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Sarcoidosis after breast implant rupture: Looking beyond granulomas

Dear Editor,

Numerous cases of patients developing an autoimmune or inflammatory disease after silicone breast implantation have been reported in the literature, such as Sjogren syndrome and systemic sclerosis [1]. In addition, five cases of sarcoid-like diseases have been described [2–6]. A meta-analysis pooling case-control and cohort studies has shown no increased risk [7], except when a diagnosis of autoimmune disease had been self-reported [8]. More recently, with the concept of autoimmune/inflammatory syndrome induced by adjuvants (ASIA, or Shoenfeld's syndrome) [9], an international register has been set up to investigate the relationship between external adjuvant exposure and development of an aberrant autoimmune response [10,11]. Lastly, in 2018, a retrospective case-control study of women with silicone breast implants showed a significant increase in the risk of developing autoimmune or inflammatory disease, including sarcoidosis with an OR of 1.98 [95% CI 1.50–2.60] [12].

A 44-year-old woman, from Caribbean origin, without any medical history, was implanted with breast implants for esthetical purpose in 2011. Seven years later, she presented with an acute vision loss and complained of chest pain. She was diagnosed with anterior bilateral granulomatous uveitis and bilateral breast implant rupture with several siliconomas within breasts and axillary nodes. Blood tests showed polyclonal hypergammaglobulinemia (17 g/L) and high levels of angiotensin-converting enzyme (214 UI/L) and lysozyme (31 mg/L), with normal C-reactive protein (CRP) level. Microbiological investigations (human immunodeficiency virus, hepatitis B and C virus serologiy, interferon-gamma release assay) were negative. Chest CT revealed diffuse interstitial lung disease with bilateral axillary lymphadenopathy (Fig. 1A). A diagnosis of sarcoidosis with pulmonary and ocular involvement was suspected, and local ophthalmic treatment with corticosteroids was initiated. Surprisingly, no link between sarcoidosis and breast implant rupture was established at this time. After surgical extraction of breast implants, she developed sub-acute respiratory symptoms. Blood test showed hypoxemia (60 Hg mm) and mild inflammatory syndrome with CRP at 48 mg/L. Chest CT revealed exacerbation of the pulmonary abnormalities, with bilateral ground-glass opacities, and peribronchovascular condensations (Fig. 1B). Bronchoalveolar lavage fluid analysis showed mixed alveolitis, without microbial agent. Transbronchial biopsy and axillary lymph node microbiopsy revealed an epithelioid and gigantocellular granuloma without caseous necrosis, but with some optically-empty vacuoles (Fig. 1C). Microbiological examinations were negatives. Rapidly, the patient complained of paresthesia and neuropathic pain in the right hand and in both feet, with gait disturbance. Clinical examination found distal motor and sensitive impairments of both legs (common fibular nerve territories), and in the right median nerve territory. Electromyoneurography identified abnormalities that were compatible with multineuritis. Biopsy of the fibular nerve was performed and found granulomatous inflammation, with no sign of foreign material. Further investigations with electron microscopy and energy dispersive X-ray (EDX) spectrometry were performed on transbronchial, lymphatic and nerve biopsy. This exam revealed silicon particles within nodes and bronchial mucosa that were located inside the optically-empty vacuoles seen in light microscopy (Fig. 1D), but there was no evidence of silicon on the nerve biopsy. The final diagnosis of systemic granulomatosis linked to silicone spread was retained. Oral corticosteroids were started at 1 mg/kg/day associated with hydroxychloroquine, with good clinical efficacy in a few weeks.

Our patient's clinical history is clearly consistent with an inflammatory disease provoked by rupture of silicone breast implants. However, the pathophysiological mechanism remains unclear. The first hypothesis is a direct granulomatous reaction against silicon particles following extensive systemic dissemination. Indeed, while local granulomatous reaction to silicone is common after implant rupture, systemic dissemination of silicone gel is also well–demonstrated and can be detected through MRI [14–16]. Of note, silicon can also migrate throughout implant shell without rupture in the form of “gel bleed”. Electron microscopy with EDX has demonstrated the presence of silicon far from the implantation site, in the liver of two living patients [17], and in multiples organs of an autopsied woman with breast implant rupture [18]. In that case, silicone had spread to brain, spinal cord, lymph nodes, lung, and digestive tract, but not in the nerves. In our case, we were able to demonstrate the presence of silicon in lung and axillary nodes as well as pulmonary parenchyma but we could not establish its presence in the eye nor in the nerve, despite disseminated granulomatous reactions.

