OMCR

Oxford Medical Case Reports, 2020;2020,7–9

doi: 10.1093/omcr/omz132
Advance Access Publication Date: 31 January 2020
Case Report

CASE REPORT

A rare coexistence of Behcet's disease and Graves' thyrotoxicosis in a young man: a case report

Hareesh Joshi[1,*,†], Imran Shahriar[1], Poonam Sharma[2], Satyanarayana V Sagi[1] and Samson O Oyibo[1]

[1]Department of Diabetes and Endocrinology, Peterborough City Hospital, Peterborough, UK, and [2]Department of Rheumatology, Peterborough City Hospital, Peterborough, UK

*Correspondence address. Department of Diabetes and Endocrinology, Peterborough City Hospital, Peterborough, Cambridgeshire, PE3 9GZ, United Kingdom Tel: 01733 678000; Fax: 01733 678532; Email: hareesh.joshi@nhs.net

Abstract

Behcet's disease is a recurrent systemic vasculitic disorder. It manifests most commonly in the form of skin lesions, oral and genital ulcers and uveitis. Graves' thyrotoxicosis is an autoimmune disorder characterized by excessive production of thyroid hormones. We present a case of a 41-year-old male of Turkish descent who had symptoms of arthralgia, rash, palpitations and weight loss. Bloods tests showed raised inflammatory markers and biochemical evidence of severe autoimmune thyrotoxicosis. The patient was HLA-B51-negative, and pathergy test was inconclusive. A diagnosis of Behcet's disease was made on constellation of clinical symptoms. The patient was treated with carbimazole and prednisolone followed by azathioprine. The coexistence of Behcet's disease and Graves' disease in the same patient is very rare. Further studies are required to determine if there is a pathological association between these two conditions.

INTRODUCTION

Behcet's disease (BD) is a systemic inflammatory disorder characterized by recurrent oral and genital ulcerations, uveitis and skin lesions. Males are more commonly affected than females with an onset in the third decade. BD has a sporadic nature, albeit familial aggregation has been linked to HLA-B51 carriers. The etiopathogenesis still remains to be understood; however, the main histopathological hallmark of the disease is vasculitis. Graves' thyrotoxicosis develops as an autoimmune response against thyroid autoantigens. This is characterized by excessive production of thyroid hormones affecting nearly 2% of the population. Thyroid receptor antibody test is specific for Graves' thyrotoxicosis. Any association between thyroid autoimmunity and BD has not been previously established. We present a case of an adult male with a rare coexistence of BD and Graves' thyrotoxicosis.

CASE REPORT

A 41-year-old gentleman of Turkish descent presented with a 3-month history of fatigue, generalized pain, worse around the knees, a generalized rash, sweating, palpitations and significant weight loss (18 kg). During this time, the patient had also noticed multiple painful mouth ulcers (10–15 in number). Two weeks prior to presentation, the patient had an episode of bilateral painful red eyes associated with mild photophobia that subsided within 48 h without treatment. He had a past medical history of urinary symptoms and incomplete bladder emptying, complex migraine for which he took Topiramate. He also gave a history of recurrent oral, urethral and scrotal ulcers, joint pains and painful eyes, accompanied by dysuria several years ago for which he had a course of steroid in Turkey. He denied any history of urinary tract infections or sexually transmitted diseases. The patient had a strong family history of thyrotoxicosis affecting both his

[†]Hareesh Joshi, http://orcid.org/0000-0001-6124-6520
Received: June 4, 2019. **Revised:** July 31, 2019. **Accepted:** November 13, 2019

Table 1: Thyroid function tests results pre- and post-treatment

Thyroid function test results	At presentation	At 6 months	At 1 year
Thyroid stimulating hormone (TSH) (0.30–4.20 mU/L)	<0.01	0.01	1.91
Free thyroxine (free T4) (12.0–22.0 pmol/L)	>100	18.2	17.8
Free triiodothyronine (free T3) (3.1–6.8 pmol/L)	47.8	6.2	5.1
Thyroid receptor antibody (<2.0 IU)	14.3	-	-

