

Rare occurrence of central diabetes insipidus with dermatomyositis in a young male

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Summary

Central diabetes insipidus (CDI) and several endocrine disorders previously classified as idiopathic are now considered to be of an autoimmune etiology. Dermatomyositis (DM), a rare autoimmune condition characterized by inflammatory myopathy and skin rashes, is also known to affect the gastrointestinal, pulmonary, and rarely the cardiac systems and the joints. The association of CDI and DM is extremely rare. After an extensive literature search and to the best of our knowledge this is the first reported case in literature, we report the case of a 36-year-old male with a history of CDI, who presented to the hospital's endocrine outpatient clinic for evaluation of a 3-week history of progressive facial rash accompanied by weakness and aching of the muscles.

Learning points:

- Accurate biochemical diagnosis should always be followed by etiological investigation.
- This clinical entity usually constitutes a therapeutic challenge, often requiring a multidisciplinary approach for optimal outcome.
- Dermatomyositis is an important differential diagnosis in patients presenting with proximal muscle weakness.
- Associated autoimmune conditions should be considered while evaluating patients with dermatomyositis.
- Dermatomyositis can relapse at any stage, even following a very long period of remission.
- Maintenance immunosuppressive therapy should be carefully considered in these patients.

Background

Central diabetes insipidus (CDI), a rather disabling and severe disease characterized by polyuria and polydipsia, is caused by defects of the posterior pituitary, resulting in deficiency of the antidiuretic hormone, vasopressin (1). CDI of an autoimmune etiology is very rare, with an incidence of one case per 9 million persons (2). Previous studies have shown that 37% of these cases show increased levels of autoantibodies to vasopressin-secreting cells (3). CDI has been shown to occur as an isolated disorder or in association with other autoimmune diseases, especially, endocrine autoimmune diseases (4, 5, 6).

Dermatomyositis (DM), another rare idiopathic inflammatory condition, also with an autoimmune etiology, primarily affects the skin, followed by inflammation and weakness of the proximal muscles. Extra-muscular manifestations involving the joints as well as the muscles of the gastrointestinal tract (leading to dysphagia), the pulmonary system, and rarely the cardiac system, also occur (1). The underlying pathogenesis of DM remains poorly understood although recent studies have demonstrated its association with antibodies that may increase the pro-inflammatory cytokines and interferon (7, 8).



After a thorough literature search, we could not find any reported case on the association of DM with an autoimmune CDI. We reported here, for the first time an interesting case of autoimmune CDI associated with DM.

Case presentation

A 36-year-old male presented to the outpatient endocrine clinic in our tertiary care hospital with complaints of a facial rash and aching muscles for 3 weeks. This was followed by a progressive weakness of the proximal muscles of both his upper and lower limbs. A systemic physical examination revealed the presence of an extensive facial rash not sparing the nasal folds. He also had periorbital erythema with edema (heliotrope rash), erythematous papular lesions on the knuckles (Gottron papules), and decreased muscle tone in both the upper and lower limbs. The signs and symptoms were classical and characteristic of DM, and the patient was diagnosed with the same.

The patient was a known case of idiopathic CDI diagnosed 5 years earlier and was on treatment with desmopressin (60 µg twice a day). He was diagnosed at a local hospital in his town, where he had presented with history of polyuria, polydipsia, nocturia, and inability to fast in the month of Ramadan (the mandatory daily 8–10 h fasting month for Muslims). He had no history of headache, visual impairment, arthralgia or myalgia, no history of any surgery or head trauma, and no known positive family history of CDI, at the time of presentation.

Investigation

The laboratory tests carried out revealed elevated white blood cell count of $14 \times 10^9/L$ (normal range: $4-11 \times 10^9/L$), increased erythrocyte sedimentation rate of 44 mm/h (0–17 mm/h), and increased C-reactive protein levels of 108 mg/L. There was substantial increase in creatine kinase (CK) levels, 4134 U/L (35–323), along with an increase in the CK-muscle/brain (CKMB) fraction, 122.8 U/L (7–25). The patient's biochemical profile showed normal serum electrolyte levels (sodium: 134 (135–145 mmol/L); urea: 5.8 (2.5–6.4 mmol/L)); and creatinine (66 (53–106 µmol/L)) and liver function tests (aspartate transaminase: 237 U/L and alanine transaminase: 82 U/L).

