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Scleroderma renal crisis following silicone breast implant rupture: a case report and review of the literature

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ABSTRACT

Systemic sclerosis (SSc) is a chronic multisystem autoimmune disorder characterised by progressive functional and structural abnormalities in blood vessels leading to microvascular dysfunction, excessive production and deposition of collagen leading to the fibrosis of skin and internal organs.

The aetiology of the disease is unknown. However, exposure to various environmental factors, such as polyvinyl chloride and silica have been thought to play a role in the development of the disease. For this reason, silicone breast implants have been postulated as a cause for a range of autoimmune diseases including systemic sclerosis. This remains as yet unconfirmed.

We report the case of a 52-year-old woman who presented with rapid development of skin thickening followed by scleroderma renal crisis (SRC) following rupture of silicone breast implants. This is the first published case of SRC in this setting. The literature on silicone and autoimmunity is reviewed.

Case presentation

In July 2008, a 47-year-old previously healthy sports co-ordinator developed ridging in her silicone breast implants four years after implantation. Subsequent ultrasound imaging in August 2008 confirmed ruptured implants which required re-implantation in August 2012. Prior to this in January 2011 she had developed Raynaud's phenomenon which became more severe following the re-implantation and was followed four months later by puffiness of her fingers and hands with rapid thickening and tightening of the skin which progressed from her fingers to above her elbows and on to the chest wall (Fig. 1).

In early April 2013 she presented to a peripheral hospital with abrupt onset shortness of breath and was noted to be in biventricular cardiac failure. Physical examination demonstrated marked peripheral oedema, chest radiograph confirmed significant pulmonary oedema and the NT-pro BNP was markedly elevated with titre >4,000pmol/l (normal range <4pmol/l). Blood pressure (BP) was 180/110 mmHg. Her biochemistry, which was normal in March 2013, confirmed acute renal failure with serum creatinine 313 μmol/L and urinalysis revealed protein (+1) and blood (+3). C-reactive protein had increased (61mg/L) and complement C3 and C4 were reduced. Her antinuclear antibody screen was positive (titre 1:640, speckled pattern) with subsequent analysis revealing RNA polymerase 3 antibody positivity. Anti-centromere and Scl-70 were negative. The clinical impression was of a rapidly progressive new onset diffuse cutaneous systemic sclerosis (dcSSc) presenting with scleroderma renal crisis (SRC).

In addition to cardiorespiratory support, she was started on captopril which was escalated rapidly to control her BP. Frusemide, labetalol and amlodipine were added to obtain good BP control, which was then stabilised at 110/70 mmHg.

Following the acute phase, her pulmonary function tests (PFTs) revealed FVC 89% predicted, FEV1 85% predicted, FEV1/FVC ratio 80% and TLCO of 44% predicted. HRCT scan done ruled out any co-existent significant fibrotic lung disease. Echocardiography (ECHO) revealed a global pericardial effusion, more marked around right heart inferiorly of 1.55cm width. Her right ventricular systolic pressure was 47.1 mm/Hg. The left ventricular ejection fraction was estimated at 60%. She was discharged after a 16-day inpatient stay. Clinic review 1 month later confirmed that her BP remained well controlled and serum creatinine had stabilised at 149 μmol/L.

Repeat PFTs and ECHO have been requested to establish the baseline cardiorespiratory status after stabilisation.

Discussion

The aetiology of systemic sclerosis is unknown. However, exposure to various environmental factors, such as polyvinyl chloride and silica have been implicated, as have viral pathogens (1). We believe this is the first published case of rapid onset dcSSc presenting with SRC in a female with a history of silicone breast implant rupture. The summarised data from 57 published cases of autoimmune disease following silicone breast implant rupture are presented in Table I. The mean time