Table 2: Diagnostic criteria for Behcet's disease according to the International Study Group

Recurrent oral aphthous ulcers (at least three times in a year)
PLUS any two of the following
Genital ulceration (active lesion or scar)
Skin lesions (erythema nodosum, folliculitis or other ulcerations)
Eye involvement (anterior or posterior uveitis or retinal vasculitis)
Positive pathergy test (skin hyper reactivity (sterile erythematous nodule or Pustule more than 2 mm in diameter in 24–48 h)

first- and second-degree relatives. He was an ex-smoker and did not drink alcohol.

On examination, the patient was found to have sweaty tremulous hands consistent with thyrotoxicosis, and a generalized erythematous, nodulo-papular rash (non-blanching) and mouth ulcers (one on the tongue and two on the soft palate). There was no evidence of synovitis or any genital ulceration. The patient had painless red eyes but no exophthalmos, consistent with mild thyroid eye disease.

Blood tests revealed biochemical evidence of severe thyrotoxicosis. His full blood count, calcium, vitamin B12, folate and ferritin levels and renal and liver function tests were normal with a high erythrocyte sedimentation rate (ESR) at 107 mm/h. The thyroid receptor antibody levels were raised, consistent with Graves' thyrotoxicosis (see Table 1). Tests for blood borne viruses including HIV, hepatitis and a total autoimmune antibody screen were all negative. The human leukocyte antigen test for B exon sequence encoding for HLAB51 and the skin test for pathergy were negative. The chest X-ray was normal. An ultrasound scan and radioiodine uptake scan of the thyroid gland showed features consistent with Graves' thyrotoxicosis. Based on the International Study Group for BD for making a diagnosis of BD (Table 2), the patient's history, symptoms and clinical findings (mouth, eye, genital and skin lesions) fulfilled the criteria for a diagnosis of BD.

The patient was commenced on 20 mg of Carbimazole daily, 10 mg of Propranolol three times a day by the endocrinologist and 20 mg Prednisolone once daily with tapering by 5 mg every week by the rheumatologist for the BD. This was followed by treatment with a steroid sparing agent (Azathioprine). The patient responded well with resolution of clinical symptoms and normalization of the thyroid functions over an 8-month period. Follow-up in ophthalmology clinic did not show any ocular abnormality nor thyroid eye signs. The patient remains on a maintenance dose of Azathioprine and Carbimazole with regular follow-up in Rheumatology and Endocrinology clinics.

DISCUSSION

BD does mimic autoimmune disorders in its response to immunosuppressive therapy, and therefore, it is not out of place to assume an association with autoimmune thyroid disorders. However, BD has been grouped under auto-inflammatory disorders where the innate immune system directly causes tissue inflammation, as opposed to activation of the adaptive immune system in autoimmune disorders [1]. Most of the clinical manifestations of BD are due to vasculitis, and it is currently grouped under variable vessel vasculitis in current definitions for vasculitides adopted by the 2012 International Chapel Hill Consensus Conference on the Nomenclature of Vasculitides [2].

Autoimmune thyroid disease is well known to be associated with several other autoimmune disorders [3]. However, two studies have shown no significant association between autoimmune thyroid disease and BD, as BD lacks the features of other autoimmune diseases, namely, anti-nuclear antibody positivity, female predominance, and the presence of Raynaud's phenomenon or glomerulonephritis [4, 5].

