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AN OVERVIEW OF CONTRAST AGENT IN DIAGNOSTIC IMAGING, ADVERSE REACTION AND AVOIDING ERROR

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Abstract:

Contrast media agents have been used to increase picture quality in MRI exams for decades, and some of the agents have a great overall safety record. A search was conducted in electronic sources, such as PubMed and Embase, for publications published up to the start of 2022 that discussed contrast media agents used in radiograph situations. The majority of adverse reactions to contrast media are regarded to be idiosyncratic or pseudoallergic in nature. They are unexpected and not dose-dependent, and they may entail the release of histamine as well as other biological mediators such serotonin, prostaglandins, bradykinin, leukotrienes, adenosine, and endothelin. Because antibodies to contrast media could not be reliably shown, there is no definitive proof that these adverse reactions to contrast media are allergic.

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INTRODUCTION:

Contrast agents, also known as contrast media, are substances used to raise the radiodensity of a certain tissue by altering the way electromagnetic radiation or ultrasonic waves pass through the body. These drugs can be administered orally, rectally, or intravenously to the patient. Contrast compounds are now widely used in current clinical practice. Concerns about the toxicity of many contrast agents have grown as their use has grown [1,2]. For patients undergoing radiographic imaging such as x-rays or computed tomography (CT) scans, contrast agents are either iodine or barium-based. The osmolality of iodinated contrast agents, which ranges from 300 to 1200 osmol/kg H2O, is used to classify them. Because iodine is the radiopaque ingredient in all iodinated contrast agents, the radiopacity induced by their administration is proportional to their iodine content. Iodinated contrast agents are most commonly delivered intravenously, however due to the capillary permeability of the contrast molecules, the substance soon redistributes to the extravascular region [3].

The majority of magnetic resonance imaging (MRI) contrast agents are based on chelated gadolinium. Unlike iodinated or barium contrast agents, which attenuate x-rays to improve imaging, gadolinium contrast agents boost the signal intensity of biologic tissues by shortening the time it takes water protons to align with the magnetic field created by the imaging machine. Gadolinium contrast agents' chelating components also allow the substance to stay in circulatory veins longer before extravasating than radiographic contrast agents [4].

Intravenous iodinated contrast media has both acute and delayed side effects, as well as organ-specific side effects (contrast-induced nephrotoxicity, and cardiovascular, pulmonary, and neurotoxicity). The mild acute general adverse effects include nausea, vomiting, moderate urticaria, pallor, and soreness in the injected extremity. Moderate side effects include severe vomiting, extensive urticaria, laryngeal edema, dyspnea, and rigors. Severe responses include pulmonary edema, cardiac arrhythmias, cardiac arrest, circulatory collapse, and unconsciousness. Mild reactions are self-limiting and last shorter time. Mild reactions, in general, do not require specific treatment. Moderate and severe adverse reactions, on the other hand, are serious events that must be handled immediately [5,6].

DISCUSSION:

Magnetic resonance imaging (MRI) and computed tomography (CT) are common diagnostic imaging modalities in veterinary medicine, where a contrast study is frequently necessary for diagnosis. Contrast media delivery can result in adverse responses that can be categorized as immediate or delayed in start, mild, moderate, or severe in terms of clinical features and intensity of symptoms, and hypersensitivity (Type B) or non-hypersensitivity (Type A) in terms of etiology [7]. When used at the manufacturer-recommended doses in patients with normal renal function, gadolinium-based contrast agents have an outstanding overall safety record, with major adverse responses occurring in roughly 0.03% of all administrations [8,9]. This reputation was maintained until 2006, when GBCA-induced nephrogenic systemic fibrosis (NSF) was first described in persons with renal insufficiency [10,11]. Since 2014, there has been an increase in the number of studies revealing increased gadolinium deposition in the brain and other tissues of patients with normal renal function after repeated GBCA exposures, raising a new safety risk with GBCAs [12,13]. To offer the safest, highest-quality care possible, radiologists must have a thorough understanding of these contrast agents. Contrast toxicity occurs when the compounds employed as contrast agents, such as iodine, barium, gadolinium, or microbubbles, cause injury to biological tissues.

Toxicity can occur when a patient's medical history is not thoroughly recognized, particularly when it comes to allergies, heart issues, or renal disease. Special populations, such as pregnant women, breastfeeding mothers, and metformin patients, should be given special care for potential harm from contrast use. To determine the appropriateness of the proposed investigation, radiologists doing contrast-enhanced imaging typically do not know the patient well and must rely on a referring physician's opinion or a time-limited informed consent process [14].

