

Krzewski Szymon, Baranowski Mateusz, Wzorek Katarzyna. Autoimmune pituitary inflammation. *Journal of Education, Health and Sport*. 2022;12(2):11-15. eISSN 2391-8306. DOI <http://dx.doi.org/10.12775/JEHS.2022.12.02.001>
<https://apcz.umk.pl/JEHS/article/view/JEHS.2022.12.02.001>
<https://zenodo.org/record/5946864>

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of December 1, 2021. No. 32343. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical Culture Sciences (Field of Medical sciences and health sciences); Health Sciences (Field of Medical Sciences and Health Sciences).

Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 1 grudnia 2021 r. Lp. 32343. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przynależy do dyscypliny naukowej: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).

© The Authors 2022;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland
Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike.
(<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.
The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 02.01.2022. Revised: 17.01.2022. Accepted: 02.02.2022.

Autoimmune pituitary inflammation

Szymon Krzewski 1 - <https://orcid.org/0000-0003-2339-6741> smn.krzak@gmail.com
Mateusz Baranowski 2 - <https://orcid.org/0000-0001-7266-738X>
mateusz.gromek.baranowski@gmail.com
Katarzyna Wzorek 3 – <https://orcid.org/0000-0003-1873-0629> kwzorek@gmail.com

1. lek. dent., Chair and Department of Pedodontics, Medical University of Lublin, Poland
2. lek. dent., Chair and Department of Periodontology Medical University of Lublin, Poland
3. mgr. Department of Radiation Therapy, Independent Public Clinical Hospital No.1 in Lublin, Poland

Key words: pituitary gland, autoimmune diseases, autoimmune pituitary inflammation

Abstract: Autoimmune Hypophysitis (AH) is often referred in the literature as lymphocytic pituitary inflammation. It is the most common form of rare, chronic inflammation states affecting this gland. In most cases it has autoimmune character. Symptoms of pituitary inflammation are mostly headaches, dysfunction of anterior and/or posterior pituitary lobe and visual disturbances. Diagnostics is extremely difficult and inflammation itself is probably diagnosed too rare. Autoimmune Hypophysitis coexist with other autoimmune endocrinopathies. The golden standard in Autoimmune Hypophysitis diagnosis is biopsy and magnetic resonance imaging (MRI) is also used. In relation to rare occurrence of the Autoimmune Hypophysitis, varied clinical picture and lack of standardized research on large group of patients there are no described standards of conduct with those patients.

Introduction:

Hypophysitis is a rare occurring disease diagnosed in less than 1 in over 9 million cases every year(1,2). It can be primary or secondary in relation to local process or systemic process. In most cases it has autoimmune character, but other causes include secondary inflammation to tumor or cyst on the sella turcica, systemic diseases, infections or drug induced causes(3).

Symptoms of pituitary inflammation are mostly headaches, dysfunction of anterior and/or posterior pituitary lobe and enlargement of pituitary and/or pituitary peduncle stated in imaging examination(3,4).

Diagnostics of this condition is extremely difficult and inflammation itself is probably diagnosed too rare(1-3). Differential diagnosis is wide and multifaceted, including primary cancer, metastasis and lymphoproliferative diseases(1-3).

At the beginning of twentieth century appeared first histological descriptions noticing lymphocytic inflammation of the gland. Autoimmune basis of this condition was confirmed in 1950's. Since then, medical knowledge in this area was expanded in many researches.

Purpose of work:

Presentation of the topic of Autoimmune pituitary inflammation, analysis of current state of knowledge and propositions about possible methods of treatment.

Description of current state of knowledge about the topic:

Autoimmune Hypophysitis (AH) is often refereed in the literature as lymphocytic pituitary inflammation. It is the most common form of rare, chronic inflammation states affecting this gland(5-7). Autoimmune Hypophysitis is observed mostly in Caucasian population. It occurs more often in women then men and it is correlated to pregnancy. Average age in the moment of diagnosis is 34,5 years old among women and 44,7 years old among men(5,8). [Table 1]

Table 1. General characteristics of Autoimmune Hypophysitis (AH) (F – female, M – male) (8)

