Two Independent Capsules Surrounding a Single Textured Implant in Ehlers-Danlos Syndrome

Summary: Textured breast implants are associated with prolonged inflammation leading to increased risk for complications such as the development of anaplastic large cell lymphoma. The underlying molecular mechanisms that drive increased inflammation toward textured implants (compared with smooth implants) remain poorly understood. Here, we present the first known case of a patient with Ehlers-Danlos syndrome (EDS) who developed two independent fibrotic capsules around a single textured silicone implant. The patient was found to have one internal capsule tightly adherent to the implant and a second external capsule that was attached to the surrounding tissue. We observed that the internal implant-adherent capsule was composed of a highly aligned and dense collagen network, completely atypical for EDS and indicative of a high mechanical stress environment. In contrast, the external nonadherent capsule, which primarily interacted with the smooth surface of the internal capsule, displayed disorganized collagen fibers with no discernible alignment, classic for EDS. Remarkably, we found that the internal capsule displayed high activation of monocyte chemoattractant protein-1, a mechanoresponsive inflammatory mediator that was not elevated in the disorganized external capsule. Taken together, these findings demonstrate that the tight adhesion between the textured implant surface and the internal capsule creates a high mechanical stress environment, which is responsible for the increased local inflammation observed in the internal capsule. This unique case demonstrates that mechanical stress is able to override genetic defects locally in collagen organization and directly connects the textured surface of implants to prolonged inflammation. (Plast Reconstr Surg Glob Open 2022;10:e4470; doi: 10.1097/GOX.0000000000004470; Published online 25 August 2022.)
the external capsule interacted with the smooth surface of the internal capsule, this unique case provided a valuable window into the factors underlying the prolonged inflammation observed around textured implants.

**CASE PRESENTATION**

A 59-year-old woman with EDS and a history of left breast implant-based reconstruction with Allergan 410 textured implant (partial submuscular augmentation without mesh or acellular dermal matrix) for cancer presented to our clinic with a severe Baker IV capsular contracture and pain. The patient was concerned regarding the potential risk for BIA-ALCL and sought to exchange her textured implant for a smooth one. Intraoperatively, the left breast implant was found to lie within two distinct capsules (Fig. 1A–C). The internal capsule was tightly adherent to the breast implant, whereas the external capsule was only adherent to the surrounding native subcutaneous tissue (Fig. 1). Interestingly, the internal capsule was present on all textured surfaces but spared the few smooth portions of the textured implant, including the identifying information tag and orientation knobs (Fig. 1B). Upon gross examination, there were no signs of infection in the capsules or the implant. In addition, no evidence for infection was observed in pathology. Complete internal capsulectomy and external capsulectomy were performed, followed by placement of a smooth round silicone 560-cm³ implant. The patient was discharged and completed a 5-day course of Keflex and had a routine postoperative course.

We found that the internal capsule was tightly adherent to the implant and appeared to be constrained and under high levels of mechanical stress relative to the external capsule, which was attached to the surrounding tissue. Hematoxylin and eosin staining of the internal capsule revealed that it was surprisingly organized and entirely comprised aligned collagen fibers with increased cellularity (see figure, Supplemental Digital Content 1A, Hematoxylin and eosin of internal capsule showing unidirectionally aligned fibers with increased cellularity. Optical fields were analyzed from six tissue sections of our case. Scale bars = 100 µm. P less than 0.05, http://links.lww.com/PRSGO/C134).

Trichrome staining demonstrated that this internal capsule was composed of thick fibrous tissue with increased collagen deposition (see figure, Supplemental Digital Content 1B, Trichrome stain, demonstrating increased collagen deposition in the internal capsule compared with the external capsule. Optical fields were analyzed from six tissue sections of our case. Scale bars = 100 µm. P less than 0.05, http://links.lww.com/PRSGO/C134). Herovici stain, differentiating between mature (red) and immature (blue) collagens, demonstrated predominantly mature collagen in the internal capsule (see figure, Supplemental Digital Content 1C, Herovici stain, demonstrating increased deposition of mature, red collagen staining in the internal capsule. Optical fields were analyzed from six tissue sections of our case. Scale bars = 100 µm. P less than 0.05, http://links.lww.com/PRSGO/C134), and picrosirius red staining confirmed a highly aligned and tightly packed collagen fiber arrangement (see figure, Supplemental Digital Content 1D, Picrosirius red staining, demonstrating the internal capsule with highly aligned and tightly packed collagen fibers, whereas the external capsule shows a disorganized network, consistent with the typical histological presentation of EDS. Optical fields were analyzed from six tissue sections of our case. Scale bars = 100 µm. P less than 0.05, http://links.lww.com/PRSGO/C134). The presentation of highly organized parallel collagen fibers is consistent with previous
histological evaluations of double capsules. However, this presentation is completely atypical of a patient with EDS, which is a disorder known for disorganized, wavy, and weak collagen architecture.

