Unusual association of diseases/symptoms

Partial central diabetes insipidus in patient with common variable immunodeficiency

Marta Cano Megías, Ana Maria Matei, Olga Gonzalez Albarran, Gilberto Perez Lopez

Endocrinology Department, University Hospital Ramon y Cajal, Madrid, Spain

Correspondence to Miss Marta Cano Megías, mcanomegias@gmail.com**Summary**

Approximately 20% of patients with common variable immunodeficiency (CVID) have any autoimmune disease, as concurrent as prior to diagnosis, even during follow-up. In recent years, cases of CVID associated to endocrine autoimmune diseases have been reported. To our knowledge, no cases of CVID with diabetes insipidus has been reported previously. The authors present the case of a 37-year-old male, diagnosed of CVID, who had thirst, polyuria and nocturia for several years. After a water deprivation test and a complete resolution of patient's symptoms with vasopressin (DDAVP) treatment, diagnosis of partial central diabetes insipidus was finally made. Patients diagnosed of CVID could develop water misbalance due to posterior hypophysis autoimmune disorder. A high index of clinical suspicion, an early diagnosis and treatment of these disease could avoid future complications and improve the quality of life of these patients.

BACKGROUND

Common variable immunodeficiency (CVID) is the form of antibody deficiency with the highest prevalence in clinical practice, affecting children and adults to an equal extent. The main feature is the hypogammaglobulinaemia due to impaired maturation of B cells. Mechanisms such as abnormalities in the function of cells involved in cellular immunity (T cells, dendritic cells), and alterations in the secretion of various cytokines are also common to cases of CVID. Approximately 70–80% of patients are diagnosed based on a previous history of recurrent sinus, lung and gastrointestinal infections. The diagnosis is made after all other known causes of humoral defects have been excluded.^{1 2}

Moreover, approximately 20% of CVID patients are diagnosed of any autoimmune disease concurrent during lifetime. The pathogenic mechanism of this autoimmunity is not well understood, because it is unclear how antibodies are produced against various organs in patients with immunoglobulin deficiency. The most common autoimmune diseases associated with CVID are: immune thrombocytopenic purpura, autoimmune haemolytic anaemia and polyarthritis (rheumatoid arthritis-like). Cases of pernicious anaemia, inflammatory bowel disease, Sjögren's disease, vitiligo and autoimmune hepatitis have also been described. Even 5% of those affected may develop non-caseating granulomas in solid organs like lungs, liver or spleen. In addition, there is an increased risk of malignancies, most frequently haematological and gastric tumours.¹
³ Here we present a patient with CVID, who may develop neurohypophysitis. We searched via Pubmed any other case reports using the key words 'CVID', 'autoimmunity', 'autoimmune endocrinopathies associated to CVID' in English. We did not found any other adult case with neurohypophysitis and CVID.

CASE PRESENTATION

A 37-year-old male was referred to our office for assessment of polyuria and polydipsia. The patient's daily water

intake was approximately 4 litres, and he had persistent sensation of thirst, cold-water craving and polyuria for more than 10 years. These symptoms had been worsen in the past 6 months before our evaluation, leading to a water intake of 8–10 litres per day, polyuria and nocturia, which impaired the rest during the night. He denied headache, head trauma or visual disturbances. He did not take any drug or herbal product, except monthly treatment with parenteral immunoglobulins.

The patient had since childhood repetitive lung and gastrointestinal infections. His mother was affected of rheumatoid arthritis. He was diagnosed of nodular sclerosis Hodgkin's disease stage IA (cervical region) 8 years ago. Six cycles of chemotherapy with adriamycin, bleomycin, vinblastine, dacarbazine (ABVD) schema were completed, followed by radiotherapy of the affected field in total dose of 30 Gy. There were no acute or delayed complications related to this therapy, achieving complete remission since then.

Some years later, the patient was referred to the immunology department for persistent hypogammaglobulinaemia in periodical blood analysis. A functional study of the immune response was performed with no reaction to vaccination and low number of memory B cells in peripheral blood was found. Thus, CVID was diagnosed and intravenous immunoglobulin replacement therapy was started with the next basal levels of serum immunoglobulin: IgG 282 mg/dl, IgA 34 mg/dl, IgM 17 mg/dl.