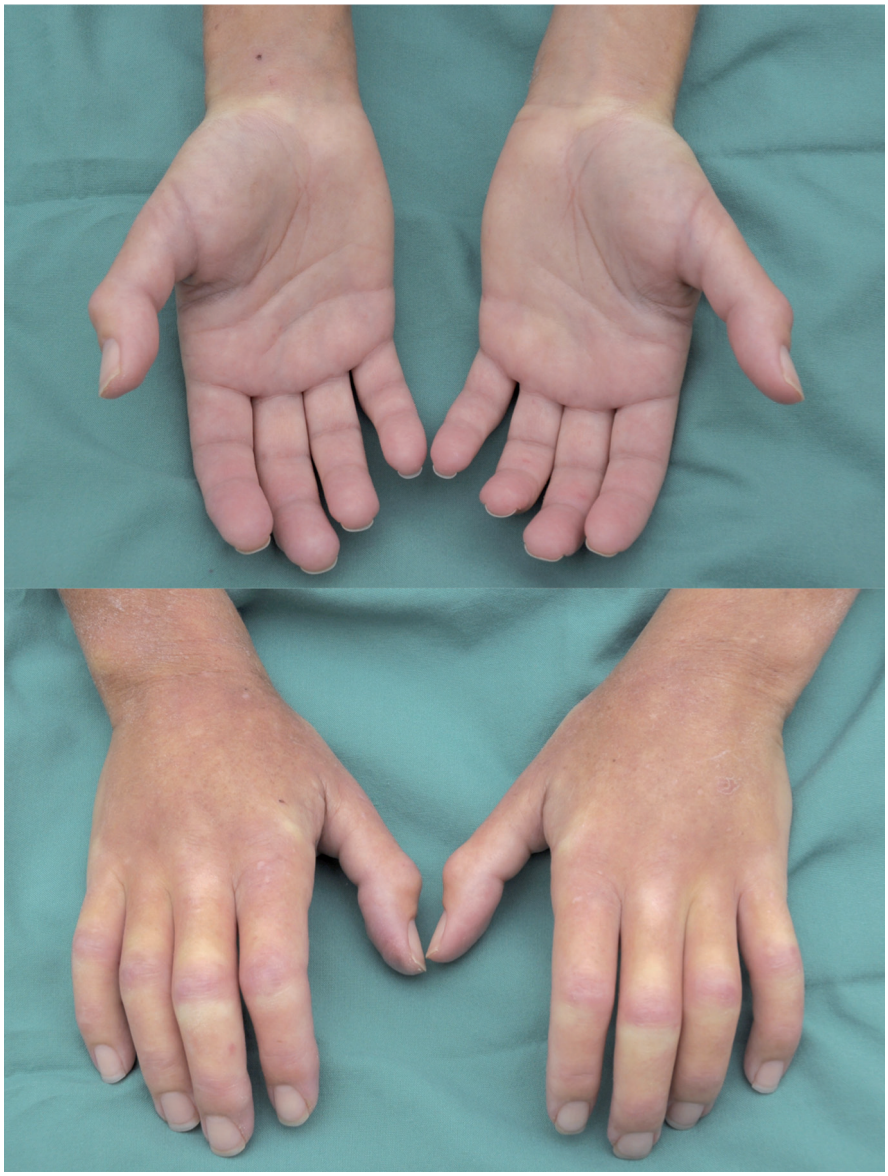

Fig. 1. The hands of our patient showing marked sclerodactyly.

from implantation to symptom onset was 13.2 years with a standard deviation of 5 years although no information on rupture was reported in the majority of the published cases. In our case, the non-Raynaud manifestation of puffy fingers and rapid progressive skin fibrosis developed 9 years after implantation (5 years after rupture), consistent with this data.

From Table I, it can also be seen that the most frequent autoimmune diseases reported following silicone implants are SSc (26%), inflammatory arthritis (15.8%), human adjuvant syndrome [HAS] (12.3%) and systemic lupus erythematosus [SLE] (3.5%). With regard to the autoantibody frequency in this sample, ANA is the most frequently reported auto-antibody (19 subjects), ds-DNA (5 subjects) and rheumatoid factor (8 subjects – with 5 having an associated inflammatory arthritis). Other antibodies reported were RNP (4 subjects), sm antibodies (1 subject) and anti-mitochondrial antibodies (3 subjects).

