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LETTER TO THE EDITOR

Sinopharm COVID-19 vaccine-induced Stevens—Johnson syndrome

Background

Stevens—Johnson syndrome (SJS) is a medical emergency. It is a rare potentially lethal adverse drug reaction. It is defined by an acute hypersensitivity reaction that causes extensive necrosis of the mucous membrane and skin [1]. The acute phase leads to an inflammation of the ocular surface. The chronic phase is marked with fibrosing conjunctivitis, corneal scarring and dry eye [2]. While the number of studies showing the efficacy of the COVID-19 vaccine are increasing day by day, its side effects remain unknown.

We report a case of Stevens—Johnson syndrome following the administration of the second dose of Sinopharm COVID-19 vaccine (Chinese-WIBP-Vero-Inactivated-Covid).

Case presentation

We report a case of a 32-year-old African man, with no pathological history, who presented six hours after the second dose of sinopharm vaccine, blistering rash on his hands, erythematous plaque with peeling dermis on his chest, back, skull, face and neck, without exposure to any other drug (Fig. 1a—d). No adverse reactions were reported after the first dose of vaccine exposure. The patient was seen in ophthalmology consultation seven days after the beginning of the symptomatology. The ophthalmologic examination found: Visual acuity 20/20, palpebral edema and erythema, BUT < 10s, bulbar conjunctival hyperemia grade 3, superficial punctate keratitis in both eyes. The patient also had signs of fibrosing conjunctivitis, two symblephara stage IIIA and IIID occupying respectively 0—25% and 75—100% of the length of the lower lid in the left eye, according to Tauber's classification [3] (Fig. 2a—c).

The treatment conducted included eye wash, a combination of corticosteroid and tobramycin eye drops and ointment, oral vitamin C, vitamin A ointment, symblepharon ring, oral doxycycline and hydrating preservative-free eye drops.

Thirty days later, we noticed a regression of palpebral erythema and edema, disappearance of conjunctival hyperemia and superficial punctate keratitis, and stabilization of the symblephara with a beginning of ectropion in the left eye (Fig. 3a and b).

Discussion

Stevens—Johnson syndrome is an acute, delayed-type hypersensitivity reaction that affects the skin and the mucous membranes. Stevens—Johnson syndrome is rare, it affects approximately 1 or 2/1,000,000 annually people per year [4].

It is the result of a T-cell-mediated disorder. T cells are activated by binding of drugs to T cell receptors (TCRs) from antigen-presenting cells (APCs). There are actually three hypotheses on T cell activation: the hapten/pro-hapten model, the pharmacological interaction (p-i) concept, and the altered peptide model [5,6]. The majority of drugs and their metabolites are pro-haptens and do not act as haptens themselves. They acquire the immunogenicity by covalently binding to carrier proteins (hapten antigen). Hapten antigens form a complex with HLA in APCs and are recognized by TCRs. This stimulation triggers the drug-specific T cell activation [7].

The $CD4^+$ T cells mostly infiltrate the dermis. While the cytotoxic $CD8^+$ T cells mainly infiltrate blister fluid and the epidermis [8,9]. The epidermal damage is considered to be a result of an apoptotic process [10]. Apoptosis is induced by cytotoxic $CD8^+$ T cells through the Fas-Fas ligand (FasL) pathway or the perforin/granzyme pathway [11]. Thereupon, Stevens Johnson Syndrome's pathogenesis is different from allergic reactions, that involves plasmocytes and IgE.

The typical clinical presentation includes mucocutaneous tenderness, hemorrhagic erosions, and erosion of the mucous membrane, erythematous macules, blisters, denuded skin and possible acute fibrosing conjunctivitis. Concerning causal agents, over 200 drugs have been incriminated [12]. Mycoplasma pneumoniae and Herpes simplex virus infections were also identified as causes. Vaccines can induce Stevens—Johnson syndrome too, despite the extreme rarity. Only a dozen of cases have been reported in the published literature, and it concerned varicella, smallpox, anthrax, tetanus, and influenza vaccines essentially [13]. Through a systematic review on ten studies, spread over 18 years, Grazina et al. explored the link between vaccination and SJS, concluding that there was not sufficient evidence to form a positive association between the two [14].

All COVID-19 vaccines have two components: virotopes and excipients. Both can cause severe drug reactions [15].