The physical examination was rigorously normal. At the office, the patient was afebrile, with a heart rate of 56 bpm, a blood pressure of 123/85 mm Hg, weight 100.7 kg, height 180 cm, (body mass index 31 kg/m²). The blood routine laboratory tests measured a glucose 71 mg/dl, creatinine 0.90 mg/dl, urea 23 mg/dl, Na⁺ 142 mmol/l, K⁺ 4.2 mmol/l, total proteins 7.3 g/dl, Ca²⁺ 9.1 mg/dl, serum calculated osmolality 291.7 mOsm/kg. Urine biochemistry test showed an osmolality 116 mOsm/kg, K⁺ 14.80 mmol/l and Na⁺ <20.00 mmol/l. Baseline hormonal pituitary studies

were also performed with the following results: growth hormone (GH) 0.10 ng/ml, cortisol 13.70 ug/dl, somatostatin C 106.00 ng/ml, adrenocorticotrophic hormone 17.90 pg/ml, testosterone 536.2 ng/100 ml, prolactin 11.10 ng/ml, follicle stimulating hormone 3.93 mIU/ml, luteinising hormone 2.87 mIU/ml, thyroid stimulating hormone 1.407 uIU/ml. Insulin hypoglycaemia test also was performed with normal result for GH and cortisol. Antiadrenal and antipituitary antibodies were negative. Antithyroid antibodies (antithyroid peroxidase, antithyroglobulin, thyroid-stimulating immunoglobulin) were negative too. The patient had no active or chronic viral infection that could explain the immunity disorder (HIV, hepatitis B, hepatitis C, cytomegalovirus, Epstein–Barr virus).

Then a water deprivation test was performed. After 8 h overnight water deprivation, the patient presented a basal urine osmolality of 280 mOsm/kg, serum calculated osmolality of 300 mOsm/Kg and a serum Na⁺ of 143.5 mmol/l. Similar serum osmolalities were measured during the next 8 h, reaching a plateau of urinary osmolality for the next three samples with a maximum value of 457 mOsm/kg. After that, 2 mcg desmopressin (DDAVP) were administrated subcutaneously, with a subsequent rise in urinary osmolality to 688 mOsm/kg (Δ231 mOsm/kg, which represents an increase of urinary osmolality of 50%). The test was stopped at this point. We registered a 4 litres urine excretion during the 16 h of water deprivation test. Thus, the patient was diagnosed of partial central diabetes insipidus.

The brain MR showed in T1-wave sequences an absence of the normal signal of the neurohypophysis, with adenohypophysis normal in size and appearance. No organic lesions were viewed that may cause this loss of signal.

TREATMENT

A treatment with DDAVP flas 120 µg once daily was prescribed, with the resolution of polyuria and nocturia and disappearance of continuous sensation of thirst. The daily water intake lowered to 2 litres per day too.

OUTCOME AND FOLLOW-UP

After 1 month of DDAVP therapy, successive controls of plasma osmolality and serum ions were within normal range, with daily water intake of 2 litres, diuresis of 3 litres and disappearance of nocturia. One year later, the patient is reviewed in our office and told us that he had increased daily water intake to 4–5 litres and diuresis to 6 litres, with reappearance of nocturia. The laboratory test showed a serum calculated osmolality of 290 mOsm/kg, Na⁺ 141 mmol/l and urine osmolality 315 mOsm/kg. The dose of DDAVP flas was increased to 120 µg twice daily, reaching again a complete resolution of these symptoms.

DISCUSSION

In recent years, there have been report of CVID's cases associated to endocrine autoimmune diseases, being type 1 diabetes mellitus the most prevalence. However, there are cases of thyroid dysfunction (Hashimoto and Graves diseases), polyglandular autoimmune syndrome and Addison's disease too.^{4–7} Younes *et al*⁴ described a case of panhypopituitarism in a 12 year-old girl, who suffered from an adrenal crisis triggered by pneumonia. Panhypopituitarism was proposed to be secondary to an

autoimmune lymphocytic hypophysitis associated with this immunodeficiency. Therefore, our case could be possibly the first one of an autoimmune process affecting just the neurohypophysis.

The lymphocytic infundibuloneurohypophysitis is a rare disorder characterised by central diabetes insipidus. It is caused by a chronic inflammatory infiltrate at this level, mediated by autoimmune mechanism in response to neurohypophyseal antigens.⁸ The presence of specific antibodies against neurohypophyseal antigens in some cases of idiopathic diabetes insipidus supports the autoimmune mechanism.^{9–10} But patients with CVID often have no detectable autoantibodies and its serum levels are hard to measure due to the use of the intravenous immunoglobulins.

