Clinical Kidney Journal, 2021, vol. 14, no. 7, 1848–1850

doi: 10.1093/ckj/sfab058
Advance Access Publication Date: 15 March 2021
Exceptional Case

EXCEPTIONAL CASE

Systemic sclerosis and microscopic polyangiitis after systemic exposure to silicone

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ABSTRACT

The relationship between silicon breast implants (SBIs) and autoimmune/inflammatory syndrome induced by adjuvants (ASIA) has been extensively analysed, with discordant results. We present a 45-year-old woman with confirmed systemic exposure to SBI who developed systemic sclerosis (SSc) followed by anti-neutrophil cytoplasmic antibody anti-myeloperoxidase vasculitis with renopulmonary syndrome. The novelty of our case is, first, confirmation of systemic exposure to SBI and, second, chronologic development of not one, but two severe autoimmune diseases. Controversy may still remain regarding SBIs and ASIA because it is unclear that previous studies confirmed systemic exposure to silicon in their cohort of patients.

Keywords: ANCA anti-MPO vasculitis, ASIA, crescentic glomerulonephritis, silicon breast implants, systemic sclerosis, thrombotic microangiopathy

BACKGROUND

Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) involves a broad spectrum of autoimmune diseases that are triggered by exposure to substances with adjuvant activity [1]. Adjuvants are compounds that enhance a specific immune reaction resulting in the generation of antibodies against specific pathogens. Substances described to have an important adjuvant activity include aluminum salts, mineral oils, collagen, hyaluronic acid and silicone, the use of which in daily clinical practice is increasingly more frequent. Shoenfeld and Agmon-Levin [1] established diagnostic criteria for ASIA in 2011. One of the main adjuvants used in clinical practice is silicone breast implants (SBIs). The relationship between SBIs and the risk of development of various autoimmune connective diseases, including sarcoidosis, Sjögren's syndrome, systemic sclerosis (SSc) and anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), has been described in several anecdotal case reports and analysed in meta-analyses and cohort studies, with discordant results [2–4].

CASE REPORT

A 45-year-old Colombian woman was admitted with lower extremity oedema, oliguria, fever and hypertension. At age 40 she underwent silicone breast implantation for cosmetic reasons. Three years later her right SBI accidentally burst. Implant explantation was postponed because of the patient's refusal. She was diagnosed with SSc at age 44, after development of chronic fatigue, polyarthralgia and Raynaud phenomena. Treatment