Our patient had positive anti-RNA polymerase III antibodies. These antibodies define a particular subtype of SSc that are commonly associated with SRC and rapidly progressive skin fibrosis (2-4). One third of patients with positive RNA polymerase III antibodies develop SRC, making them a marker of poor prognosis.

The Women's Health Cohort Study reported by Hennekene *et al*., was one of the largest studies comprising 398,528 subjects where 10,830 had silicone breast implants (5). Of these 324 developed systemic sclerosis, which corresponds to a slightly elevated risk of CTD. This study was however excluded from the meta-analysis (6) which reviewed nine case control studies, nine cohort studies and two cross-sectional studies and concluded that there was no apparent causal relationship between silicone breast implants and the development of CTD. Had the Hennekene's study been included in this analysis then the adjusted relative risk would have increased from insignificant 1.01 to significant 1.3 (5, 7).

Silicone was thought to be biologically inert and was introduced in the 1960s as a safe component in a wide variety of medical products which include artificial heart valves, joint implants and breast implants. Subsequently, silicone implants have been postulated as a cause for a range of autoimmune diseases including systemic sclerosis, adjuvant induced arthritis and the autoimmune syndrome induced by adjuvants (6, 8-11).

A capsule forms around the implanted silicone as a result of the inflammatory response to foreign antigens and there have been cases noted with anti-silicone antibodies (12). Bekerecioglu *et al*. looked at the capsular tissue around silicone implants in fifteen asymptomatic patients with previous silicone implants following burns and compared it to healthy controls (13). He found significantly higher concentrations of immunoglobulins (IgG and IgM) as well as anti-silicone antibodies in tissues around the implant, supporting the case that silicone is not biologically inert.

Silicone has subsequently been detected outside the capsule formed around the implant. Chastre *et al*. showed microscopic silicone particle migration without rupture in transsexual patients who developed pneumonitis following subcutaneous silicone injections (14). This was further supported by the work of Rees *et al*. who showed phagocytes enriched with silicone particles dispersed in various tissue planes follow-

Table I. Autoantibody profiles in foreign substance implants (with or without rupture).

USA, Endo N *et al*. (8)	Age (yr)	Mean age (yrs)	Gender	Duration of implant (yrs)	Foreign substance	Rupture Y/N	Diagnosis
1	42		F	6	Silicone	-	Foreign body granulomata
2	44		F	11	Silicone	-	RA
3	38		F	9	Silicone	-	Inflammatory arthritis
4	46		F	10	Silicone	-	fibrositis
5		45	F	13	Silicone	-	radiographic degenrative changes
6		45	F	11	Silicone	-	Inflammatory arthritis
7		45	F	One month	Silicone	-	fibrositis
8		45	F	23	Silicone	-	adult still's disease

USA, Claman *et al*. (16)	Age (yr)	Mean Age (yrs)	Gender	Duration of Implant	Foreign substance	Rupture Y/N	Diagnosis
1		49.9 ± 10.7	F	15.3 ± 4.3	Silicone	-	CREST
2		49.9 ± 10.7	F	15.3 ± 4.3	Silicone	-	CREST
3		49.9 ± 10.7	F	15.3 ± 4.3	Silicone	-	CREST
4		49.9 ± 10.7	F	15.3 ± 4.3	Silicone	-	Diffuse SSc
5		49.9 ± 10.7	F	15.3 ± 4.3	Silicone	-	Diffuse SSc
6		49.9 ± 10.7	F	15.3 ± 4.3	Silicone	-	Diffuse SSc
7		.9 ± 10.7	F	15.3 ± 4.3	Silicone	-	SLE
8		49.9 ± 10.7	F	15.3 ± 4.3	Silicone	-	SLE
9		49.9 ± 10.7	F	15.3 ± 4.3	Silicone	-	Sjögren's
10		49.9 ± 0.7	F	15.3 ± 4.3	Silicone	-	RA
11		49.9 ± 10.7	F	15.3 ± 4.3	Silicone	-	RA

