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Case Report

# Dermatofibrosarcoma Protuberans following COVID-19 and Influenza vaccination: A Case Report

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**Abstract:**

Coronavirus Disease 2019, commonly known as COVID-19, is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Symptoms range from mild (fever, cough, fatigue) to severe (shortness of breath, organ failure), with complications often observed in individuals with underlying health conditions or compromised immune systems. The introduction of vaccines to combat the disease is recent, necessitating ongoing evaluation of potential long-term effects. In contrast, influenza vaccination, with over 70 years of use, allows a better understanding of its long-term impacts. This case discusses a 40-year-old male patient who developed Dermatofibrosarcoma Protuberans (DFSP) in his right arm with rapid progression, following the simultaneous administration of the COVID-19 vaccine AstraZeneca and the trivalent Influenza vaccine at the same day and anatomical site, the proximal brachial region of the right upper limb. The patient underwent resection and histopathological analysis of the lesion, which revealed a skin/subcutaneous sarcoma compatible with grade 1 DFSP. The temporal relationship between the emergence of the lesion and the vaccination raises questions about potential uncommon immune-mediated adverse effects, discussed in this article through clinical analysis and a review of studies reporting similar reactions. This case highlights the importance of reporting and investigating rare adverse events that may be associated with vaccines to identify and better understand these complications.

**Key words:** dermatofibrosarcoma protuberans; vaccine; covid-19; influenza; skin/subcutaneous sarcoma; immune-mediated reaction

## Abbreviations:

**DFSP** : Dermatofibrosarcoma Protuberans

**FISS** : Feline Injection-Site Sarcoma

**MMR vaccine** : Measles, mumps and rubella vaccine

## Introduction:

Vaccination is one of the most effective strategies for the prevention of infectious diseases, significantly contributing to the reduction of global morbidity and mortality. In the context of the COVID-19 pandemic, the introduction of vaccines specifically targeting the coronavirus marked a milestone in public health, helping mitigate the devastating effects of the disease. At the same time, vaccination against influenza, with over seven decades of use, remains crucial for preventing severe complications. Although vaccines are generally safe, reports of rare adverse effects, including sarcomas at injection sites or adjacent areas, have emerged with the widespread use of the COVID-19 vaccine. In light of this, this case report describes a rare cutaneous sarcoma of the Dermatofibrosarcoma Protuberans (DFSP) type with accelerated progression following the simultaneous administration of the AstraZeneca COVID-19 vaccine and the trivalent influenza vaccine at the same anatomical site. The aim of this article is to discuss the potential associations between vaccination and the development of the lesion, with emphasis on clinical findings, surgical management, and histopathological analysis, contributing to a better understanding of the mechanisms involved in immune-mediated

responses post-vaccination and helping to expand knowledge for supporting future research on uncommon adverse events. Dermatofibrosarcoma protuberans (DFSP) is a rare type of soft tissue sarcoma with a low metastasis rate but high local recurrence. It typically presents as a firm plaque in shades of pink and purple on the trunk and proximal extremities, with slow progression. Surgical excision with clear margins is the preferred treatment, and radiotherapy may reduce local recurrence, especially in cases where wide margins are impractical (1).

## Case:

Male patient, 40 years old, self-identified as black, obese, rural worker, former alcoholic, diagnosed with systemic arterial hypertension controlled with Losartan, Atenolol, and Hydrochlorothiazide, with a surgical history of cholecystectomy in 2018 without complications. The documents provided by the patient indicate a vaccination history including: one dose of the diphtheria and tetanus vaccine, the yellow fever vaccine, one dose of the hepatitis B vaccine, the MMR vaccine, and the trivalent influenza vaccine. Regarding COVID-19 immunization, the patient received two doses of the Coronavac vaccine and one dose of the AstraZeneca vaccine. In 2022, following the simultaneous (i.e., same arm and day) administration of the AstraZeneca and trivalent influenza vaccines in the brachial region of the right upper limb, the patient initially experienced localized pain. One month later, he noticed the development of a small exophytic nodule in the proximal and lateral region of the right upper limb, specifically in the long head of the biceps muscle. The nodule exhibited rapid growth, acquiring characteristics of a tumor mass, and was accompanied by pain, bleeding, redness, ulceration, a putrid odor, and purulent discharge (Figure 1).

