia areata patients with a medical history of Down syndrome, personal history of atopy, a family history of thyroid disease, or clinical



Figure 1. Past and present medical history of the patient, together with the results of the antibody screening.

findings (goiter) suggestive of potential thyroid dysfunction in the individual patient") we investigated the thyroid function taking into account the positive allergy history; these conclusions are recently reaffirmed in the study by Popa et al.⁴. The thyrogastric syndrome is still a current and frequent pathology. The association between chronic atrophic gastritis and autoimmune thyroid disease seems to share a common pathogenetic mechanism involving a complex interaction between genetic susceptibility, embryological derivation, and environmental factors⁵. The concept that autoimmune diseases are characterized by shared (common) threads is well illustrated by their propensity to co-associate in a patient or direct relatives, as coexistences or overlaps. Similarly, laboratory abnormalities can be associated with other altered laboratory parameters, indicators of associated pathologies. For example, adult patients with autoimmune thyroid disease have hypergastrinaemia in 35% of cases^{6,7}: of these patients with autoimmune thyroiditis, an association with autoimmune gastritis was observed in 100% of cases, with anemia in 82%, while 68% of these patients have gastric parietal cell antibodies⁸. Autoimmune thyroid diseases are also a feature of type 3 polyglandular autoimmune syndromes: the recent review by Betterle C et coll.⁹ describes the wide spectrum of the combinations and the intricate relationships between this condition and the other distinct autoimmune diseases, excluding Addison's disease. These combinations are collectively termed type 3 Autoimmune Polyglandular Syndrome (APS-3). According to the old classification of Neufeld and Blizzard, this syndrome is divided into a subtype 3a (characterized by the presence of type 1 diabetes), a subtype 3b (associated with pernicious anemia, vitiligo, and chronic atrophic gastritis) and a sub-type 3c (with alopecia and myasthenia)¹⁰. The APS of adults manifests itself as one of the major autoimmune diseases (such as adrenal failure, Grave's disease, or type 1 diabetes) and minor autoimmune disorders (vitiligo and indeed the presence of alopecia) preceding the development of autoimmune deficiency of major endocrine glands¹¹. Nonetheless, patients with autoimmune thyroid disease may also develop other autoimmune diseases (not currently included in APS 3), and may present in

circulation one, or more, tissue-specific autoantibodies without the presence of any disease (incomplete forms) (Figure 2). For a period of time, Hamilton DV described the association of Hashimoto's thyroiditis and pernicious anemia with systemic lupus erythematosus¹²; a few years later the same association was described but in the presence of Sjogren's syndrome and CREST syndrome¹³ or miastenia¹⁴⁻¹⁶. An increased association of pernicious anemia with other autoimmune diseases, such as type 1 diabetes (3%-4%), and in particular, autoimmune thyroiditis (3%-32%) has been reported, too. Among an unpublished series of Lahner E et coll. of 177 patients with pernicious anemia, 41% had associated autoimmune thyroiditis and 10% presented with vitiligo or alopecia¹⁷⁻²⁰. The scientific literature also reports patient case reports suffering from autoimmune-type chronic active hepatitis associated with vitiligo, nail dystrophy, alopecia areata and a variant of liver kidney microsomal (LKM) autoantibodies²¹. The relationships between a broad spectrum of autoimmune diseases imply a need for surveillance of patients for potential secondary autoimmune disease processes, therefore, after a diagnosis of alopecia areata is made, a detailed personal and family history for atopy, thyroid disease, coeliac and other autoimmune disorders should be obtained as also recommended by the most recent Italian guidelines on the subject²² and how it was done in the clinical case examined.

Conclusions

Taking charge of a patient with alopecia is a recurrent task by dermatologists and aesthetic physicians. Less frequently, this problem may be brought to the attention of a general practitioner, internist, or endocrinologist. The behavior adopted made it possible to reveal, starting from alopecia, thyrogastric syndrome and to exclude other possibly associated pathologies: type 1 diabetes, myasthenia gravis, multiple sclerosis, Schidt's syndrome. The possible association of alopecia with other pathologies of the "autoimmune galaxy" obliges the doctor to pay the utmost attention, in addition to the treatment of blemishes, to protect the health of the patients and the prevention of possible organ damage.



Figure 2. Diagram of autoimmune diseases and associated diseases, grouped into four large groups, with autoimmune-based thyroid disorders.

Originality of the Manuscript: The submitted manuscript was not simultaneously sent to another journal or it is not presently being evaluated by another journal. A part of the content of the manuscript has been previously published in the 36th National Congress of the Italian Society of Aesthetic Medicine (SIME), 15-17 may 2015.

Conflict of Interests: The authors state that they have no conflicts of interest.

Grant or Other Financial Support: None.

Patient Consent: Anonymous data collection. Patient consent form is not necessary.