SEX – F:M = 8:1
Age in moment of diagnosis (years) – F 34,5; M 44,7
Race – Caucasian: Japanese = 3:1
Correlation with pregnancy – often occurring 6 months before and 6 months after the birth
Genotype – HLA DR4 (44%), HLA DR5 (23%)
Other autoimmune disease is present
Occurring of other autoimmune disease among patient's family

Clinical image of Autoimmune Hypophysitis varies individually. There are four categories of symptoms occurring in cycle of remission and relapse. The earliest and most common are headaches and visual disturbances. They are the result of pressure of enlarging pituitary gland on the surrounding structures of the brain. Second category of symptoms is associated with deficiency of hormones which are produced by anterior lobe of pituitary gland. The most common is deficiency of Corticotropin (ACTH) and also: Thyroid Stimulating Hormone (TSH), Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), Prolactin (PRL), Growth Hormone (GH). Third category are the symptoms of diabetes insipidus – polydipsia and polyuria, caused by damage of posterior lobe of pituitary gland. Least often are symptoms of hyperprolactinaemia in form of menstrual disorders, potency disorders and galactorrhea(5-8).

The knowledge about pathogenesis, frequency of occurrence and natural course of the condition is mostly unconfirmed according to the principles of good clinical practice and evidence-based medicine. Due to growing doctor's awareness, development of diagnostic, non-invasive imaging of pituitary gland and transsphenoidal surgery as well as use of animal's models in research, the knowledge is expanding and disease itself is diagnosed more often. The best conformation of this fact are growing numbers of AH's descriptions in literature(5-9).

Defining pathological characteristic of Autoimmune Hypophysitis is lymphocytic inflammatory infiltration. Usually it covers whole gland, deforming its natural structure and causes impairment of function. Besides lymphocytes, the other inflammatory cells are present and they can play a major role in immunopathology. Most authors suggest the autoimmune character of the disease, but the viral etiology is also considered. Immunohistochemical research shows presence of polyclonal lymphocytes T and B, without dominant type of lymphocytes which is typical for autoimmune diseases (6,10).

Other evidences suggesting autoimmune basis of Autoimmune Hypophysitis include improvement of patient's condition in response to treatment with immunosuppressants – mostly glucocorticosteroids, but also metotrexate or azathioprine. Presence of Antipituitary Antibodies (APA) and coexistence with other diseases with proven autoimmune nature (5-8,11).

Moreover, other autoimmune diseases are frequently found in the families of Autoimmune Hypophysitis patients. Probably it has connection with genetic predisposition and presence of HLA-DR4 and HLA-DR5 alleles. [Table 2] (6,10)

Table 2. Autoimmune criteria in pituitary inflammation (6)

Criteria	Presence in AH
Lymphocytic infiltration of target organ	Yes
Characteristic image in CT and MRI suggesting Lymphocytic infiltration of target organ	Yes
Evidence of disease induction among experimental animals	Yes
Presence of autoantibodies directed against target organ	Yes
Identification of specific autoantibodies	Debatable
Coexistence with other autoimmune diseases and/or in presence of other specific autoantibodies	Yes
Cycles of remission and relapse	Yes
Good respond to immunosuppressive treatment	Yes

According to the literature, in over 20% of cases Autoimmune Hypophysitis coexist with other autoimmune endocrinopathies such as: Autoimmune Thyroid Diseases (AITD), Hashimoto's Thyroiditis (HT) –7,4%, Graves' Disease (GB) – 1,6%, Polyglandular Autoimmune Syndrome type II (PAS II)- 1,8%, Diabetes Mellitus Type 1 (DM1)- 0,8% and Addison's disease (AD)- 0,5%.

This research was conducted among adult population and there is lack of data for pediatric population. Among patients with organ-specific and non specific autoimmune diseases marks of Antipituitary Antibodies can be used in order to diagnose patients, who may develop autoimmune pituitary inflammation. (5-7, 11, 12)

The specific autoantibody against which the autoimmune response is developing was not identified until this day. The role of alpha-enolase is raised, considering its coexpression in placenta, which could be the explanation for strong relation of the disease to pregnancy. (13)

Antibodies that are recognising alpha-enolase are described in many other diseases, such as endometriosis, lupus erythematosus and Wegener's granulomatosis. (5) As in the case of others

endocrine glands, autoantibodies of the pituitary gland are mainly lipoproteins, located in intracellular membrane of endoplasmic reticulum. (8)

