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CASE REPORT

Delayed prosthetic seroma: a localized inflammatory response to COVID vaccination and infection?

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Abstract
We present a patient whom we believe developed a late abdominal mesh collection in response to COVID-19 mRNA vaccination booster and COVID-19 infection. A polypropylene mesh was placed during her right breast reconstruction operation 2 years ago where she underwent a right transverse abdominis rectus muscle (TRAM) free flap. She recovered uneventfully from this operation. This lady, though vaccinated, developed respiratory symptoms and tested positive for COVID-19 infection 3 days after her booster injection. She then noticed right-sided abdominal swelling 3 days after the onset of respiratory symptoms. She only presented 1 month later due to a 7-day history of pain at the site of abdominal swelling. A computed tomography scan confirmed the presence of a seroma, and she underwent ultrasound-guided percutaneous drainage. A COVID Antigen Rapid Test of the fluid returned positive, though the PCR swab returned negative. There have been no published reports of periprosthetic mesh seroma after COVID-19 vaccination or infection to date. We wanted to share our experience so that other surgeons may be aware of this potential presentation given the current ongoing pandemic.
Level of evidence: Level V, risk/prognostic.

Keywords COVID-19 · SARS-CoV-2 · COVID-19 infection · COVID-19 vaccination · Prosthetic mesh · Seroma

Introduction

The COVID-19 pandemic has reshaped the world we live in. Its varied clinical presentations outside of the respiratory system continue to baffle physicians. There have been reports of late periprosthetic breast implant seroma in relation to COVID vaccination or infection [1–4]. It is hypothesized that an immunological response during infection or after a vaccination result in an influx of inflammatory cells such as neutrophils and T cells resulting in a seroma. There have been findings of a positive viral load found within blood serum, urine, and feces [5]. As of our knowledge, there have been no reports of a positive viral load found within periprosthetic fluid.

We present a case of a lady who took a COVID-19 booster injection and simultaneously developed COVID-19 infection 3 days after the booster. She then developed periprosthetic mesh seroma immediately after developing respiratory symptoms due to COVID-19 infection.

Case report

A 56-year-old Chinese female with a history of diabetes had undergone right breast reconstruction with a free right transverse rectus abdominis muscle (TRAM) flap for invasive ductal carcinoma almost 2 years ago. A PROLENE® Polypropylene Mesh (Ethicon, Johnson & Johnson) was used for rectus sheath repair. She recovered uneventfully with no donor site scar complications. She did not require adjuvant chemo or radiotherapy. She had taken the Pfizer-BioNTech COVID-19 booster injection early November 2021. Unfortunately, she developed respiratory symptoms 3 days after the booster injection and tested positive for COVID-19. Three days after the development of respiratory symptoms, the patient noticed right-sided abdominal swelling which coincided with the location of the Prolene mesh (Fig. 1). She presented only 1 month later after the onset of abdominal swelling. This was associated with a 7-day history of pain.

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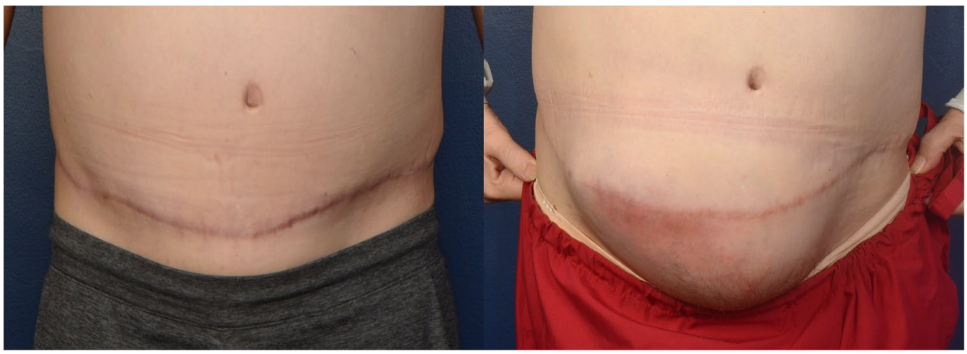

Fig. 1 Left: patient seen 3 months before her COVID-19 booster injection and subsequent COVID-19 infection. Her abdomen had healed well with no wound dehiscence. There is no hypertrophic or keloidal scars. Right: patient seen with a 1-month complaint of abdominal swelling after COVID-19 booster injection and infection. There is a large fluctuant swelling at the right lower abdomen which corresponds to the site of the Prolene mesh

On examination, a large fluctuant mass was seen at the right lower abdomen at the surgical scar site. There was slight erythema and was mildly tender. Her inflammatory markers were slightly elevated with a white cell count of 10.3^9/L (range 4–10^9/L) and C-reactive protein of 75 mg/L (range 0–5 mg/L). A computed tomography (CT) scan showed a large $16 \times 12 \times 8$ cm hypodense collection in the subcutaneous layer of the abdominal wall, above the Prolene mesh (Fig. 2). She underwent ultrasound guided aspiration and percutaneous drain insertion which yielded 720 mL of frank pus (Fig. 3).