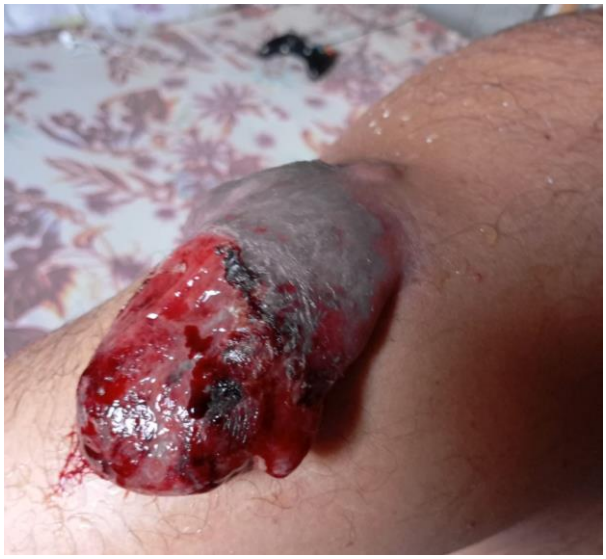

**Figure 1:** Ulcerated exophytic tumor in the brachial region 10 months after vaccination

During the progression of the lesion, the patient sought treatment at low-complexity health services in his hometown. However, due to the unfamiliarity of the lesion among professionals, no definitive treatment was provided. The only measures taken were dressing the lesion, prescribing analgesics, and referring the patient to a specialized regional service, the Clinics Hospital of the Federal University of Minas Gerais. Two years after receiving the AstraZeneca vaccine, the patient was seen at the Ambulatory Surgery Service of the Clinics Hospital of the Federal University of Minas Gerais, presenting the lesion. Upon medical evaluation, the following was noted: an ulcerated exophytic tumor with infection, measuring approximately 15x10x5 cm (Figure 2),

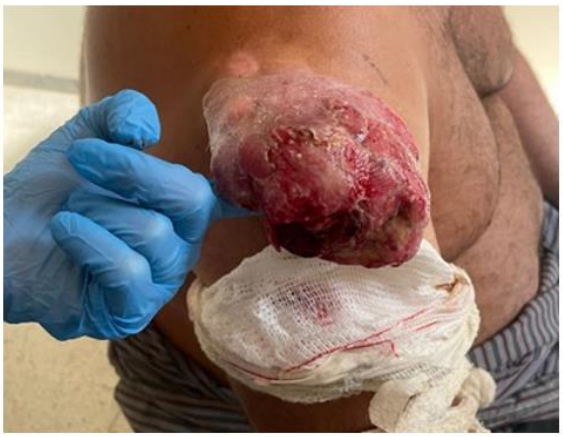

**Figure 2:** Ulcerated exophytic tumor in the brachial region 2 years after vaccination

as well as a second adjacent lesion measuring 2x1x0.5 cm (Figure 3).

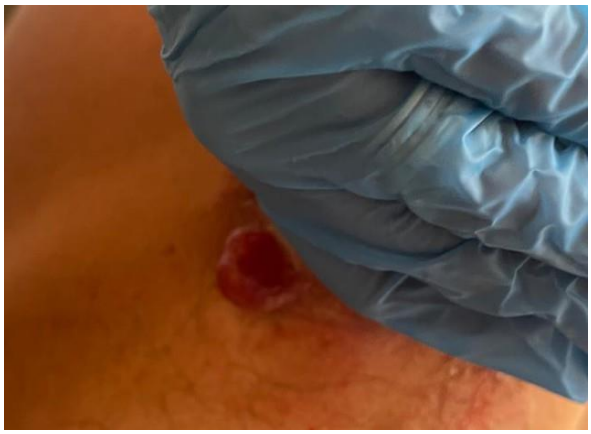

**Figure 3:** Adjacent exophytic tumor

The patient was referred for surgical excision and biopsy of the lesions. After consultation, the patient underwent surgery for lesion excision. Antisepsis of the right deltoid region was performed with chlorhexidine, and a sterile fenestrated surgical drape was positioned to isolate the lesion (Figure 4).