A complete evaluation of the anterior pituitary function was carried out. His hormonal profile was positive for subclinical hypothyroidism (TSH=8 mIU/L, free T4=18 pmol/L, and negative thyroid antibodies). The other pituitary hormones, prolactin, luteinizing

hormone, and follicle-stimulating hormone were within normal range or 'inappropriately normal' in the face of low total testosterone due to high-dose steroid given for dermatomyositis that suppress gonadal axis (Table 1). IGF-1 levels were also measured and found to be normal.

His autoimmune status was also evaluated by testing for the presence of autoantibodies. The autoimmune profile was positive for antinuclear antibodies with a titer of 1:320, while the other antibodies including anti-ds DNA, RF, RNP, SS-A, SS-B, anti-Scl-70, and anti-Smith were all negative.

Electromyography (EMG) was carried out on the patient using the Dantec Keypoint (Natus, CA, USA). Studies of the muscles showed evidence of myopathy with increased muscle membrane irritability (fibrillations/positive sharp waves) suggestive of muscle fiber necrosis. Additional MRI of the lower limbs was also done to evaluate DM, which demonstrated a picture of extensive myositis.

The MRI investigation of the hypothalamo-pituitary region (MRI sella turcica) was carried out to confirm his earlier diagnosis of CDI and showed a small pituitary gland with no evidence of pituitary adenomas and an absent native hypersignal or bright spot of the posterior pituitary (neurohypophysis), which is a characteristic feature of CDI (Fig. 1A and B). The diagnosis for CDI in the patient was reevaluated and confirmed in our facility biochemically by withholding the night dose of

Table 1 Laboratory investigations.

Investigations	Values		Reference range
	On steroid	Off steroid	
Pituitary hormones			
Prolactin, mIU/L	346.4		86–324
LH, IU/L	5.570	5.740	1.7–8.6
FSH, IU/L	3.070	2.540	0.8–9
Estradiol, pmol/L	21.710	133.20	37–143
Testosterone, nmol/L	2.090	11.21	9.9–27.8
Free T4, pmol/L	18		10.3–25.8
TSH, mIU/L	8		0.25–5
Random urine chemistry			
Urine osmolality, mosmol/kg	56		50–1400
Urine sodium, mmol/L	6		40–220
Immunology			
Thyroglobulin Abs, Units	0.00		<60
TPO Abs, Units	61.35		<100

Investigations of pituitary function revealed central picture of hypogonadism due to steroid use for dermatomyositis. Normal gonadal function was found off steroid. Investigations of urine chemistry revealed low urine osmolality going with DI (off desmopressin).

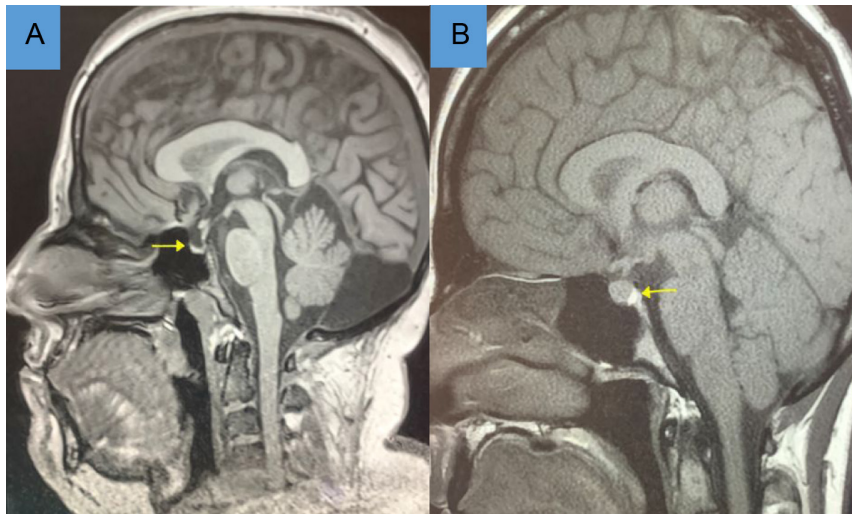


Figure 1

(A) The T1 sagittal MRI without contrast in our patient, showing the absent bright spot of the posterior pituitary. (B) T1 sagittal brain MRI without contrast in a normal patient, showing the normal bright spot of the posterior pituitary. MRI, magnetic resonance imaging.

desmopressin and restricting his fluid intake to check the urine osmolality. This was confirmed to be low 56 (mosmol/kg) and urinary sodium was 6 mmol/L with urine output of 2500 mL since midnight to 0800 h next day. The short period biochemical profile evaluation of over 8 h superseded the need to proceed with water deprivation test as the patient could not tolerate it due to significant dehydration. The final diagnosis of DM was confirmed on the basis of the EMG and MRI findings.