An Antigen Rapid Test (Abbott PANBIO™) was performed on the fluid and returned positive (Fig. 4). However, a SARS-CoV-2 (COVID-19 agent) PCR swab test was negative. The bacterial cultures showed *Group B Streptococcus*. She was treated with the appropriate antibiotics, and the mesh was salvaged. The drain fluid quality gradually turned to haemoserous (Fig. 5), and the drain was subsequently removed when the amount decreased.

A positive COVID-19 N-protein serology confirmed that she had a previous COVID-19 infection.

Discussion

This is the first case of late periprosthetic mesh collection which potentially occurred in response to COVID vaccination and infection that we know of to date. There have been recent case reports of late breast implant seromas in relation to COVID vaccination or infection alone [1–4]. Another study also co-related delayed inflammatory reactions to hyaluronic acid dermal fillers after exposure to COVID-19 infection [6]. A case of sudden development of Baker IV capsular contracture for breast augmentation after COVID-19 vaccination has also been reported [7]. However, there has been no proven explanation for these complications. We hypothesize that a heightened inflammatory response during infection or after vaccination result in an influx of inflammatory cells. There could be a preferential migration

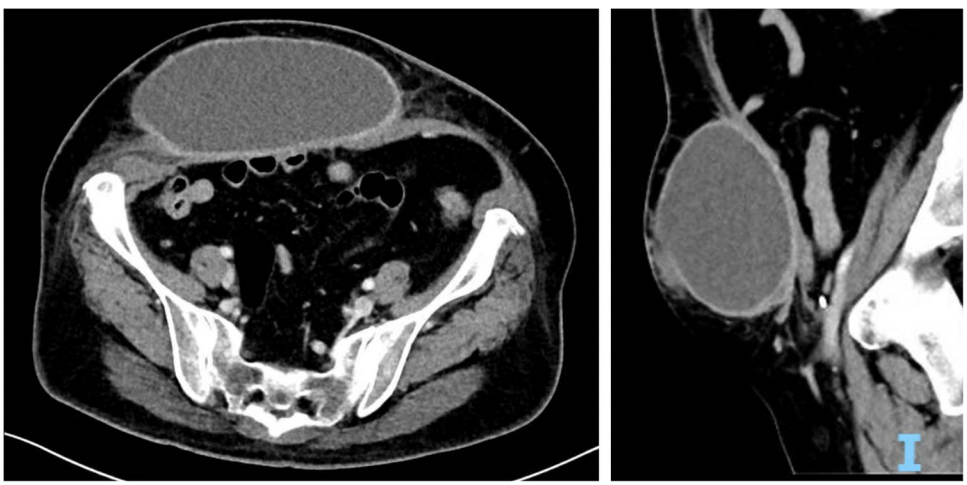

Fig. 2 Computed tomography scan showing a large hypodense collection sited mainly over the right abdomen where the Prolene mesh was placed (left: axial view, right: sagittal view)