On the other hand, there are reports of the coexistence of BD with other autoimmune disorders such as, Sjogren's syndrome, ankylosing spondylitis, systemic lupus erythromatosis, Takayasu's disease and immunoglobulin-A nephritis [6–9]. Several possible explanations emerge from these studies. Of note, most patients in these studies were females, and the association may have been a coincidental finding. Furthermore, there is a significant overlap of clinical features between different conditions such as oral ulcers, uveitis and arthralgia, which can occur in a number of these conditions. However, the hypothesis concerning the role of antibodies in BD may share a common ground in the pathogenesis of other autoimmune diseases, namely, the presence of the anti-endothelial cell antibodies found in patients with BD. These antibodies to the alpha-enolase protein in endothelial cells have been demonstrated in various autoimmune and inflammatory conditions such as ANCA-positive vasculitis, inflammatory bowel disease, discoid lupus erythematosus, systemic lupus erythematosus, systemic sclerosis, mixed connective disease and autoimmune liver disease [10].

We have presented a rare case of a coexistence of BD and Graves' thyrotoxicosis in the same patient. Although the limited data do not demonstrate concrete evidence of any association between the two conditions, this case does highlight the question of whether their coexistence is due to a pathogenic association rather than mere coincidence.

ACKNOWLEDGEMENTS

None

CONFLICT OF INTEREST STATEMENT

None declared.

FUNDING

No funding was received for the work involved in this article.

ETHICAL APPROVAL

No ethical approval was required.

CONSENT

Written consent was obtained from the patient for the publication of this case report.

GUARANTOR

Samson Oyibo is the guarantor for this article.

REFERENCES

1. Zen M, Gatto M, Domeneghetti M, Palma L, Borella E, Iaccarino L, *et al.* Clinical guidelines and definitions of autoinflammatory disease: contrast and comparisons with autoimmunity: a comprehensive review. *Clin Rev Allergy Immunol* 2013;**45**:227–35. http://dx.doi.org/10.1007/s12016-013-8355-1.
2. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, *et al.* 2012 revised International Chaper Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum* 2013;**65**:1–11. http://dx.doi.org/10.1002/art.37715.
3. Boelaert K, Newby PR, Simmonds MJ, Holder RL, Carr-Smith JD, Heward JM, *et al.* Prevalence and relative risk of other autoimmune diseases in subjects with autoimmune thyroid disease. *Am J Med* 2010;**123**:183.e1–9. doi:http://dx.doi.org/10.1016/j.amjmed.2009.06.030.
4. Aksu K, Oksel F, Keser G, Ozgen AG, Ynal V, Kabalak T, *et al.* Thyroid functions in Behcet's disease. *Clin Endocrinol* 1999;**50**:406–7.
5. Cebeci F, Onsun N, Pekdemir A, Uras AR, Kayatas K. Thyroid autoimmunity and Bechet's disease: is there a significant association? *Sci World J* 2013;**2013**:956837. http://dx.doi.org/10.1155/2013/956837.
6. Cho SB, Chun EY, Bang D, Lee KH, Lee ES, Lee S. Coexistence of Behcet's disease and autoimmune disease: clinical features of 11 cases. *J Dermatol* 2005;**32**:614–6. https://dx.doi.org/10.1111/j.1346-8138.2005.tb00809.x.
7. Cimen OB, Sahin G, Bicer A, Erdogan C. Behcet's syndrome coexisting with clinically occult ankylosing spondylitis. *Z Rheumatol* 2002;**61**:440–2.
8. Lee WS, Kim SJ, Ahn SK. Behcet's disease as a part of the symptom complex of SLE? *J Dermatol* 1996;**23**:196–9. doi: https://doi.org/10.1111/j.1346-8138.1996.tb03997.x.
9. Martini A. Behcet's disease and Takayasu's disease in children. *Curr Opin Rheumatol* 1995;**7**:449–54.
10. Lee KH, Chung HS, Kim HS, Oh SH, Ha MK, Baik JH, *et al.* Human alpha-enolase from endothelial cells as a target antigen of anti-endothelial cell antibody in Behcet's disease. *Arthritis Rheum* 2003;**48**:2025–35. doi: https://doi.org/10.1002/art.11074.