Further risk of contrast toxicity is incurred by off-label use of contrast agents. Current regulations from the Food and Drug Administration (FDA) in the United States have a limited number of approved contrast agents for specific uses in specific body areas. Because the FDA has not yet been able to comprehensively test all contrast agents in all populations for all purposes, the actual clinical use of contrast agents by necessity must encompass off-label use not yet assessed by the FDA. Diagnostic needs in MR angiography, cardiac, and pediatric populations are among those least addressed by the FDA that remain frequently required in clinical practice [15].

The incidence of adverse events following the injection of low-osmolarity iodinated or gadolinium-based contrast agents is expected to be less than 1% [16]. Adverse reactions are further classified as

physiologic or allergiclike [17]. Allergiclike reactions are rarer than physiologic reactions and are usually moderate. Serious or severe responses to contemporary nonionic, low-osmolarity iodinated contrast agents are expected to occur at a rate of 0.04% and have been documented in up to 0.4% of injections with earlier ionic chemicals [18,19]. In comparison, gadolinium-based contrast agents have a 10-fold lower rate of adverse reactions [20]. Physiologic effects, such as headache, nausea, vomiting, and vasovagal responses, frequently require just supportive care. Allergiclike reactions, on the other hand, can range from modest discomfort to life-threatening episodes and, depending on their severity, may necessitate prescription therapy. Although the incidence of adverse and true allergiclike reactions is low, the number of contrast-enhanced imaging studies performed in a typical imaging practice makes them not uncommon; adequate precautions and preparations must be in place to provide prompt and appropriate treatment when they occur. The treatment schedule is determined by the individual symptoms of the patients as well as the intensity of the reaction [20].

PHYSIOLOGIC REACTIONS & VASOVAGAL REACTION:

The mechanism of physiologic reactions, also known as chemotoxic reactions, remains unknown. These reactions are assumed to be linked to molecular properties such as osmolarity or the molecular binding of certain activators [21,22]. Physiologic reactions, unlike allergiclike reactions, frequently exhibit dosage and concentration dependence. Adverse events affecting the circulatory system occur more frequently in people with underlying heart illness [17]. Otherwise, no specific risk variables have been identified that have been consistently linked to an increased incidence of physiologic reactions. Preserving intravenous (IV) access, monitoring vital signs, and administering supplemental oxygen at a rate of 6 to 10 L per minute are general precepts in the treatment of all adverse responses. It is also critical to be familiar with the institution's specialized emergency response system as well as the placement of appropriate medication and equipment [22].

Noncardiogenic pulmonary edema is extremely uncommon and occurs in persons with normal cardiac activity. It's unclear whether this is an allergic reaction or a physiologic reaction. In addition to delivering supplementary oxygen and monitoring the patients' pulse oximetry, the head of the bed should be elevated and IV furosemide supplied, if practicable. When pulmonary edema develops, the emergency response team should be activated, and the patient should be transferred to an appropriate treatment facility [23].

Although the specific mechanism of an allergiclike (also known as anaphylactoid or idiosyncratic) contrast media reaction is unknown, they are handled in the same way as other true allergy medication reactions. They can occur within 1 hour (acute or immediate) of injection and last for up to 1 week (delayed). Regardless of when the reaction occurs, treatment is determined by the severity and types of symptoms displayed [17,23].

A vasovagal reaction is a complicated neurologic reflex that is characterized by hypotension and can be induced by a range of stimuli [24]. It is one of the most prevalent physiologic reactions and can occur at any time during the investigation, including before the contrast agent is administered. It is frequently eased by recumbence and usually only requires reassurance and elevation of the patients' legs without any extra intervention. If the induced bradycardia persists or patients become symptomatic, a gradual IV infusion of 0.6 to 1.0 mg of atropine might be given. Rapid IV fluid resuscitation (0.9% normal saline or lactated Ringer solution) infusion to a total volume of 500 mL to 1 L is recommended [24].

GADOLINIUM DEPOSTION IN THE BRAIN:

In 2014, Kanda et al. [25] published a Japanese study that found a link between hyperintensity in the globus pallidus and dentate nucleus on unenhanced T1-weighted MR images in individuals who had previously received doses of Gadopentate dimeglumine or Gadodiamide (linear GBCAs) [120]. Even after only four lifetime doses of Gadodiamide, this association was detected in persons with normal renal or hepatobiliary function [26]. Later, in other experiments, Errante et al. got comparable results [27]. Furthermore, Inductively Coupled Plasma Mass Spectrometry (ICP-MS) autopsy investigations revealed gadolinium buildup in cerebral tissues [27,28]. More specifically, the majority of the retained Gd was discovered in endothelial cells, with a lesser portion of it settling in neurons after crossing the blood-brain barrier. So yet, no histological alterations in brain cells or clinical symptoms have been linked to this buildup. Macrocyclic GBCAs appear to be less associated with this occurrence, but this is still under investigation [29].

