

## **Nephrogenic Systemic Fibrosis: Portrait in the Medical Literature**

**G. Pirovano<sup>1</sup>, C. Schultz<sup>2</sup>, J. R. Parker<sup>2</sup>, M. A. Kirchin<sup>3</sup>, and A. Spinazzi<sup>1</sup>**

<sup>1</sup>Worldwide Medical Affairs, Bracco Diagnostics Inc., Princeton, NJ, United States, <sup>2</sup>Medical Communications, Bracco Diagnostics Inc., Princeton, NJ, United States, <sup>3</sup>Medical Communications, Bracco Imaging, Milan, Italy

### **Purpose**

Nephrogenic systemic fibrosis (NSF) is a potentially fatal, scleroderma-like disease associated with the administration of gadolinium-based contrast agents (GBCAs). The first case of NSF was published in 2000; since that time, many case reports or series of patients with NSF have been published. We identified and analyzed all unique cases of nephrogenic systemic fibrosis (NSF) published in the peer-reviewed literature in order to gain an increased understanding of the demographics and associated risk factors for development of this disease.

### **Materials and Methods**

All cases of NSF reported in the literature (PubMed; 2000 to 2010) were reviewed and tabulated. For each independent NSF case from the literature, the following information was extracted: age, sex, country of origin, degree of renal impairment, details of GBCA exposure (including type if known and total cumulative dose prior to onset of NSF symptoms), date of onset of symptoms, and time from last GBCA exposure to onset of symptoms.

### **Results**

From the literature search, 133 articles were identified that reported 705 unique NSF cases from 19 countries. Of these 705 cases, 605 (85.8%) were biopsy-proven cases of NSF. The most common age range was 60-69 years-of-age, and there were slightly more males (51.5%) than females (48.5%). The vast majority of cases reported a degree of renal impairment of Stage 4 or 5 chronic kidney disease (CKD), with 1 case of Stage 2/3a/3b (eGFR 34.6-69.9), and another of Stage 3a/3b CKD (eGFR 40.0 to 58.2). Of the 436 cases for which renal impairment was reported, 14 (3.2%) reportedly suffered from acute renal failure. Patients receiving only Omniscan or Magnevist accounted for 93.3% of reported NSF cases. In all 705 cases, no unconfounded cases with Dotarem, MultiHance, or ProHance were reported. In terms of cumulative dose prior to NSF onset, patients received doses ranging from low to very high, but the most common doses were moderate-to-high (0.2-0.29 mmol/kg or 10-29 mmol). In most cases, symptoms appeared 1-3 months after the last administration of contrast. Importantly, no cases were identified with an onset of disease symptoms after 2007.

### **Significance of the Conclusions**

Analysis of all NSF cases published in the medical literature provides a unique profile of a relatively new clinical entity, and largely echoes the findings of smaller groups of cases. Such findings have contributed significantly to shaping guidelines designed to prevent the onset of new NSF cases. To date, most radiologists have instituted a number of preventive measures, including prescreening to identify at-risk patients, switching to a more stable GBCA, lowering the GBCA where appropriate, and using noncontrast or alternative diagnostic modalities in patients at risk. Such measures have led to a substantial, if not complete, reduction in the incidence of new NSF cases.