Post-COVID-19 biologically false-positive VDRL: A report

Dear editor,

The venereal disease reference laboratory (VDRL) test of syphilis detects antibodies to a non-specific cardiolipin-lecithin-cholesterol antigen. It is a biological false positive (BFP) when VDRL is reactive, but a specific treponemal test is non-reactive. The usual BFP rate has been 1–2%, while prevalence as high as 26% has also been reported.\textsuperscript{1,2} Treponemal antibody tests, such as T. pallidum haemagglutination (TPHA), have a meagre false-positive rate (< 1%), making them highly dependable.\textsuperscript{3}

A 27-year-old, unmarried male blood donor with an incidental positive VDRL test was referred to us from the blood bank for further evaluation. The patient was asymptomatic and had no medical or surgical history. He voluntarily donated blood multiple times in the last 5 years, the last one being 4 months previously with normal serology on all occasions. He was diagnosed with COVID-19 with moderate pneumonia 3 months prior, for which he was hospitalized and managed conservatively, and he recovered within 15 days. He was not vaccinated for COVID-19. He reported no sexual contact in the last year and no high-risk sexual behaviour. His vitals, lymph nodes, skin and mucosa, and other systems were normal on examination. Repeat VDRL was reactive with a titer of 1:2, while TPHA was negative. At 10 weeks, the titer increased to 1:4, and became non-reactive at 16 weeks. Other viral markers and laboratory tests parameters were within normal limits.

Lipoidal (cardiolipin-lecithin-cholesterol complex), a non-specific antigen, is found in Treponema pallidum, the causative organism for syphilis. Antibodies called reagins develop against it, which the VDRL test detects. Since lipoidal antigen is present in humans’ mitochondrial and nuclear membrane, VDRL tests can come positive whenever the normal human cells are destroyed in any systemic infections other than syphilis, causing a biological false-positive reaction. Thus, any reactive VDRL is consistently confirmed by one of the treponemal tests, most commonly TPHA. BFP can be seen in infections, vaccinations, pregnancy, age-related changes, neoplasms or autoimmune disorders, etc.\textsuperscript{1}

However, before concluding on VDRL reactivity as BFP, a thorough history and evaluation for any chronic illness, autoimmune or collagen disease, substance abuse, hepatitis or neoplasms is necessary. Many febrile illnesses like tuberculosis, malaria, filariasis and physiological conditions including pregnancy, age, vaccination can result in temporary false-positive reactions. A repeat of syphilis serology can be asked after 10 weeks, as by that time, the immune system should have recovered.\textsuperscript{3} Our patient was completely asymptomatic, and his history was not suggestive of any medical or surgical illness; neither did he receive any vaccination recently nor have a history of substance abuse. He also tested VDRL negative several times as part of blood donation screening. The only new incident between the last and present positive tests was COVID-19 pneumonia. Most of the viral infections causing BFP reactions are associated with polyclonal-gammopathy. Acute monoclonal gammopathy is also reported in COVID-19\textsuperscript{5}; BFP reactions can be attributed to this phenomenon.

The VDRL becomes reactive within a few weeks of infection, peaks within the first year and then gradually decreases. In our case, the modified TPHA test for syphilis done after the VDRL reactivity tested negative. It took 16 weeks for the test to become non-reactive without any treatment in the present case.

To the best of our knowledge, BFP VDRL reports linked to COVID-19 infections are absent or scarce. The present incident highlights the need for more research in this area, including COVID-19 infection, which caused the current pandemic, among the diseases that generate BFP nontreponemal tests.

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Ethical approval

Case report/letters do not require institutional review or ethical approvals in our institute. Consent for publishing the test reports was obtained from the patient.
Informed consent
Consent for publication of the report is taken.

Data availability
The test results (reports) are available with the corresponding authors and can be shared at a reasonable request.

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