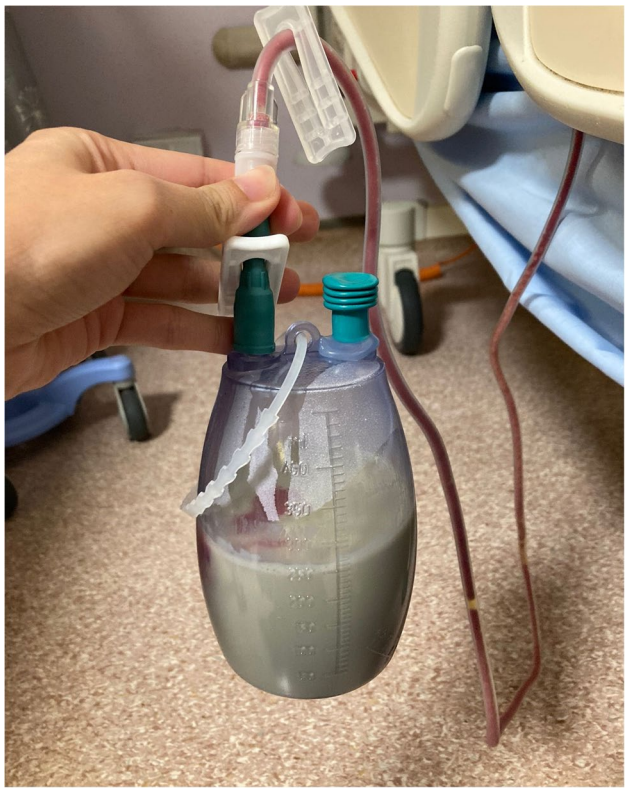

Fig. 3 Frank pus following ultrasound guided aspiration

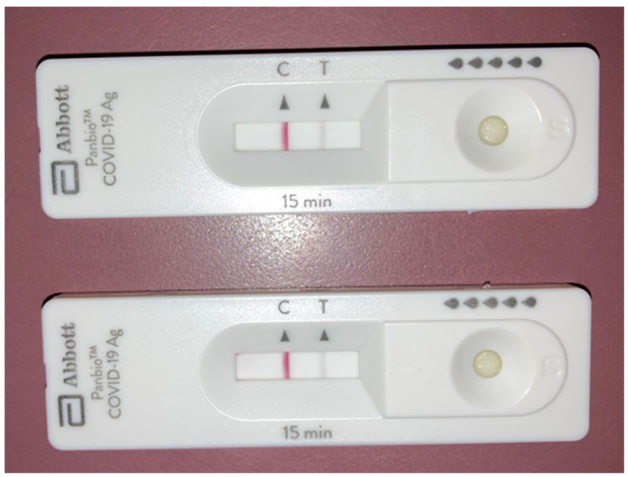

Fig. 4 Positive Antigen Rapid Test (ART) performed twice on the aspirated pus fluid

of neutrophils, macrophages, and T cells to the prosthesis, leading to seroma formation. In our case report, this lady unfortunately had both a COVID-19 booster injection as well as infection shortly after. It is difficult to pinpoint whether it was the booster injection or infection that was the inciting reason for the late seroma development. They could

Fig. 5 Drain fluid subsequently turned haemoserous and was removed when the amount decreased

have been synergistic resulting in an exceptionally amplified inflammatory response.

We wanted to investigate if we could detect the COVID viral load in the periprosthetic fluid since the virus has been reported to be detected within blood serum, urine, and feces [5]. The inflammatory response could have resulted in leaky blood vessels, and the virus could have seeded the prosthesis. We tested the aspirated fluid for COVID-19 spike protein and RNA. Interestingly, the Antigen Rapid Test (ART) returned positive twice (Fig. 3). However, the SARS-CoV-2 PCR swab test was negative even though it was repeated. There could be a few explanations for this. First, it has been shown that the Abbott PANBIO™ ART kit has a sensitivity of 71.8%. This means that it has a false-positive rate as high as almost 20%. This would be supported by the negative PCR swab test that was performed subsequently, meaning to say that no viral load was present. Second, it is plausible that there could be actual viral load detected in the periprosthetic fluid. However, super-imposed bacterial infection due to her diabetic status and late presentation may have diluted or degraded the virus making it undetectable on the PCR swab. Third, the usage of the ART kit or PCR swab has not been validated on seroma fluids (in our case pus). This

would make our results difficult to interpret. However, given that the virus' RNA may be detected in blood serum, urine, and feces, it is not impossible for the viral particle to extravasate and preferentially seed a prosthesis due to increased capillary permeability from a pro-inflammatory response.

We acknowledge that our patient's bacterial culture returned positive for *Group B Streptococcus*. Her presentation can be argued to be simply a flare of a subacute bacterial infection. However, given other case reports of breast implant seromas in relation to COVID-19 vaccination and infection, we find the temporal relation to her COVID-19 booster injection and infection to be too much of a coincidence. It is very uncommon for mesh infections to occur this late [8], especially when her post-operative recovery was uneventful. She moreover did not require adjuvant chemo or radiotherapy. We believe that she developed a transudative sterile seroma which then became secondarily infected due to chronicity and diabetes.

The authors have reported a combination of treatment modalities for periprosthetic seroma in breast implants [1, 3]. These include conservative management such as non-steroidal anti-inflammatories, antibiotics, and cryotherapy; as well as minimally invasive procedures such as percutaneous drainage. In our case, we decided for percutaneous drainage as the collection seen on the CT scan was large. Her slightly elevated inflammatory markers also raised the concern for infection. We wonder if this could have been treated conservatively if she had presented earlier with a smaller and still sterile seroma collection.

Our findings and current literature seem to suggest a co-relation between late periprosthetic seromas and COVID-19 vaccination or infection. This could have implication for other types of foreign materials such as prosthetic joints, hernia meshes, or endovascular grafts. Much work needs to be done to prove causality. However, we suspect that we will continue to see increasing numbers of "unexplained" periprosthetic seromas and should perhaps have a high index of suspicion of COVID-19 infection or recent vaccination.

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Declarations

Consent to participate Informed consent was obtained from the patient included in the study.

Ethical approval All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This paper contains 1 case report. The Singapore SingHealth Centralised Institutional Review Board has confirmed that no ethical approval is required.

Conflict of interest Stephanie Li-shan Chan, Michael Ku Hung Hsieh, James Wan Loong Mok, and Tze Yean Kong declare no conflict of interest.

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