Treatment

Treatment in this case consisted of high-dose prednisone administration followed by mycophenolate or methotrexate, as steroid-sparing agents.

The patient started immediately on a high dose of methyl prednisolone, 120 mg daily, following which the CK and CKMB levels reduced along with significant improvements in the muscle tone. Immunosuppressants were also started, with the aim of treating the facial rash and at the same time providing a steroid-sparing effect. Hydroxychloroquine (800 mg daily) and mycophenolate mofetil (1 g) were given and levothyroxine (50 µg daily) was also started for the accompanying hypothyroidism. The dose of methyl prednisolone was then tapered down to 60 mg daily over a 3-month period, and he was then subsequently maintained on the same dose. His skin rash also disappeared during that time.

Outcome and follow-up

He responded well to the treatments. Six months post treatment, improvements were observed in the hematological parameters with reduction in

C-reactive protein and serum CK levels. He was subsequently maintained on oral prednisolone (60 mg daily), mycophenolate mofetil (1 g twice daily), hydroxychloroquine (800 mg daily), and desmopressin (60 µg twice daily).

Discussion

Immuno-endocrine disorders are characterized by the deficiency of specific hormones along with the presence of circulating autoantibodies to the specific hormone-producing cells (5). These disorders are often seen in combination with other autoimmune conditions, but the association of CDI with DM is rare. In this case report we presented an interesting case of DM in a patient with CDI. Autoimmune CDI has rarely been described in the literature and is usually induced by the global damage of the hypothalamic regions by autoantibodies to the arginine vasopressin-secreting cells (AVPcs) (3, 9). Pivonello *et al.* showed the likelihood of AVPc autoantibodies (Abs) positivity of 99% in their study, when all of the following were present: the age at disease onset of <30 years, history of autoimmune disease, and the presence of pituitary stalk thickening, and an 80–82% likelihood when two of the above parameters were present (10). This test was not performed in our case because the test is still not routinely performed in the laboratory, but is primarily done for research purposes only. We were unable to confirm the presence of the factors indicated by Pivonello *et al.*, although we suspect that they might have been positive in our case. CDI has been found in association with thyroiditis (11) or as part of polyglandular syndrome. It has also been found in association with histiocytosis X (12). DI was shown



to be linked with other autoimmune connective tissue disorders such as systemic lupus erythematosus, Sjögren's syndrome, and systemic sclerosis (13). On the other hand, DM is also known to overlap with autoimmune thyroiditis (10, 14), type I diabetes mellitus, celiac disease, myasthenia Gravis (15, 16, 17), and also together with both T1DM and thyroiditis (18).

The presence of the classical signs of DM in our patient, which included heliotrope rash, periorbital oedema, and Gottron papules were the basis for further laboratory and imaging tests that were carried out for the confirmation of the diagnosis. As suspected, the patient was found to have very high levels of serum C-reactive protein and serum CK, along with a specific increase in the muscle-specific CKMB isoenzyme. The EMG and MRI tests carried out also revealed evidence of myopathy, muscle fiber necrosis, and extensive myositis which further confirmed the diagnosis. The MRI of the brain also revalidated the presence of CDI, which was confirmed by the absence of the physiological neurohypophyseal hyperintense signal or bright spot, characteristic of CDI regardless of the etiology (11, 12).

To our knowledge this is the first reported case in the literature DM and idiopathic CDI in a young male; both presented together due to the presence of an autoimmune component. Moreover, our patient had two other features suggestive of autoimmune CDI (the age of disease onset of <30 years and the presence of autoimmune disease, DM). These findings and presence of associated autoimmune conditions should be considered while evaluating patients with dermatomyositis to provide a favorable therapy with better prognosis and recovery.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this case report.

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Patient consent

Consent has been obtained from the patient for publication of the submitted article and accompanying images.

Author contribution statement

Aishah Ekhzaimy, patient's physician, recruited the patient, did the investigation, and collected the data. She prepared the final manuscript and reviewed the article. Afshan Masood was involved in reviewing the

manuscript. Seham Alzahrani was involved in data collection of the patient. Waleed Al-Ghamdi was involved in writing the manuscript. Daad AlOtaibi was involved in reviewing the data of the patient. Muhammad Mujammami obtained the patient's consent.

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