Received: 7.2.2021; Editorial decision: 11.3.2021

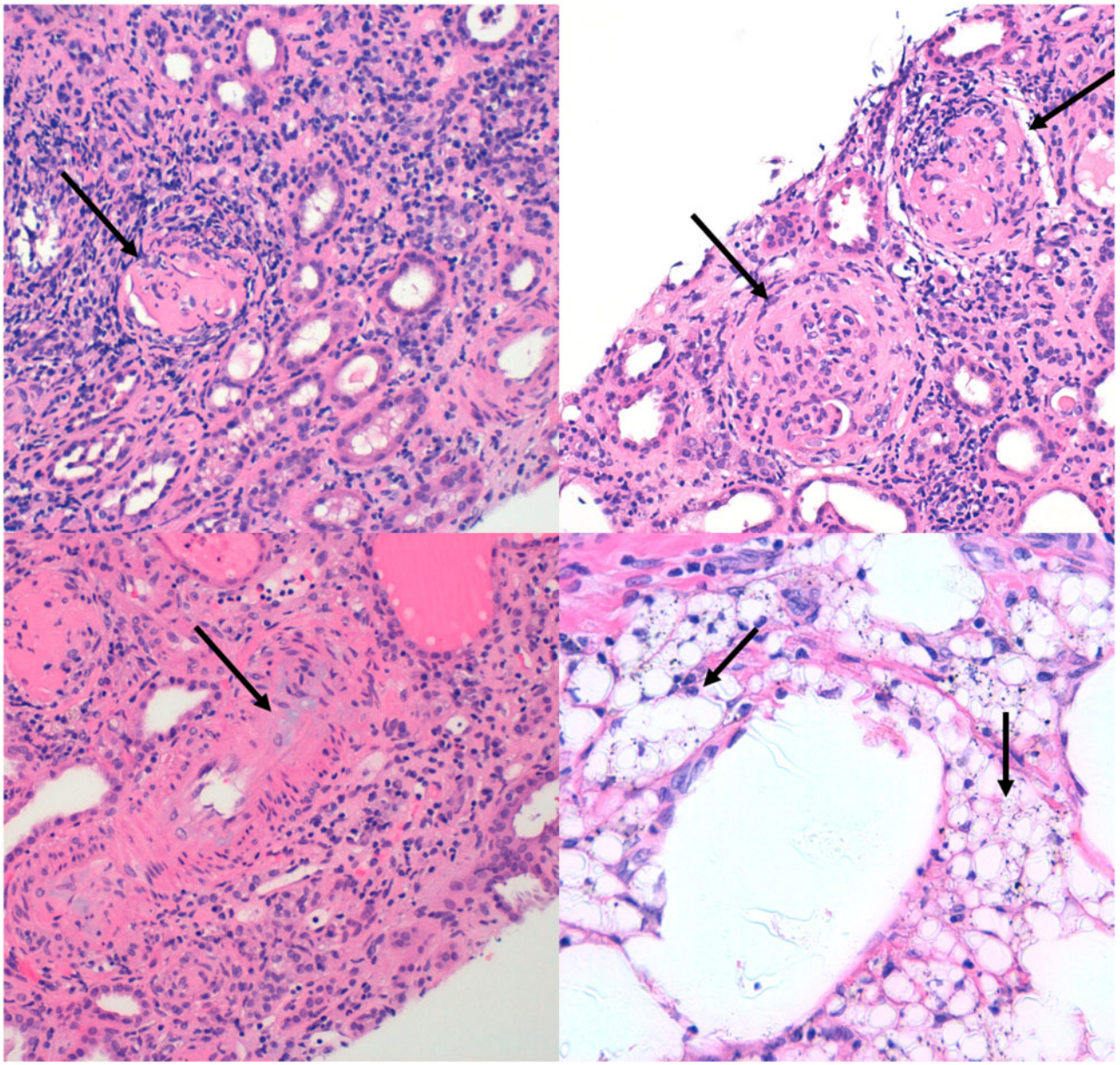

FIGURE 1: Anatomopathological findings. (Top left) Renal biopsy showing mesangial proliferation and predominant mononuclear infiltration (20× optical microscopy, haematoxylin and eosin stain). (Top right) Renal biopsy showing crescentic glomerular proliferation (40× optical microscopy, haematoxylin and eosin stain). (Bottom left) Renal biopsy showing vascular wall thickening and obliteration (20× optical microscopy, haematoxylin and eosin stain). (Bottom right) Armpit node biopsy showing macrophages with intravacuolar silicon inclusions, typical findings of silicon-induced granulomas (10× optical microscopy, haematoxylin and eosin stain).

consisted of oral prednisone and methotrexate, which she discontinued 1 month prior to her current hospitalization. Previous renal function was normal on repeated measures.

Physical examination revealed hypertension (204/101 mmHg) and peripheral oedema. Biochemical analyses showed a serum creatinine of 17 mg/dL, pH 7.22, bicarbonate 13.5 mmol/L, potassium 5.63 mmol/L, C-reactive protein 157 mg/dL (5.9 g/dL) and a normal platelet count. ANCA anti-myeloperoxidase was positive (97 IU/mL), with normal anti-MBG, complement and rheumatoid factor. Body tomography revealed bilateral pleural and pericardial effusion as well as free liquid in the abdomen and the presence of nodes in the right armpit and internal right mammary chain. Coronavirus disease 2019 polymerase chain reaction was negative.