Japan, Kumagai *et al*. (17)	Age (yr)	Gender	Duration of Implant	Foreign substance	Rupture Y/N	Diagnosis
1	45	F	19	Paraffin	-	SSc
2	49	F	16	Paraffin	-	SSc
3	51	F	17	Paraffin	-	SSc
4	36	F	9	Paraffin	-	SSc
5	35	F	16	-	-	SSc
6	44	F	22	Silicone	-	MCTD
7	26	F	2	Paraffin	-	MCTD+SSc
8	41	F	7	Paraffin	-	Limited morphea
9	41	F	13	Silicone	-	RA
10	52	F	16	Silicone	-	RA
11	48	F	20	Silicone	-	RA
12	55	F	15	Paraffin	-	HAS
13	40	F	5	-	-	HAS
14	53	F	17	Silicone	-	HAS
15	43	F	20	Silicone	-	HAS
16	39	F	14	Silicone	-	HAS
17	41	F	7	Silicone	-	HAS
18	45	F	15	-	-	HAS

Israel, Levy *et al*. (9)	Age (yr)	Gender	Duration of Implant	Foreign substance	Rupture Y/N	Diagnosis
1	60	F	4	Silicone	Y	SSc
2	37	F	5	Silicone	-	SSc
3	57	F	15	Silicone	-	Raynaud's phenomenon
4	79	F	17 (6 years loss of follow-up included)	Silicone	Y	Limited SSc

Turkey, Bekerecioglu *et al*. (13)	Age (yr)	Gender	Duration of Implant	Foreign substance	Rupture Y/N	Diagnosis
1	25	M	-	Silicone	-	Burns
2	32	M	-	Silicone	-	Burns
3	42	M	-	Silicone	-	Burns
4	54	M	-	Silicone	-	Burns
5	15	M	-	Silicone	-	Burns
6	33	M	-	Silicone	-	Burns
7	28	M	-	Silicone	-	Burns
8	21	M	-	Silicone	-	Burns
9	17	F	-	Silicone	-	Burns
10	12	F	-	Silicone	-	Burns
11	14	F	-	Silicone	-	Burns
12	4	F	-	Silicone	-	Burns
13	30	F	-	Silicone	-	Burns
14	14	F	-	Silicone	-	Burns
15	35	F	-	Silicone	-	Burns

N: negative; P: positive; – : not known; F: female, M: male; RA: rheumatoid arthritis; MCTD: mixed connective tissue disease; SLE: systemic lupus erythromatosus; SSc: systemic sclerosis; lcSSc: limited cutaneous SSc; dcSSc: diffuse cutaneous SSc; HAS: human adjuvant syndrome.

ANA	DsDNA Abs	RNP Abs	Sm Abs	SSA Abs	SSB Abs	AMA	RF	ACA	Scl-70	Pr3	MPO	Anti-silicone
N	-	-	-	-	-	N	N	-	-	-	-	-
1/320	-	-	-	-	-	N	1/320	-	-	-	-	-
1/160	-	-	-	-	-	1/100	N	-	-	-	-	-
N	-	-	-	-	-	N	N	-	-	-	-	-
1/40	-	-	-	-	-	N	N	-	-	-	-	-
1/40	-	-	-	-	-	1/32	1/160	-	-	-	-	-
N	-	-	-	-	-	1/400	N	-	-	-	-	-
N	-	-	-	-	-	N	N	-	-	-	-	-