References

- 1. Wambier CG, King BA. Rethinking the classification of alopecia areata. J Am Acad Dermatol. 2019; 80(2):e45.
- Camacho-Martínez FM. Hair loss in women. Semin Cutan Med Surg. 2009; 28(1):19-32.
- 3. Patel D, Li P, Bauer AJ, Castelo-Soccio L. Screening Guidelines for Thyroid Function in Children With Alopecia Areata. JAMA Dermatol. 2017; 153(12): 1307-1310.
- Popa A, Carsote M, Cretoiu D, Dumitrascu MC, Nistor CE, Sandru F. Study of the Thyroid Profile of Patients with Alopecia. J Clin Med. 2023; 12(3):1115.
- Lahner E, Conti L, Cicone F, et al. Thyro-entero-gastric autoimmunity: Pathophysiology and implications for patient management. Best Pract Res Clin Endocrinol Metab. 2020; 34(1):101373.

- 6. Vierhapper H, Nowotny P, Bieglmayer Ch, Gessl A. Prevalence of hypergastrinemia in patients with hyper- and hypothyroidism: impact for calcitonin? Horm Res. 2002; 57(3-4): 85-9.
- 7. Paloheimo L, Hendolin P, Carita Eklund C, et al. Biohit GastroPanel® test in Screening of the Patients with Autoimmune Thyroid Disease (AITD) for Autoimmune Atrophic Gastritis (AAG). Available on the site: https:// www.biohithealthcare.com/wp-content/uploads/2018/12 /gp-screening-of-aitd-patients-21-1.pdf
- Rosatello A. Le malattie sempre meno rare nella medicina moderna. Associazione ONLUS RARE-CEF. Available on the site: https://www.yumpu.com/it/document/view /16296746/rosatello-sindrome-tireogastricapdf-rarecef -onlus-alba
- 9. Betterle C, Furmaniak J, Sabbadin C, Scaroni C, Presotto F. Type 3 autoimmune polyglandular syndrome (APS-3) or type 3 multiple autoimmune syndrome (MAS-3): an expanding galaxy. J Endocrinol Invest. 2023; 46(4): 643-665.
- Betterle C, Zanchetta R. Update on autoimmune polyendocrine syndromes (APS). Acta Biomed. 2003; 74(1):9-33.
- Larina AA, Shapoval'iants OS, Mazurina NV, Troshina EA. Diagnostics and treatment of polyglandular syndrome of adults. Klin Med (Mosk). 2012; 90(8):64-6.
- Hamilton DV. Systemic lupus erythematosus in a patient with Hashimoto's thyroiditis and pernicious anaemia. J R Soc Med. 1978; 71(2):147-9.
- Saad-Dine Y, Macurak RB, Beasley EW, Ward JA. Hashimoto's thyroiditis, pernicious anemia, Sjogren's syndrome, and CRST syndrome – a case report. J Med Assoc Ga. 1981; 70(3):187-9.
- Durston JH. Myasthenia gravis, Hashimoto's disease and pernicious anaemia. Postgrad Med J. 1969; 45(522): 290-1.
- Kurata Y, Yamada A, Kyo S, et al. A case of Hashimoto's thyroiditis, myasthenia gravis and pernicious anemia (author's transl)]. Rinsho Ketsueki. 1980; 21(7):1033-7.

- 17. De Block CE, De Leeuw IH, Van Gaal LF. Autoimmune gastritis in type 1 diabetes: a clinically oriented review. J Clin Endocrinol Metab. 2008; 93(2):363-371.
- Lahner E, Annibale B. Pernicious anemia: new insights from a gastroenterological point of view. World J Gastroenterol. 2009; 15(41):5121-8.
- Kjaergaard AD, Teumer A, Marouli E, et al. Thyroid function, pernicious anemia and erythropoiesis: a two-sample Mendelian randomization study. Hum Mol Genet. 2022; 31(15):2548-2559.
- 20. Tzellos TG, Tahmatzidis DK, Lallas A, Apostolidou k, Goulis DG. Pernicious anemia in a patient with Type 1 diabetes mellitus and alopecia areata universalis. J Diabetes Complications. 2009; 23(6):434-7.
- Sacher M, Blümel P, Thaler H, Manns M. Chronic active hepatitis associated with vitiligo, nail dystrophy, alopecia and a new variant of LKM antibodies. J Hepatol. 1990; 10(3):364-9.
- Rossi A, Muscianese M, Piraccini BM, et al. Italian Guidelines in diagnosis and treatment of alopecia areata. G Ital Dermatol Venereol. 2019; 154(6):609-623.

Correspondence:

Received: 18 July 2024

Accepted: 28 October 2024

Valerio Massimo Magro, MD

MD, Echocardiography Unit Department of Internal Medicine and Geriatry, University of Campania "Luigi Vanvitelli", Piazza L. Miraglia 2, 80100, Naples, Italy Trained in aeshetic medicine at the International School of

Aesthetic Medicine, Isola Tiberina - Gemelli Isola Hospital, Rome, Italy

E-mail: valerio_magro@hotmail.com