The adenohypophyseal function is usually normal in these patients. If anterior pituitary hormone deficits are associated, they usually have transient involvement and imply a deficit of GH, that could be diagnosed after an insulin hypoglycemic test.⁸ Our patient had not got high basal plasma osmolality, against what could be expected, due to the preservation of thirst's sensation and free access to water at any time. Moreover, he did not suffer from any acute medical illness that conditioned losing of thirst sensation or access to water (disrupting the defence mechanism of diabetes insipidus to avoid sodium and/or water misbalance).

The brain MR shows a diffuse thickening of the pituitary stalk that eventually could diminish as the lymphocytic infiltrate is replaced by fibrosis.¹¹ Loss of signal intensity in T1-images has also been described. Since the increase of signal is due to the phospholipids membrane of the antidiuretic-containing granules, the absence of bright spot on MR reflects a lack of function of the neurohypophysis. In our patient, MR T1-wave images showed this characteristic finding and no thickening of the pituitary stalk. Therefore, it rather suggests a long-term process, which may be related to an advanced lymphocytic neurohypophysitis.

Learning points

- CVID is the form of antibody deficiency with the highest prevalence in clinical practice. It occurs mainly with a previous history of recurrent sinus, lung and gastrointestinal infections.
- Approximately 20% of patients with CVID have an autoimmune disease concurrent or before diagnosis, including endocrine autoimmune diseases, being the most common type 1 diabetes mellitus.
- Patients with CVID may be susceptible to develop neurohypophysitis with a water balance disorder.
- An early diagnosis and treatment of these autoimmune diseases can avoid future complications and improve the quality of life of these patients.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. Agarwal S, Cunningham-Rundles C. Autoimmunity in common variable immunodeficiency. *Curr Allergy Asthma Rep* 2009;9:347–52.

2. **Cunningham-Rundles C**, Bodian C. Common variable immunodeficiency: clinical and immunological features of 248 patients. *Clin Immunol* 1999;**92**:34–48.
3. **Wang J**, Cunningham-Rundles C. Treatment and outcome of autoimmune hematologic disease in common variable immunodeficiency (CVID). *J Autoimmun* 2005;**25**:57–62.
4. **Younes JS**, Secord EA. Panhypopituitarism in a child with common variable immunodeficiency. *Ann Allergy Asthma Immunol* 2002;**89**:322–5.
5. **Topaloglu AK**, Yuksel B, Yilmaz M, *et al*. Coexistence of common variable immunodeficiency and autoimmune polyglandular syndrome type 2. *J Pediatr Endocrinol Metab* 2001;**14**:565–6.
6. **Metin A**, Tezcan I, Ozyurek H. IDDM in an adolescent patient with common variable immunodeficiency. *Diabetes Care* 1998;**21**:1029.
7. **Iglesias P**, Ferreira A, Diez JJ. Common variable immunodeficiency in adult woman with IDDM. *Diabetes Care* 1997;**20**:677–8.
8. **Rivera JA**. Lymphocytic hypophysitis: disease spectrum and approach to diagnosis and therapy. *Pituitary* 2006;**9**:35–45.
9. **Scherbaum WA**. Autoimmune hypothalamic diabetes insipidus ("autoimmune hypothalamitis"). *Prog Brain Res* 1992;**93**:283–92.
10. **De Bellis A**, Bizzarro A, Amoresano Paglionico V, *et al*. Detection of vasopressin cell antibodies in some patients with autoimmune endocrine diseases without overt diabetes insipidus. *Clin Endocrinol (Oxf)* 1994;**40**:173–7.
11. **Beressi N**, Beressi JP, Cohen R, *et al*. Lymphocytic hypophysitis. A review of 145 cases. *Ann Med Interne (Paris)* 1999;**150**:327–41.

This pdf has been created automatically from the final edited text and images.

Copyright 2012 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit

<http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Cano Megías MC, Matei AM, Gonzalez Albarran O, Perez Lopez G. Partial central diabetes insipidus in patient with common variable immunodeficiency. *BMJ Case Reports* 2012;10.1136/bcr.11.2011.5067, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow

Keep up to date with all published cases by signing up for an alert (all we need is your email address) <http://casereports.bmj.com/cgi/alerts/etoc>