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On the Cover

What's the diagnosis? A 42 year old renal transplant patient presented with a painful, swollen left leg. A plain radiograph revealed muscle calcification consistent with nephrogenic systemic fibrosis (NSF) (cover image). The patient has Von Hippel-Lindau syndrome and was previously on hemodialysis following bilateral nephrectomies for renal cell carcinoma. During this time he had multiple gadolinium-enhanced MRI scans for resection of cerebellar haemangioblastomas.

NSF results from CD34 positive fibrocyte infiltration, causing thickened and hard skin and muscles. Gadolinium has been implicated as a causative agent. The pathogenesis of NSF is incompletely understood however one of the proposed mechanisms suggests that a number of factors, including circulating iron and hyperphosphataemia, lead to an increased dissociation of free gadolinium (Gd³⁺) from its chelate. Both free Gd³⁺ and poorly soluble precipitates such as GdCl₃ can cause a release of profibrosing cytokines such as TGF β and MCP-1. Different preparations of gadolinium contrast agents confer different risk: the Royal College of Radiologists advises the lowest volume of the most stable agent least likely to release Gd³⁺. Currently the only treatment for NSF is recovery of renal function. Our patient received a kidney transplant, but despite this his muscle and skin changes have worsened.

(Image and text provided by Emma O'Lone and William White, Royal London Hospital, Renal London, London, United Kingdom and Muhammad Magdi Yaqoob, William Harvey Research Institute, Translational Medicine and Therapeutics London, London, United Kingdom)