There are three main approaches to producing COVID-19 vaccine. Their differences lie in whether they use the whole

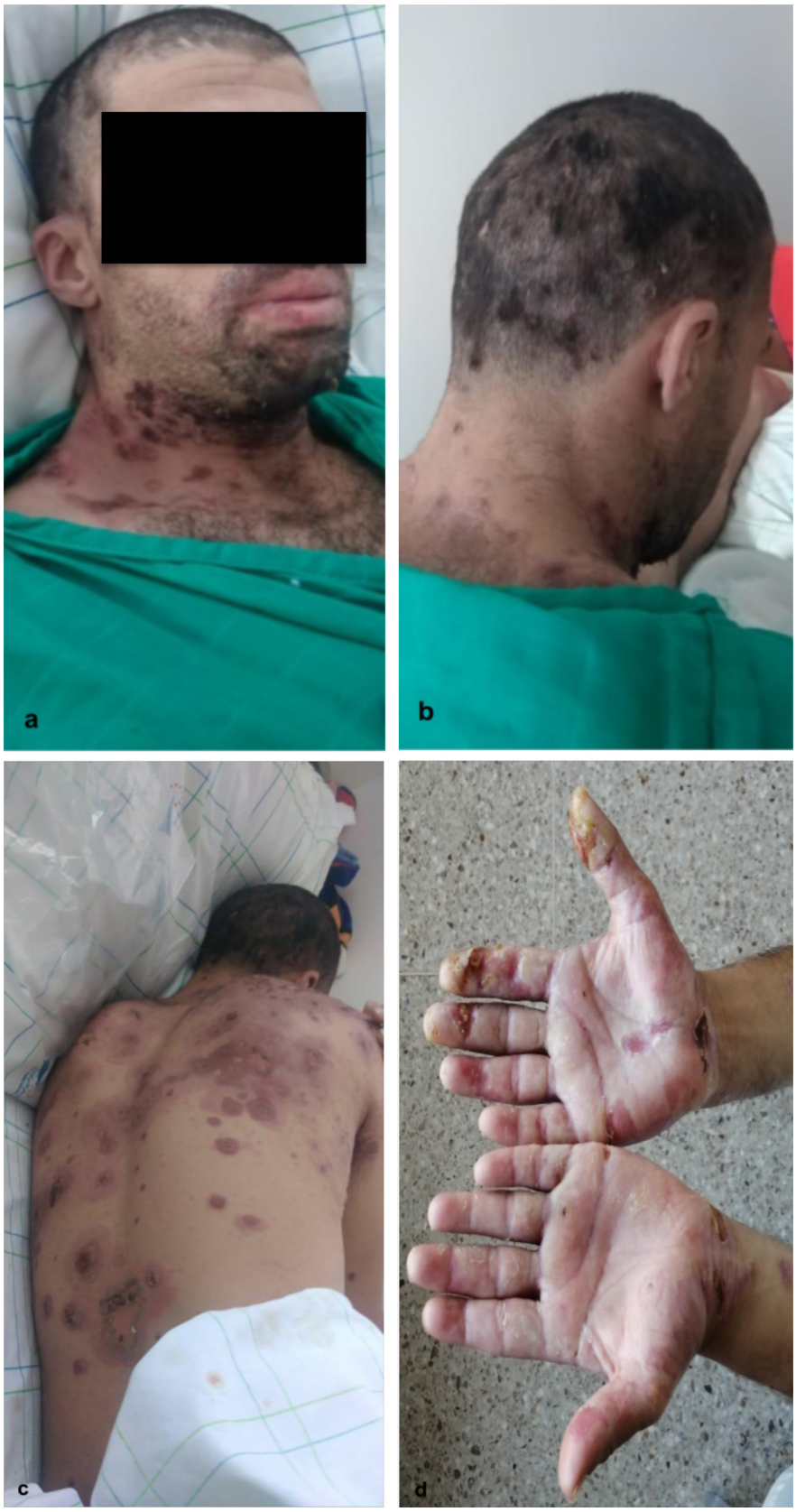

Figure 1. a and b: multiple purpuric patches with epidermal detachment affecting the neck, the skull and palpebral edema and erythema; c: multiple purpuric plaques with epidermal detachment affecting the back; d: multiple purpuric plaques with epidermal detachment affecting the palms.

