Late Seroma in Breast Implants: A Coronavirus Disease 2019 Phenomenon?

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Abstract
The coronavirus disease 2019 (COVID-19) pandemic has been challenging in all aspects of the medical field with new clinical presentations constantly arising. Plastic surgeons are not immune to this and need to be aware of their implications. There has been a recent report of late periprosthetic seroma (breast implant) as a clinical manifestation of COVID-19 infection. To our knowledge, this phenomenon has not been further reported. We present a 53-year-old immunocompromised lady who developed late seroma after COVID-19 infection. She eventually required explantation of the implant and is awaiting autologous reconstruction. It is likely that we will increasingly continue to see this phenomenon of implant complications as a result of COVID-19 infection and should be watchful, especially regarding potential immunocompromised patients.

Keywords
► late seroma
► seroma
► breast implant
► coronavirus
► coronavirus disease 2019

Introduction
Coronavirus disease 2019 (COVID-19) has been reported to have numerous multisystem and multiorgan involvement outside the respiratory symptom. This is postulated to be due to a heightened systemic inflammatory response after exposure to the COVID-19 spike protein. This may potentially result in a supposed “delayed” influx of immunologic cells such as macrophages, neutrophils, and T cells in relation to a foreign breast implant which then presents as a late seroma. A recent paper reports two patients who developed late seromas after COVID-19 infection.1 Other authors have also presented their experience with this phenomenon after COVID-19 vaccination as well.2-4 We present our case of an immunocompromised lady who developed a late seroma of her tissue expander following COVID-19 infection.

Case
A 53-year-old female who underwent left skin-sparing mastectomy and tissue expander insertion (Mentor CPX4 Smooth Breast Tissue Expander) 7 months ago for invasive ductal carcinoma presented to our clinic with sudden onset of left breast swelling and erythema (► Fig. 1). She was still undergoing adjuvant chemotherapy. Physical examination revealed fluctuance at the lateral aspect of the breast with surrounding skin erythema. She did not have any history of fever. An ultrasound showed a large fluid collection at the 3 o’clock position (► Fig. 2). Her biochemical markers showed neutropenia with an absolute neutrophil count of 0.42 × 10^9/L (range: 2.00–7.50 × 10^9/L). She had normal albumin of 38 g/L (range: 35–50 g/L). She underwent ultrasound-guided aspiration and percutaneous drain insertion which yielded 450 mL of straw-colored viscous fluid. Fluid cultures were negative for bacteria.
and acid-fast bacilli, but fungal culture revealed *Candida parapsilosis* complex. She was treated with oral fluconazole and the drain was removed after 5 days. In view of positive fungal cultures, the patient was counseled for autologous reconstruction after completion of adjuvant chemotherapy during her outpatient follow-up. She subsequently underwent removal of tissue expander pending delayed autologous reconstruction. Tissue cultures taken from the capsule grew *Candida parapsilosis* complex. She was kept on oral fluconazole for 2-week duration and has since recovered uneventfully. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; COVID-19 agent) polymerase chain reaction nasopharyngeal swab test taken as a routine for all hospitalized patients was positive though the patient was asymptomatic with no respiratory symptoms.

**Discussion**

COVID-19 infection in an immunocompromised patient can result in a plethora of multisystem dysfunction. In our patient, while she had no respiratory symptoms, her sole complaint was of breast swelling and erythema 7 months after index surgery. It is hard to correlate the exact time of COVID-19 infection and seroma development in our patient as she was otherwise asymptomatic. Her immunocompromised state may have influenced this. Núñez et al reported the development of seroma in one patient within 4 days and the second patient almost immediately after onset of COVID-19 symptoms.\(^1\) Both patients had ultrasound-guided puncture of the fluid collection. The second patient was reported to have the recurrence of the seroma when there was a worsening of the respiratory symptoms. This required surgical drainage when her respiratory condition improved. Both cases had negative fluid cultures, and implants were salvaged. In our case, while the bacteria cultures were negative, the fungal culture grew *Candida parapsilosis* complex. This influenced the decision for explantation of tissue expander and delayed autologous breast reconstruction after completion of adjuvant chemotherapy.

Periprosthetic breast implant seromas have been postulated to be related to trauma, hematoma, subclinical infection, implant rupture, and rarer but of concern, breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). The detection of CD30+ve atypical cells is diagnostic of BIA-ALCL and helps differentiate a benign seroma from a malignant seroma. Practically, the approach toward a benign seroma is largely dependent on the presence of infection as this affects implant salvage versus explantation. Typically, percutaneous drainage of the seroma is attempted and if seroma recurs, patients are usually brought to surgery for surgical drainage. Relevant to our case report, there has been no literature which has analyzed the cytology of a COVID-19 infection-related seroma. Unfortunately, we did not analyze the fluid that was drained as well. It is arguable that the patient was immunocompromised and, hence, has a higher propensity for opportunistic infection leading to a seroma. However, she had recovered uneventfully postoperatively and had been on chemotherapy for at least 5 months before the seroma developed acutely. Given the timeline of COVID-19 infection and acute seroma formation, we find it too much of a coincidence and hypothesize that the inflammatory response from COVID-19 triggered a seroma formation.

Besides developing late periprosthetic seroma after COVID-19 infection, there have been reports of late seromas immediately after COVID-19 vaccination. This included both mRNA vaccines and viral vector vaccines.\(^2-4\) Maximillian et al have summarized their findings of seven patients in the Letter to the Editor. It includes the time of onset of symptoms after vaccination, type of vaccine, and treatment. The range of time of onset was 2 to 19 days. The type of vaccine included Pfizer-BioNTech, AstraZeneca, and Johnson & Johnson’s Janssen. Three patients required the removal of the implants, whereas four patients were treated conservatively with various combinations of nonsteroidal antiinflammatories, antibiotics, painkillers, and cryotherapy.

Another reported effect following COVID-19 vaccination is capsular contracture.\(^5\) The patient underwent augmentation mastopexy with a smooth-walled implant. She had her
vaccination 5 months postoperatively and developed Baker IV capsular contracture requiring capsulectomy and implant exchange. Intraoperative findings showed a dense fibrotic capsule.

Similarly to implants, there has been a report of delayed inflammatory reactions to hyaluronic acid fillers following COVID-19 vaccination. The authors speculate that the potential mechanism is the blockade of angiotensin 2 converting enzyme receptors (ACE2), which are targeted by the SARS-CoV-2 virus spike protein to gain entry into the cell. Spike protein interaction with dermal ACE2 receptors favors a pro-inflammatory, loco-regional TH1 cascade, promoting a CD8+ T cell-mediated reaction to incipient granulomas, which previously formed around residual HA particles.6 This reaction has been included in the U.S. Food and Drug Administration Briefing Document for the Moderna mRNA COVID-19 vaccine.7 The recommended treatment is high-dose corticosteroids to suppress the inflammatory cascade response.

The influence of COVID-19 on the plastic surgeons’ practice is rapidly evolving. While the number of case reports is currently low, we can expect to see more patients with late implant complications. Patients with implant complications should still be treated based on current evidence-based guidelines and local protocol, taking into account emerging evidence of COVID-19 infection and implant interactions.

Authors’ Contributions
S.L.S.C. drafted the paper, preformed data collection and literature review. W.L.J.M. conceptualised and finalised the paper.

Patient Consent
Informed consent for publication was obtained from the patient.

Conflict of Interest
None declared.

Reference
1 Núñez PM, González MP, Cordero ÁJ. Late seroma of the breast in association with COVID-19 infection: two case reports. Eur J Plast Surg 2021;1–4:1–4