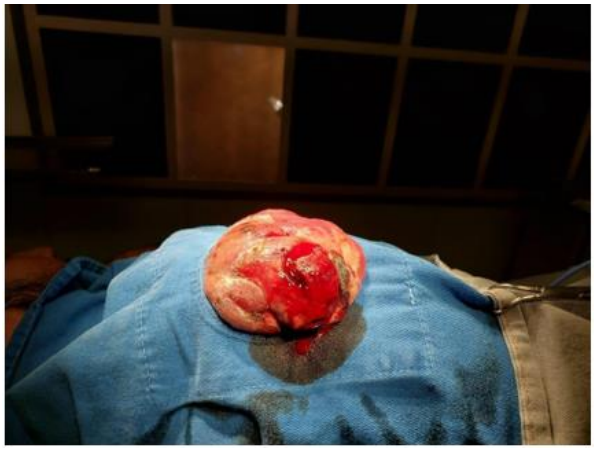

**Figure 4**: tumor isolated by fenestrated surgical drape

Regional anesthesia was administered using 1% lidocaine with vasoconstrictor for local anesthesia and to reduce bleeding. A peritumoral incision was made, followed by careful hemostasis to control abundant bleeding. During the procedure, a large amount of friable tissue surrounding the lesion was noted. Next, a new incision was made with electrocautery, and the lesion was excised via biopsy without safety margins. The excised tissue was sent for priority histopathological analysis for rapid diagnosis. Topical prophylactic antibiotics were applied to the lesion site. The surgical wound was sutured subcutaneously with Vicryl 3-0, and the skin was closed with simple Nylon 3-0 sutures (Figure 5).

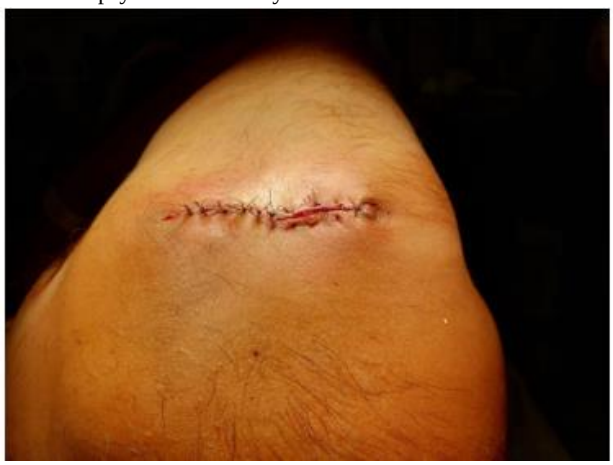

**Figure 5:** operative scar immediately after the excision

All remaining tissues were carefully washed with saline solution and soap to prevent infection, and a compressive dressing was applied. Dipyrone and Ibuprofen were prescribed for potential postoperative symptoms. At the postoperative wound review one week after the procedure, the lesion showed effective tissue repair with hyperemia and local pain (Figure 6).