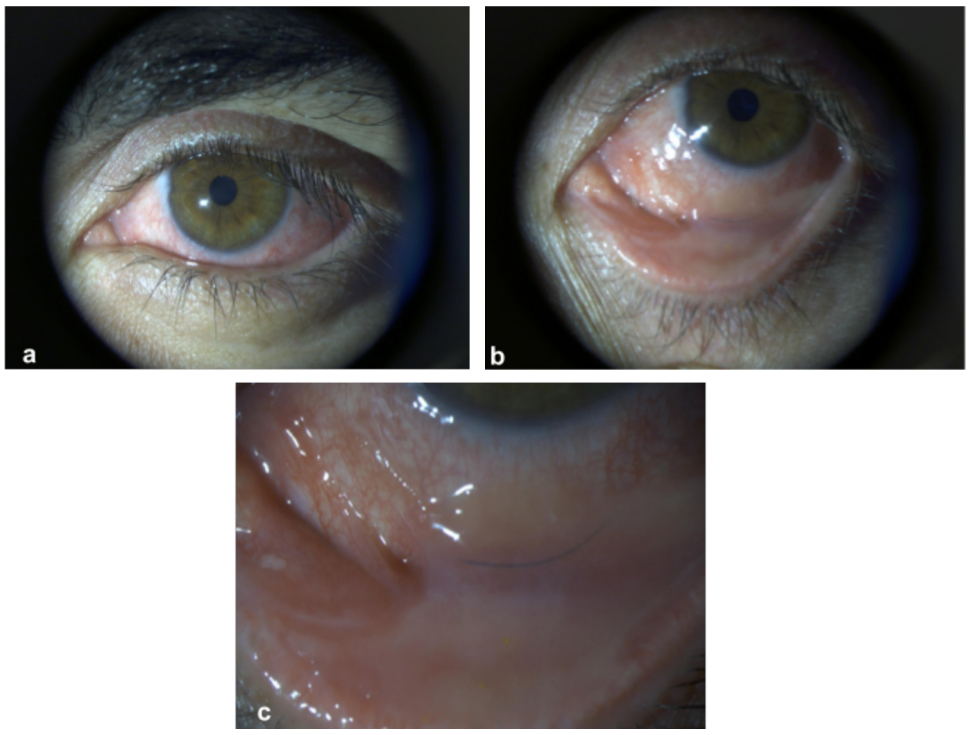

Figure 2. Pictures at day-7 of Stevens—Johnson syndrome showing conjunctival hyperemia (a), symblepharon × 10 (b), × 16 (c).

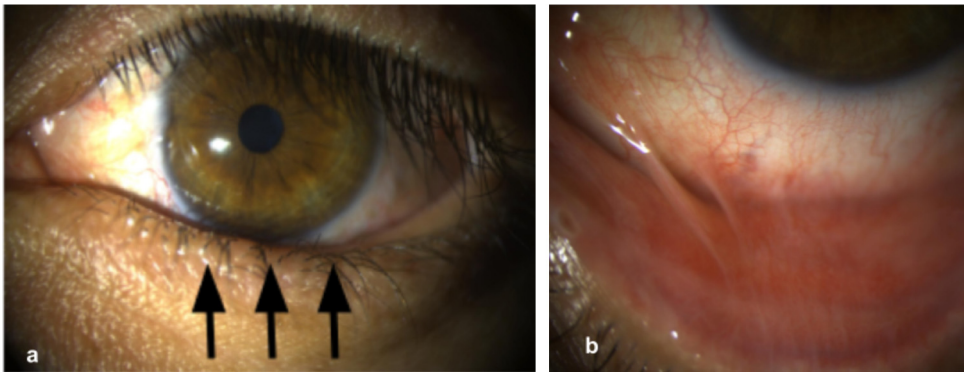

Figure 3. Pictures at day 30 of Stevens—Johnson syndrome (a) showing a beginning of an ectropion ''arrows'', (b) showing two symblepharа.

virus; or the part that triggers the immune system; or the genetic material that provides the instructions for making specific proteins and not the whole virus [16].

Sinopharm vaccine belongs to the first category. It results from the inactivation of a strain of SARS-CoV-2 (strain WIV04, Chinese Academy of Sciences National Genomic Data Center accession number SAMC133237, and GenBank accession number MN996528), by β-propiolactone, cultivated on vero monkey cells. It also contains saline solution and hydroxyde of aluminium as adjuvant [17]. Concerning the second category, we find the Janssen vaccine, the AstraZeneca vaccine and the Sputnik V vaccine. The Janssen vaccine consists of a recombinant type 26 adenoviral vector (Ad26.COV2-S) incapable of replicating and expressing the Spike glycoprotein (also called S protein or spike protein) of the SARS-CoV-2 coronavirus [18], whilst the AstraZeneca contains chimpanzee Adenovirus virus particles (I.U.) encoding the SARS-CoV-2 Spike glycoprotein [19]. The Sputnik V vaccine is based on adenovirus ''serotypes 5 and 26'' DNA, in which the *SARS-CoV-2* gene is integrated, which also leads to encoding the SARS-CoV-2 Spike glycoprotein [20]. The third category is a new process. It is based on a messenger RNA that encodes the viral spike protein, like the COMIRNATY Pfizer-BioNTech vaccine and SPIKEVAX COVID-19 Vaccine Moderna [21,22].

Actually, severe cutaneous reactions post-COVID-19 vaccination have been reported. McMahon et al. had defined a subset of vaccine-related eruption of papules and plaques, as well as 12 other patterns, following COVID-19 vaccination [23]. Ten months after the beginning of the COVID-19 vaccination campaign, five cases of Stevens—Johnson syndrome have been reported on PubMed [24—28].

Conclusion

We report a case that illustrates an exceedingly rare complication of the COVID-19 vaccine. Given the important benefit of the vaccine in the current pandemic, such rare reactions should not deter people from receiving the vaccine.

Disclosure of interest

The authors declare that they have no competing interest.

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