ANA	DsDNA Abs	RNP Abs	Sm Abs	SSA Abs	SSB Abs	AMA	RF	ACA	Scl-70	Pr3	MPO	Anti-silicone
P	-	-	-	-	-	-	-	P	-	-	-	-
P	-	-	-	-	-	-	-	P	-	-	-	-
N	-	-	-	-	-	-	-	P	-	-	-	-
P	-	-	-	-	-	-	-	-	-	-	-	-
P	-	-	-	-	-	-	-	-	-	-	-	-
N	-	-	-	-	-	-	-	-	-	-	-	-
P	-	-	-	-	-	-	-	P	-	-	-	-
P	-	-	-	-	-	-	-	N	-	-	-	-
P	-	-	-	-	-	-	-	N	-	-	-	-
P	-	-	-	-	-	-	-	-	-	-	-	-
N	-	-	-	-	-	-	-	-	-	-	-	-

ANA	DsDNA Abs	RNP Abs	Sm Abs	SSA Abs	SSB Abs	AMA	RF	ACA	Scl-70	Pr3	MPO	Anti-silicone
N	N	1/40	1/40	-	-	-	N	-	-	-	-	-
N	N	N	N	-	-	-	N	-	-	-	-	-
N	N	N	N	-	-	-	N	-	-	-	-	-
N	N	-	-	-	-	-	P	-	-	-	-	-
N	N	-	-	-	-	-	N	-	-	-	-	-
1/640	160	1/32000	N	-	-	-	N	-	-	-	-	-
1/320	64	1/2000	N	-	-	-	P	-	-	-	-	-
N	N	-	-	-	-	-	N	-	-	-	-	-
N	N	-	-	-	-	-	P	-	-	-	-	-
N	N	-	-	-	-	-	P	-	-	-	-	-
1/40	N	-	-	-	-	-	P	-	-	-	-	-
N	N	-	-	-	-	-	N	-	-	-	-	-
N	N	-	-	-	-	-	N	-	-	-	-	-
N	N	-	-	-	-	-	N	-	-	-	-	-
N	N	N	N	-	-	-	N	-	-	-	-	-
N	N	N	N	-	-	-	N	-	-	-	-	-
N	N	N	N	-	-	-	N	-	-	-	-	-
N	1/40	1/40	N	-	-	-	N	-	-	-	-	-

ANA	DsDNA Abs	RNP Abs	Sm Abs	SSA Abs	SSB Abs	AMA	RF	ACA	Scl-70	Pr3	MPO	Anti-silicone
P	P	-	-	-	-	-	-	-	P	-	-	-
1/5000	-	-	-	-	-	-	-	-	P	-	-	-
1/5000	-	-	-	-	-	-	-	P	-	-	-	-
1/160	P	-	-	-	-	-	P	P	-	-	-	-

ANA	DsDNA Abs	RNP Abs	Sm Abs	SSA Abs	SSB Abs	AMA	RF	ACA	Scl-70	Pr3	MPO	Anti-silicone
N	N	N	N	N	N	N	N	N	N	N	N	P
N	N	N	N	N	N	N	N	N	N	N	N	P
N	N	N	N	N	N	N	N	N	N	N	N	P
N	N	N	N	N	N	N	N	N	N	N	N	P
N	N	N	N	N	N	N	N	N	N	N	N	P
N	N	N	N	N	N	N	N	N	N	N	N	P
N	N	N	N	N	N	N	N	N	N	N	N	P
N	N	N	N	N	N	N	N	N	N	N	N	P
N	N	N	N	N	N	N	N	N	N	N	N	P
N	N	N	N	N	N	N	N	N	N	N	N	P
N	N	N	N	N	N	N	N	N	N	N	N	P
N	N	N	N	N	N	N	N	N	N	N	N	P
N	N	N	N	N	N	N	N	N	N	N	N	P
N	N	N	N	N	N	N	N	N	N	N	N	P
N	N	N	N	N	N	N	N	N	N	N	N	P

ing intradermal silicone injection in animal experiments (15).

The link between silicone breast implants, systemic sclerosis and other connective tissue diseases is attractive but tenuous on current evidence. There is clear biological plausibility however larger longer term studies are required to see if there is any definite association of ruptured silicone implants to occurrence of CTD or other autoimmune disorders.

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