To confirm that the adherence of the internal capsule tissue to the implant resulted in elevated mechanical stress, we stained for αSMA, which identifies myofibroblasts that are commonly found in areas of contracture. We observed a significant increase in myofibroblasts in the internal capsule. Immunofluorescence staining of the internal capsule shows a higher activation of alpha-smooth muscle actin (αSMA) positive (green) myofibroblasts compared with external capsule. Optical fields were analyzed from six tissue sections of our case. Scale bars = 100 µm. P less than 0.05, http://links.lww.com/PRSGO/C134.

In contrast, the external capsule comprised loosely dispersed collagen fibers of varying diameters with an irregular fiber outline and no observable alignment, which is classic for type I EDS, see figure, Supplemental Digital Content 1A–D, http://links.lww.com/PRSGO/C134. In as much as elevated mechanical stress is associated with inflammatory signaling, we subsequently performed immunofluorescence staining for monocyte chemoattractant protein-1 (MCP1), an important inflammatory signaling molecule, and observed significantly higher expression in the internal capsule. Immunofluorescence staining shows increased expression of cytokine MCP1 (red) in the internal capsule, indicating a highly inflammatory environment. Optical fields were analyzed from six tissue sections of our case. Scale bars = 100 µm. P less than 0.05, http://links.lww.com/PRSGO/C134.

DISCUSSION

Although double capsules have been reported in some patients before, this is the first known case of a patient with EDS with two independent implant capsules surrounding a single textured silicone implant. It seems likely that the two capsules resulted from the shearing of a single capsule at some point in the past, probably due to the COL5A genetic defect present in this patient’s type I EDS. We found that the internal capsule was adherent to the underlying textured surface and mechanically constrained...
by the implant. The significant increase in the number of myofibroblasts in the internal capsule confirmed the presence of a high mechanical stress environment. In contrast, the external capsule primarily interacted with the smooth surface of this internal capsule. This provided the opportunity for the implant and the implant-adherent internal capsule to move within the external capsule. The external capsule demonstrated significantly lower numbers of myofibroblasts, confirming the presence of a lower mechanical stress environment. This resulted in a stark difference in collagen architecture between the two capsules. The internal capsule had highly aligned collagen fibers, similar to those described in pacemaker leads, which are subject to high mechanical forces. In contrast, the external nonadherent capsule displayed a loose collagen phenotype classic for type I EDS. Remarkably, we found that the internal capsule displayed high activation of MCP-1, a mechanoresponsive inflammatory mediator that was not elevated in the disorganized external capsule. Taken together, these findings demonstrate that the tight adhesion between the textured implant surface and the internal capsule creates a high mechanical stress environment, which is responsible for the increased local inflammation observed in the internal capsule (Fig. 2).

The presentation of highly organized collagen fibers in the internal capsule is completely atypical of a patient with EDS, which is a disorder known for disorganized, wavy, and weak collagen architecture. Despite the presence of EDS, the internal capsule in this patient displayed highly organized and parallel collagen fibers, which is typical for a textured breast implant under a high mechanical stress environment and is consistent with previous reports on other double capsules. Thus, this unique case demonstrates that mechanical stress is able to locally override genetic defects in collagen organization and directly connects the textured surface of implants to prolonged inflammation. These findings may have important implications for implant-related adverse events, such as BIA-ALCL and the yet ill-defined syndrome known as breast implant illness, which may represent the sequela of a prolonged inflammatory state induced by the textured surface of breast implants.

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