

Nephrogenic systemic fibrosis: fibrotic plaques and contracture following exposure to gadolinium-based contrast media

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DESCRIPTION

A 55-year-old man with a history of end-stage renal disease secondary to systemic lupus, status post-deceased donor kidney transplants in 1988 and 2008, presented to the transplant dermatology clinic. Detailed examination revealed cobblestoning (figure 1) and faintly erythematous, hyperpigmented, indurated plaques on both legs and arms (figure 2) with slight fissuring in the left antecubital fossa (figure 3). The patient had accompanying stiffness and contracture of the left arm (figure 3), which were attributable to nephrogenic systemic fibrosis (NSF).

In March 2005, the patient received gadodiamide, a linear gadolinium-based (0.2 mmol/kg) MRI contrast agent, for an MRI study and subsequently developed severe skin fibrosis of his extremities with a cobblestoning appearance. The

dermatopathy began on his left arm and progressively involved his right arm, both hands and both legs as well. NSF was diagnosed in May 2005 after skin biopsy revealed increased fibrosis with scattered histiocytes, including multinucleated giant cells, at the interface between the dermis and subcutaneous tissue and fibrosis extending along the fibrous septae of the subcutaneous fat.

In 2005, the patient developed chronic left foot drop and peripheral neuropathy due to NSF. The neuropathy progressed to involve his right foot in late 2008. Nerve conduction velocity and electromyography studies revealed sensorimotor polyneuropathy with asymmetric denervating changes, consistent with a mononeuropathy multiplex. The patient developed chronic left elbow joint contracture, a sign of advanced NSF. Joint contractures from NSF are thought to be due to periarticular skin thickening, rather than from synovitis or arthritis.¹

Systemic fibrosis in NSF can involve many internal organs, including the lungs, myocardium and pericardium.¹ The patient had so far had neither pulmonary nor cardiac symptoms, nor other signs of systemic involvement. There had been neither softening, improvement, nor progression of his NSF since 2008.

NSF is a rare fibrosing disorder characterised by skin thickening on the extremities and trunk and dermal fibrosis.^{1 2} This disease only occurs in patients with kidney failure.² Development of NSF is most commonly linked to gadolinium exposure, as in gadolinium-based contrast agents (GB-CAs).¹ GB-CAs are excreted nearly exclusively by the kidney. Patients' glomerular filtration rates determine the risk of NSF development after gadolinium exposure, which has been reported to be approximately 3–7% in patients with reduced renal function.³

There is no proven therapy for NSF, although it is thought that renal transplantation may halt the progression of NSF.² Additionally, the likelihood of developing NSF varies between the two types of GB-CAs: cyclic and linear.² Linear agents are flexible open chains with a relatively weak bond to gadolinium, while cyclic agents cage the gadolinium in a cavity and offer better protection, stability and binding to gadolinium.² Cyclic GB-CAs are less likely to release free gadolinium, which is toxic in vivo and are thought to be safer and less likely to cause NSF than linear agents are.² If GB-CAs must be used in patients with renal failure, cyclic GB-CAs are recommended over linear agents.² Our patient developed NSF after exposure to a linear GB-CA.



Figure 1 Skin with 'cobblestone' or 'woody' appearance, typical of nephrogenic systemic fibrosis.



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Figure 2 Hyperpigmented fibrotic indurated plaques on the patient's right arm (A), left leg (B) and right leg (C).



Figure 3 Fissuring in the left antecubital fossa and stiff contracture of the patient's left arm.

Learning points

- ▶ Nephrogenic systemic fibrosis (NSF) is characterised by skin thickening on the upper and lower extremities and trunk, with a 'cobblestone' appearance of the affected skin.
- ▶ NSF may involve fibrosis of internal organs, such as the lungs and heart.
- ▶ NSF only occurs in patients with kidney failure and its development is most commonly linked to gadolinium exposure, as in gadolinium-based contrast dyes for MRI scans.

Contributors AH substantially contributed to the analysis and interpretation of data for the study, drafted the manuscript, approved the final version and is accountable for all aspects of the study. SGK substantially contributed to the design and acquisition of data for the study, revised the manuscript, approved the final version and is accountable for all aspects of the study. JGZ substantially contributed to the acquisition of data for the study, revised the manuscript, approved the final version and is accountable for all aspects of the study. MJL substantially contributed to the conception and acquisition of data for the study, revised the manuscript, approved the final version and is accountable for all aspects of the study.

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