Renal biopsy results showed necrotizing capillaritis, circumferential cellular extracapillary proliferation in 100% of glomeruli, 50% tubular atrophy and vascular endothelial damage, showing proliferation and thickening of the tunica intima in arcuate and interlobular arteries, causing narrowing and obliteration of the vascular lumen (Figure 1).

Seventy-two hours into her hospitalization, the patient developed alveolar haemorrhage and worsening pericardial effusion, resulting in echocardiographic signs of cardiac tamponade. Initial treatment consisted in haemodialysis and hypertensive emergency, followed by methylprednisolone pulses, rituximab and plasmapheresis. Cyclophosphamide was added due to worsening of alveolar haemorrhage and polyserositis.

After stabilization, excision of the right armpit nodes was performed. Foreign body granulomatosis with silicon inclusions was observed in the anatomopathological analysis (Figure 1).

The pleural and pericardial effusions resolved and ANCA decreased. However, 6 months later the patient continues to be dependent on haemodialysis, with maintenance treatment with mycophenolic acid.

DISCUSSION

The relationship between SBIs and the development of connective tissue diseases has been repeatedly described; however, evidence of this association continues to be controversial. Some case–control and cohort studies and meta-analyses have not found a significant risk associated with SBIs [2]. In contrast, a cohort study and a more recent meta-analysis including 32 studies [3] showed a significant association between SBIs and the risk of rheumatoid arthritis and Sjögren's syndrome. Similarly, recent data from the US Food and Drug Administration (FDA) large post-approval studies (LPASs) on long-term follow-up of 99 993 breast implants (56% of which were SBIs), described significantly higher rates of Sjögren's syndrome, scleroderma and rheumatoid arthritis [4].

Discrepancies observed among different studies could be due to two reasons. First, standardized incidences observed in LPAS cohorts of patients, although higher than those observed in the general population, were relatively low. This suggests that the sample sizes of previous case–control studies were insufficient to provide adequate statistical power to find differences related to exposure to SBIs. Second, SBIs do not necessarily involve systemic exposure to silicon. However, the prevalence of silent or occult SBI rupture has been found to be 77% in a median implant age of 10 years [5].

Our reported case shows a chronological relationship between the systemic exposure of SBIs and subsequent development of aggressive systemic manifestation of ASIA. We suggest the focus of further studies be shifted towards establishing a possible relationship between a confirmed systemic exposure to silicon and autoimmune disease.

PATIENT CONSENT

The patient gave her consent for publication of this case report.

FUNDING

Grant number: PI18/00356 - Instituto de Salud Carlos III - FEDER "Una manera de hacer Europa" - CERCA Programme/ Generalitat de Catalunya - IRBLleida - Fundació Dr. Pifarré

CONFLICT OF INTEREST STATEMENT

All authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available within the article and its supplementary material.

REFERENCES

1. Shoenfeld Y, Agmon-Levin N. 'ASIA' – autoimmune/inflammatory syndrome induced by adjuvants. *J Autoimmun* 2011; 36: 4–8
2. Tugwell P, Wells G, Peterson J *et al*. Do silicone breast implants cause rheumatologic disorders?: A systematic review for a court-appointed National Science Panel. *Arthritis Rheum* 2001; 44: 2477–2484
3. Balk E, Earley A, Avendano E *et al*. Long-term health outcomes in women with silicone gel breast implants: a systematic review. *Ann Intern Med* 2016; 164: 164–175
4. Coroneos CJ, Selber JC, Offodile AC , 2nd *et al*. US FDA breast implant postapproval studies: long-term outcomes in 99,993 patients. *Ann Surg* 2019; 269: 30–36
5. Brown SL, Middleton MS, Berg WA *et al*. Prevalence of rupture of silicone gel breast implants revealed on MR imaging in a population of women in Birmingham, Alabama. *AJR Am J Roentgenol* 2000; 175: 1057–1064