The other hypothesis is a full-blown sarcoidosis triggered by silicon as an external adjuvant, in a predisposed patient, which could be included in the context of an ASIA [13]. Ocular dissemination of silicon has not been reported and, in our case, clinical presentation was consistent with a sarcoid uveitis but we could not perform further exploration. Nerve biopsy also revealed granulomas, but without showing any trace of silicon. Although this may result from technical failure, it is likely that granulomatous reactions developed away from the triggering foreign body, supporting the hypothesis of a sarcoidosis in the setting of an ASIA.

Consent

The patient gave here written consent for publication.

Declaration of Competing Interest

The authors declare no conflicts of interest.

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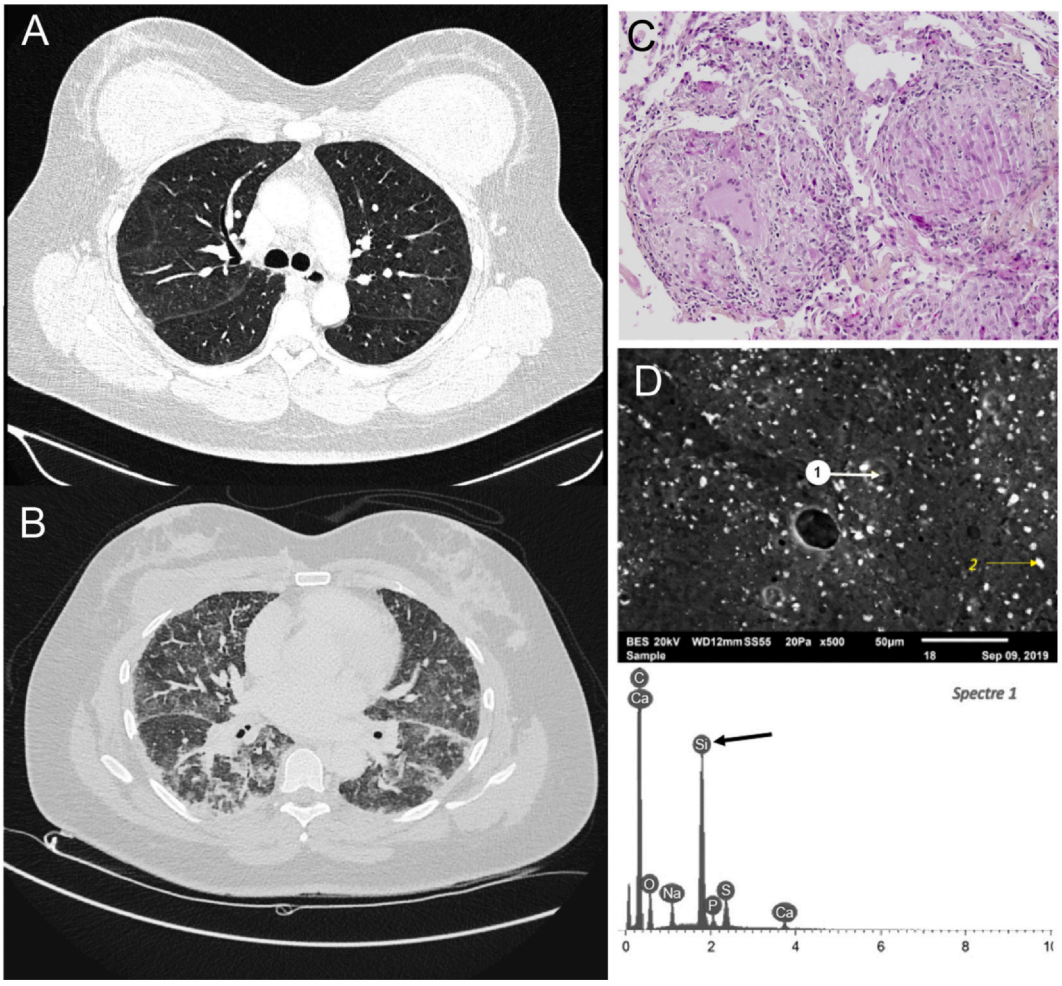

Fig. 1. (A) Chest CT at diagnosis of breast implants rupture with moderate diffuse interstitial lung disease and silicone implants with periprosthetic inflammatory reaction (*), and (B) after extraction of implants with severe diffuse interstitial lung disease. (C) Transbronchial biopsy HES X 200 showing infiltration of lung parenchyma by small, well formed, noncaseating granulomas composed of epithelioid histiocytes and multinucleated giant cells. (D) Electron microscopy with spectral analysis of transbronchial biopsy, showing empty vacuoles with presence of silicon on the bordure [1], related to silicon deposit (arrow).

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