

COVID-19 vaccination and penile Mondor disease. There is any relationship?

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Dear Editor,

the pandemic spread of Coronavirus 2 infection (SARS-CoV-2), determining the coronavirus disease 2019 (Covid-19), had devastating consequences globally with several waves affecting social and economic life. The use of masks, physical distancing, testing of exposed or symptomatic persons, contact tracing and isolation have helped limit the transmission where they have been rigorously applied; however, these actions have proved not sufficient to limit the virus spread. The vaccinations are needed to reduce the morbidity and mortality of Covid-19 (1). Two vaccine types have been developed using two different technologies: viral vectors (*Vaxzevria*; *AstraZeneca*) and mRNA (*Comirnaty*-Pfizer and *mRNA-1273-Moderna*). Aside from transient local and systemic reactions, no safety concerns were identified from vaccination. Nevertheless, there are several concern in the public opinion about the possible consequences on uro-genital system, both in men and women. We know that exist evidence suggesting no embryo and gametes infections by SARS-CoV-2 and no consequences on fertility potential after vaccination (2). Thrombosis is the most severe and nontypical adverse effects of vaccine. Similarly to Covid-19 infection, in which we recognized a predisposition to both venous and arterial thromboembolism due to excessive vascular and systemic inflammation, endothelial dysfunction, cytokine storm, hypoxia and immobilization, after vaccination there is a growing evidence of thrombotic vaccine-related events (2). During the first wave in 2020, we had already reported an increase in outpatient evaluations of patients complaining of a vascular andrological disease, known as *penile Mondor disease* (PMD) (1). The PMD occurs with palpable subcutaneous cord-like indurations beneath the penile skin (Figure 1).

Usually, PMD is an under-reported benign, self-limited disease that resolves spontaneously in four to eight weeks. The PMD under reporting may be because the lesion is often non painful and self-resolving. Most patients refrain from seeking medical attention, and when they do, sometimes even physicians pay little attention to the lesion. The PMD pathogenesis can be demonstrated by Virchow's triad. Triggering factors for endothelial damage intersect with underlying risk of blood stasis and hypercoagulability. For example, PMD may occur after frequent, vigorous, prolonged sexual activity, prolonged erection, urogenital infection and sexually transmitted diseases, pelvic surgery, penile trauma, prolonged sitting position, hematologic disease or thrombophilia. The intersection between the three Virchow's factors allows for blood clot formation in PMD typically isolated to the superficial dorsal vein with associated phlebitis (3, 4). Covid-19 infection is also related to PMD, based on several cases report published in the last years (5). Nothing is reported in the literature regarding the possible relationship between vaccination against Covid-19 and PMD. However, in our daily clinical practice, in the last three months, we have recorded an increase in outpatient assessments of PMD. We refer to 5 cases whose clinical data are reported in Table 1.

Table 1.
Clinical data of 5 cases.

Patient	Age	Vaccine type	Vaccination month	Outpatient evaluation month	Coagulation	Abnormal sex activity	History clinic
1	25	Pfizer	July	October	Normal	No	Silent
2	37	Moderna	September	December	Normal	No	Silent
3	21	Moderna	August	November	Normal	No	Silent
4	24	Pfizer	August	December	Normal	No	Silent
5	28	Pfizer	July	October	Normal	No	Silent

Figure 1. Clinical appearance (left, thin arrow) and ultrasound feature (right, arrow) of Penile Mondor disease.



Anamnesis and physical examinations were conducted to evaluate any possible cause of PMD. All patients underwent fast abdominal ultrasound and penile ecocolor-Doppler in flaccidity. Laboratory tests with particular interest on coagulation state were performed. Only the symptomatic patients (2/5) were treated with analgesic. Only one case (1/5) received low molecular weight heparin for 15 days. All patients reported complete recovery from symptoms and subcutaneous cord-like indurations complained at the presentation. PMD usually affects men at 20 to 40 years of age and in our little case series age ranged between 24 and 37 years. All performed vaccination 4 or 5 months before with mRNA-Comirnaty-Pfizer (3 cases) and mRNA-1273-Moderna (2 cases).

No patients declared prolonged or unusual sexual activity. The clinical histories were silent for any possible hypercoagulability status. Vaccinations were the only possible pathogenetic factors linking the 5 young patients. The questions arising from this real-life experience are basically two. Is it therefore possible that there is a pathogenetic link between PMD and vaccination anti Covid-19? Is there any possibility of identifying subjects predisposed to the onset of this vascular disease after vaccination? Although the PMD clinical course is very often self-limiting, in a scenario characterized by an annual anti-Covid vaccination, may be important to always inform young male about the eventuality of developing PMD and alert general practitioners and referral specialists about the possible increase in the PMD response. From a diagnostic or therapeutic point of view, we don't identify the need to change the usual attitude. We must continue to reassure the patient and to treat symptomatic cases since PMD can cause significant patient anxiety and embarrassment and may be easily confused with more concerning conditions. Our aim is to urge the andrological scientific community to perform a large-scale data collection that allows us to define a correct answer to our questions.

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