The golden standard in Autoimmune Hypophysitis diagnosis is biopsy. Because of the invasive nature of this procedure, patients often do not give consent to this. In diagnostics of Autoimmune Hypophysitis magnetic resonance imaging (MRI) is also used, in order to differentiate this disease to pituitary tumor. (2)

Summary:

In relation to rare occurrence of the Autoimmune Hypophysitis, varied clinical picture and lack of standardized research on large group of patients there are no described standards of conduct with those patients. We can highlight various strategies applied together or separated, depending on patient's symptoms: wait-and-see attitude together with observation in case of patients without clinical symptoms, hormonal replacement therapy in case of patients with hypopituitarism or therapy with dopaminergic drugs in case of patients with hyperprolactinaemia. Conservative therapy with glucocorticosteroids and in recent years also with other immunosuppressants such as metotrexate or azathioprine, in order to reduce the size of the gland, is considered as controversial. Surgical treatment in case of pressure symptoms is performed via sphenoid sinus. In case of ineffectiveness of above methods radiotherapy may also be used. (4,8,14).

References

1. Joshi MN, Whitelaw BC, Carroll PV. MECHANISMS IN ENDOCRINOLOGY: Hypophysitis: diagnosis and treatment. *Eur J Endocrinol.* 2018 Sep;179(3):R151–63.
2. Bellastella G, Maiorino MI, Bizzarro A, Giugliano D, Esposito K, Bellastella A, et al. Revisitation of autoimmune hypophysitis: knowledge and uncertainties on pathophysiological and clinical aspects. *Pituitary.* 2016 Dec;19(6):625–42.
3. Langlois F, Varlamov EV, Fleseriu M. Hypophysitis, the Growing Spectrum of a Rare Pituitary Disease. *J Clin Endocrinol Metab.* 2022 Jan 1;107(1):10–28.
4. de Vries F, van Furth WR, Biermasz NR, Pereira AM. Hypophysitis: A comprehensive overview. *Presse Médicale.* 2021 Dec;50(4):104076.
5. Caturegli P, Newschaffer C, Olivi A, Pomper MG, Burger PC, Rose NR. Autoimmune Hypophysitis. *Endocr Rev.* 2005;26(5):599–614.
6. De Bellis A, Bizzarro A, Bellastella A. Pituitary antibodies and lymphocytic hypophysitis. *Best Pract Res Clin Endocrinol Metab.* 2005;19(1):67–84.
7. Hashimoto K, Takao T, Makino S. Lymphocytic adenohypophysitis and lymphocytic infundibuloneurohypophysitis. *Endocr J.* 1997;44(1):1–10.
8. Bellastella A, Bizzarro A, Coronella C, Bellastella G, Sinisi AA, De Bellis A. Lymphocytic hypophysitis: a rare or underestimated disease? *Eur J Endocrinol.* 2003;149(5):363–76.
9. Cauley K, Dalal A, Olson B, Onyiuke H. Lymphocytic hypophysitis. *Conn Med.* 2005;69(3):143–6.
10. Rose NR, Bona C. Defining criteria for autoimmune diseases (Witebsky's postulates revisited). *Immunol Today.* 1993;14(9):426–30.

11. De Bellis A, Bizzarro A, Conte M, Perrino S, Coronella C, Solimeno S, et al. Antipituitary antibodies in adults with apparently idiopathic growth hormone deficiency and in adults with autoimmune endocrine diseases. *J Clin Endocrinol Metab.* 2003;88(2):650–4.
12. Nishino M, Yabe S, Murakami M, Kanda T, Kobayashi I. Detection of antipituitary antibodies in patients with autoimmune thyroid disease. *Endocr J.* 2001;48(2):185–91.
13. O’Dwyer DT, Clifton V, Hall A, Smith R, Robinson PJ, Crock PA. Pituitary autoantibodies in lymphocytic hypophysitis target both γ - and α -Enolase – a link with pregnancy? *Arch Physiol Biochem.* 2002;110(1–2):94–8.
14. Krysiak R, Okopień B, Herman ZS. Zapalenie przysadki mózgowej. *Przegląd Lek.* 2007;64(515–20):7–8.