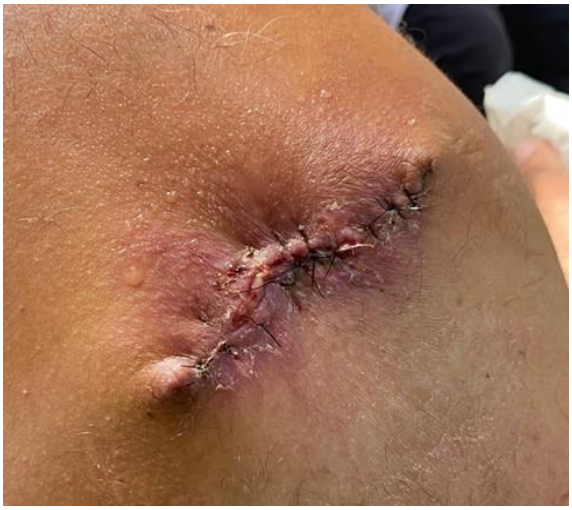

**Figure 6:** operative scar one week after tumor excision

Prophylactic Cefalexin 500 mg was prescribed every 6 hours for 10 days, with a follow-up appointment scheduled for the following week. The official histopathological report from the Clinics Hospital of the Federal University of Minas Gerais described the analysis of the collected specimens: a tissue fragment measuring 2.0 x 1.0 x 0.3 cm and a main sample measuring 9.5 x 8.0 x 4.0 cm, partially covered with skin presenting hemorrhage and erythematous nodules. Sections of the specimens showed evidence of a malignant mesenchymal neoplasm with spindle cell proliferation, discreetly hyperchromatic nuclei, forming bundles and storiform arrangements permeating adipocytes in a "chicken wire" pattern. Areas with a myxoid pattern and up to 10 mitoses per high-power field were observed, with no necrosis detected. The lesion reached the surgical margins. The report concluded it was a fusocellular sarcoma of the skin/subcutaneous tissue, consistent with grade 1 Dermatofibrosarcoma Protuberans (FNCLCC/WHO). The patient was referred for complementary immunohistochemical analysis. At the postoperative follow-up four weeks after surgery, the patient reported no complaints and denied pain, hyperemia, or discharge at the healing site. The surgical sutures had fallen off naturally. Physical examination of the operative scar showed effective wound closure, with the presence of dark and dry scabs and no inflammatory signs (Figure 7).

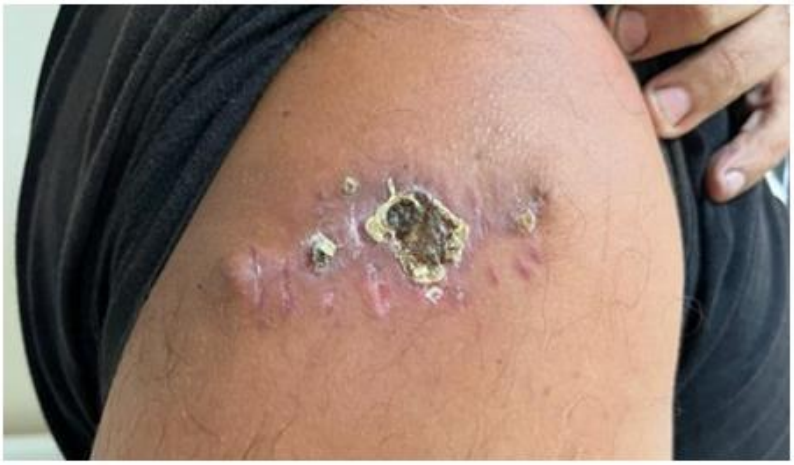

**Figure 7:** operative scar four weeks after tumor excision

The patient was referred to the oncology surgery service. The patient returned eight weeks after surgery, showing good wound healing (Figure 8).

