ACR Committee on Drugs and Contrast Media Brief Statement on Nomenclature for Symptoms Associated with Gadolinium-Based Contrast Agent Exposure (SAGE)

In addition to established early-onset (acute hypersensitivity reactions and physiologic reactions) and late-onset (nephrogenic systemic fibrosis [NSF]) adverse effects related to GBCA exposure, reports of other symptoms, or Symptoms Associated with GBCA Exposure (SAGE), have temporally emerged alongside published evidence of long-term gadolinium retention after GBCA administration. Early-onset (<24 hours from GBCA exposure) and late-onset (≥24 hours from GBCA exposure) SAGE have been reported by several hundred patients without clear linkage to an established or unifying diagnosis. Reports of these symptoms have been myriad and nonspecific ranging from "brain-fog" and malaise to neurologic (e.g. "spells") and musculoskeletal (e.g. arthralgias) complaints [1-3]. It is difficult to establish a causal relationship between GBCA exposure, gadolinium retention, and SAGE [4]. The FDA and other regulatory and professional societies including the ACR, ASNR, and ISMRM have concluded there is no compelling causal evidence that directly links tissue gadolinium retention or any other GBCA-specific etiology with these early- and late-onset SAGE complaints [5-8]. Further, all legal efforts to date to prove this causal relationship have failed, and most single-plaintiff and attempted class action litigation have been dismissed or dropped [9-11]. The FDA and GBCA manufacturers have initiated several long-term studies of GBCA safety aimed at better understanding undiagnosed SAGE complaints to determine if they are causally or coincidentally associated with GBCA exposure [5]. At present, no accepted diagnosis exists to link these two entities.

Use of the acronym SAGE is designed to enable researchers and clinical providers to describe symptoms temporally associated with exposure to GBCA without prematurely attributing those symptoms to a specific disease. It is hoped this proposed nomenclature will better articulate the current state of knowledge (i.e., enabling discussion without premature disease attribution) and improve communication in related research.

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