

Behçet's disease and subacute thyroiditis after a rabies inoculation: a case report and review of the literature

Sirs,

Behçet's disease (BD) is a systemic vasculitis with unknown pathogenesis, characterised by recurrent oral and urogenital ulcerations, erythematous nodular lesions, and vascular, neurologic, ocular lesions (1). Similarly, subacute thyroiditis (SAT) is a self-limited inflammatory disorder with unknown aetiology. Here we firstly report a patient with BD and SAT triggered by a rabies inoculation.

A 26-year-old woman visited our department with recurrent oral aphthous ulcerations and genital ulcerations after a rabies inoculation. Five months before she had been bitten by a dog and received a 5-dose rabies vaccination (inactivated aG virus strain from primary hamster kidney cells). After the first dose, she developed a high fever with a highest axillary temperature of 39.2°C. Additionally, she developed pain and swelling of the anterior neck, oral and genital ulcerations, erythema nodosum on both legs, and pseudofolliculitis on thoracodorsal areas after the third dose.

Local laboratory investigations showed a slight leukocytosis. Her erythrocyte sedimentation rate (ESR) was 32 mm/h and C-reactive protein (CRP) was 16.9 mg/L. Her perinuclear anti-neutrophil cytoplasmic antibody (P-ANCA) was doubled with negative results of other specific autoantibodies. There was no evidence of infections. Thyroid ultrasound revealed irregular hypoechoic areas on both lobes, while thyroid function was unexamined. The diagnosis of BD and suspected SAT was considered in the local hospital. Subsequently, a 3-month herbal treatment improved some symptoms but not ulcerations and pseudofolliculitis. She then visited our department. Her P-ANCA increased by 3 times with negative in other autoantibodies. Her thyroid-stimulating hormone slightly elevated with normal free thyroxines and ESR and CRP were normal. According to the International Criteria for Behçet's Disease published in 2014, her oral and genital aphthosis and skin lesions led to the diagnosis of BD without necessity for further invasive investigation (2). We kept the diagnosis of SAT and commenced treatment with thalidomide. BD recovered after 6 weeks, while the hypo-echoic areas decreased in thyroid ultrasound with sustained subclinical hypothyroidism 10 weeks later. BD is a rare and long-neglected complication for vaccination. To the best of our knowledge, only 5 publications described vaccination-triggered BD, as summarised in Table I. These included 2 case reports (3, 4), 2 cohort studies (5, 6) involving BD and quadrivalent human papillomavirus vaccine (qHPV) in adolescent girls and adult women separately, and one international descriptive study (7) using data from spontaneous

Table I. Previously reported Behçet's disease after vaccination.

First author	Year	Country	Study design	Population (sex/age)	Vaccine
Granel (3)	1999	France	Case report	Female/39	Polyvalent
Molloy (4)	2004	Ireland	Case report	Female/32	Typhoid
Arnheim (5)	2013	Denmark and Sweden	Cohort study	Female/11-17, 5 cases	qHPV
Felicetti (7)	2015	International	Descriptive study	Not available	Meningococcal, pneumococcal, tetanus, influenza, hepatitis, measles, varicella zoster, papillomavirus
Hviid (6)	2018	Danish and Sweden	Cohort study	Female/18-44, 2 cases	qHPV

qHPV: quadrivalent human papillomavirus vaccine.

online reporting systems for adverse events following immunisation. Overall, vaccination-triggered BD was reported in over 10 various vaccines (Table I).

Unlike all previous studies using recombinant or subunit antigens in inoculations, inactivated vaccines were administered for our patient. While previous case reports presented vaccination-triggered BD with either critical or unusual manifestations, our patient only had characteristic skin lesions. An increased P-ANCA was observed in our patient, however, its clinical significance was limited for the non-specificity of P-ANCA which could sometimes be detected in healthy individuals (8). This high heterogeneity indicated unspecific manifestations of vaccination-triggered BD. Interestingly, although BD is more common in Middle-East and far-east Asia (1), no vaccination-triggered BD was reported there except for this one, suggesting the existence of neglected cases.

Likewise, vaccination-triggered SAT may often be overlooked for recognised as common adverse effects with non-specific manifestations such as neck pain, fatigue, myalgia, and fever, as reviewed by Momani (9). It was only rarely reported in influenza and hepatitis B virus vaccination and most patients had an uneventful recovery (9, 10). To date, no rabies vaccination triggered SAT was reported.

Our case added to the literature as the first case with BD and SAT triggered by a rabies inoculation. In conclusion, it is necessary for physicians to recognise these rare complications for vaccines.

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