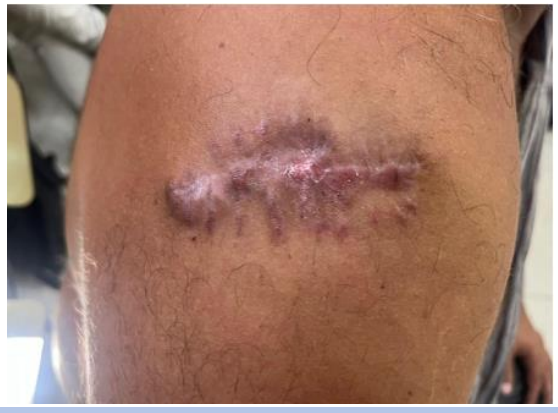

**Figure 8:** operative scar eight weeks after tumor excision

## Results and Discussion:

Immunizations play a key role in the prevention of infectious diseases, but in rare cases, they may trigger cutaneous and subcutaneous adverse events. Although most of these reactions are benign and transient, some sporadic reports have documented the development of atypical proliferative lesions, including soft tissue sarcomas, at vaccine injection sites or adjacent areas. Such occurrences raise the hypothesis that an exaggerated immune response may be associated with oncogenesis in previously sensitized tissues. This clinical case describes the rare development of a grade 1 dermatofibrosarcoma protuberans (DFSP), a fusocellular soft tissue and subcutaneous sarcoma, at the site of simultaneous (i.e., same arm and day) administration of the AstraZeneca and trivalent influenza vaccines. The tumor exhibited rapid and progressive growth over the course of two years. DFSP is a rare soft tissue tumor, typically located on the trunk or proximal extremities, with an incidence of 0.8 to 4.5 new cases per million people annually, and can manifest in both sexes equally and at all age ranges. Typically diagnosed between the third and fifth decades of life, these lesions tend to grow slowly but may ulcerate and become painful(1), as observed in the described case. The temporal proximity between vaccination and tumor development, along with the coincidence of the tumor's location at the injection site, suggests a possible causal association, despite the rarity of the event. Clinical reports have documented the appearance of proliferative lesions at vaccination sites, raising questions about the interaction between the immune stimulus of the vaccine and oncogenesis. However, the absence of robust studies with appropriate methodologies and representative sample sizes prevents confirmation of this relationship. Most available evidence comes from a few case reports, making it difficult to generalize the findings. Although some hypotheses have been raised, such as the action of vaccine adjuvants or an exacerbated inflammatory response in predisposed tissues, these mechanisms remain speculative. The rarity of tumors like DFSP also complicates the conduct of large-scale epidemiological studies. To support these assertions, Bae et al. (2023) documented the occurrence of pleomorphic undifferentiated sarcoma near the COVID-19 vaccination site in a 73-year-old woman, following the second dose of the Moderna vaccine (2). Although causality has not been proven,the temporal association and the location of the lesion also raised the hypothesis that the immunological stimulus from the vaccine could have contributed to tumor development (2). Additionally, Martínez-Ortega et al. (2024) reported the occurrence of Kaposi's sarcoma in an HIV-negative individual seven days after receiving the third dose of the AstraZeneca vaccine, suggesting a possible link between vaccination and reactivation of oncogenic factors, such as the herpesvirus associated with sarcoma (3). Soyfer et al. (2021) discussed the phenomenon of "radiation recall", in which an inflammatory response is reactivated in previously irradiated tissues after vaccination with the Pfizer-BioNTech COVID-19 vaccine. While not directly related to sarcomas, this phenomenon illustrates how immune stimuli can affect sensitized tissues (4). Although no documented reports suggest an association between the trivalent influenza vaccine and the development of malignant tumors, Toci et al. (2022) observed the development of an injection granuloma mimicking soft tissue sarcoma after the administration of the seasonal flu vaccine (5). Similarly, Quintero et al. (2022) reported a granulomatous mass that resembled a sarcoma after COVID-19 vaccination with the Moderna vaccine (6). Furthermore, studies since 1990 have investigated the development of high-grade sarcomas as rare adverse effects of vaccination in felines, with the hypothesis that these tumors may be induced by an intense and chronic inflammatory response to the vaccine or injection. The malignant transformation of fibroblasts and myofibroblasts as a result of this inflammation is supported by the characteristic histological appearance of Feline Injection-Site Sarcoma (FISS), which includes the presence of increased inflammatory cells, multinucleated giant cells, central areas of necrosis, and, in some cases, a grayish-blue material inside macrophages, compatible with aluminum-based vaccine adjuvants (7). The connection between vaccination and the development of cutaneous sarcomas, such as Dermatofibrosarcoma Protuberans, remains hypothetical due to the lack of conclusive evidence. The rarity of these events, combined with the absence of solid scientific evidence, prevents definitive conclusions but emphasizes the importance of ongoing surveillance. Reporting adverse reactions, even the most uncommon ones, is crucial for monitoring vaccine safety, allowing the early identification of patterns that may suggest potential risks. Further investigations are essential to understand the underlying mechanisms of these reactions and determine if a causal relationship truly exists. In the meantime, it is important to reinforce confidence in vaccination as an indispensable strategy for global public health.

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