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CASE REPORT Open Access

Retrospective diagnosis of Behcet's disease prompted by a false-positive D-dimer

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Abstract

A 42-year-old lady underwent extensive investigations looking for thrombosis, cancer or vasculitis following repeated D-dimer testing with values greater than 60,000 µg/ml; the negativity of the imaging ruled out cancer or thrombosis, but a review of her clinical history suggested she had features of Behcet's disease several years earlier, leading also the hypothesis that the elevated D-dimer could have been a false positive, as subsequently demonstrated. Careful history taking is mandatory for the early interpretation of symptoms linked to Behcet's disease, and a high degree of suspicion for a false positivity must be applied to asymptomatic people with unusually high levels of D-dimer.

Keywords: Behcet's disease, D-dimer

Introduction

Behcet's disease (BD) is characterized by recurrent oral and genital ulcers, cutaneous, musculoskeletal, vascular, neurologic, gastrointestinal and ophthalmic manifestations [1], and its diagnosis can often be challenging [2]: we retrospectively diagnosed BD in a lady on account of a falsely raised D-dimer (DD).

Case description

A 42-year-old lady diagnosed with transverse myelitis in 2014 underwent three episodes of saphenous vein thrombophlebitis since 2016; on the last two occasions, her DD was grossly elevated at 63,104 µg/L and 65,240 µg/L (INNOVANCE D-Dimer; Siemens Healthcare Diagnostics, Marburg, Germany): these prompted a CT pulmonary angiogram and whole body CT in January and May 2019 respectively, negative for pulmonary embolism and cancer, and a PET of her brain and spine that was negative for active vascular lesions. At her clinic attendance in December 2019, on specific questioning, she admitted having suffered from mouth ulcers (2–3 times a year, more frequently in her twenties), recurrent macular-like erosions between 2 and 5 mm in diameter on her labia, pimples on thighs and trunk and a thick leg lesion around 4/5 cm in diameter on two occasions, diagnosed as erythema nodosum by her general practitioner. In January 2020, P-ANCA, C-ANCA, C_3, C_4, ACE, antiphospholipid antibodies, and thrombophilia screen (protein C and S, antithrombin, Factor V Leiden and prothrombin 20210 mutations) were negative, but a pathergy test and HLA-B51 were positive. We hypothesized that the DD was falsely elevated: in February 2020, it was greater than 80,000 µg/L, and dilutions at 1/30 and 1/90 still yielded results of 73,692 and 29,900 µg/L instead of the expected 2660 and 888 µg/L respectively; when the assays were repeated after pre-incubation of the patient plasma containing the anti-mouse antibody with 10% mouse serum (Dako, Denmark), the baseline test yielded a result of 650 µg/L (upper cut-off 520 µg/L), and the two dilutions yielded very low negative results (22 µg/L), indicating that incubation with the mouse serum removed the interference due to the anti-mouse antibody in the patient's plasma. Moreover, repetition of the baseline tests with an immunoassay that employs an anti-mouse blocking agent (STA®-Liatest® D-Di Plus, Stago, UK) yielded a normal result.

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Discussion

With regard to the clinical history of our patient, BD should have been already suspected at the time of the patient's transverse myelitis [3], but it was confirmed only when the elevated plasma concentration of DD was further investigated and specific questions relating to BD were asked. With regards to the raised DD, some individuals harbour in their blood heterophile anti-mouse antibodies that may interfere with the DD immunoassays yielding false-positive results [4] as previously noted: a healthy young girl with left calf swelling underwent several negative Doppler ultrasounds for a repeatedly positive DD over 8 weeks (1600–2900 ng/ml) [5]; a 40-year-old man with Castleman's disease died of sepsis with suspected disseminated intravascular coagulation (DIC) for a raised DD (15,558 ng/mL) though post-mortem did not reveal DIC [6]; a 42-year-old gentleman with chest pain and elevated DD (34,470 ng/mL) underwent a CT pulmonary angiogram negative for embolism [7] and a 3-year-old girl developed migraine and vertigo a week after a chicken pox; her DD was falsely elevated (8998ng/ml) but in the presence of negative cerebral vascular investigations [8].

With regard to the clinical symptoms of our patient, the specific questioning alongside the positive pathergy test and the HLA B51 allowed a retrospective diagnosis of BD: an earlier recognition would have facilitated the initiation of immune suppression that might have prevented her recurrent thrombophlebitis and the chain of unnecessary investigations that followed; moreover, a discerning clinician should always challenge an unusually high DD level that does not match clinical symptoms in the presence of negative imaging.

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Competing interests
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