While it has long been recognized that free Gd3+ can deposit in tissues other than the skin even when the kidneys are functioning correctly [30,31], the more recent discovery of gadolinium accumulating in the

brain has raised concerns about safety. Kanda et al. [32] and Errante et al. [27] discovered a link between increased signal strength in the globus pallidus and dentate nuclei on unenhanced T1-weighted images and the number of past GBCA exposures in 2014 (**Fig. 1**).

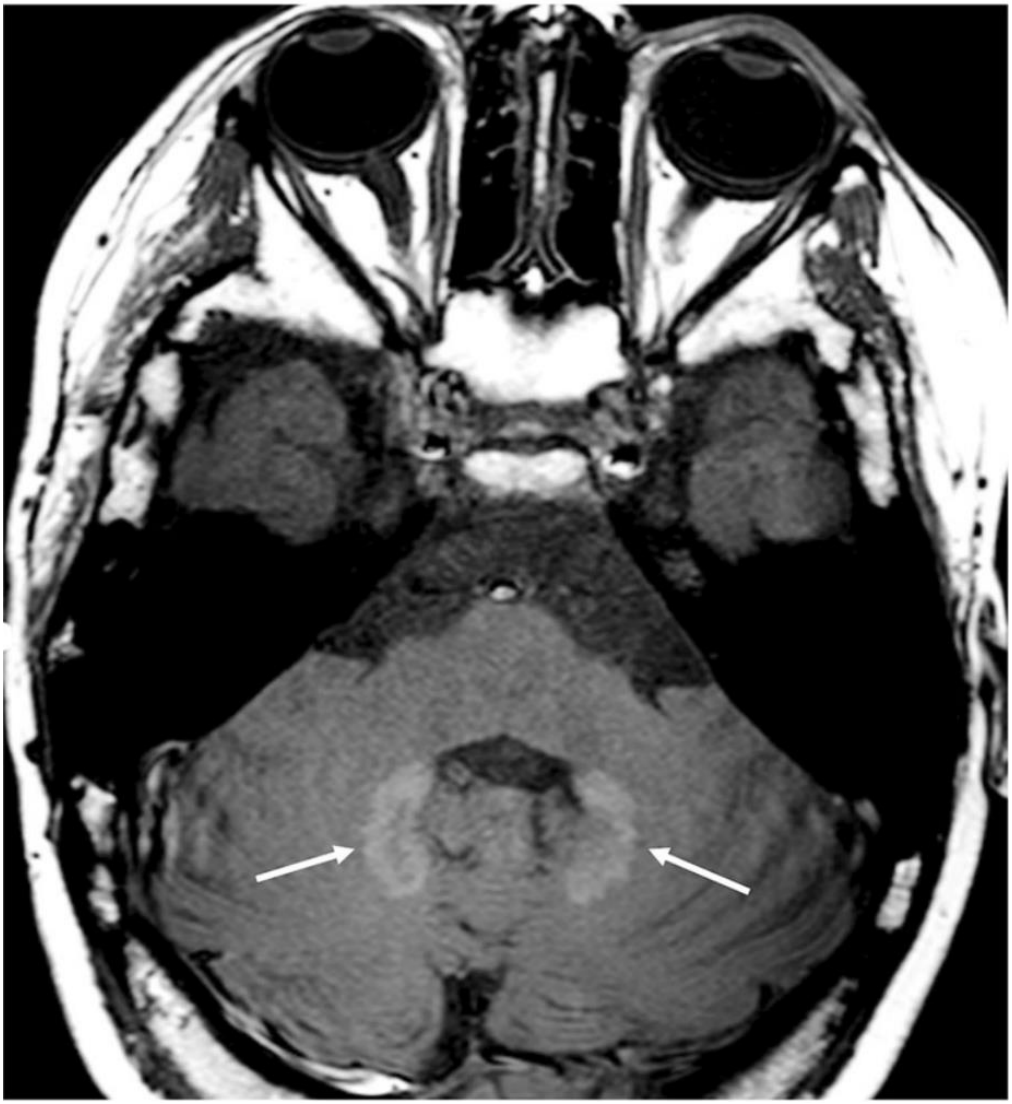

Fig. 1: Gadolinium deposition following 23 doses of gadopentetate dimeglumine.

CONCLUSION:

Adverse reactions to contrast media are uncommon, and real allergic-like reactions are even rarer and more often moderate in severity. If treatment is required, it is determined by the signs and symptoms as well as the severity of the reaction. Premedication is primarily used in individuals who have had a previous reaction and require a further contrast-enhanced examination that will expose them to the same or a comparable substance. To avoid adverse reactions to contrast media, proper preprocedural patient screening, procedure selection, and suitable prophylactic measures should be used. In the event of an adverse reaction to contrast media, awareness, training, and management preparedness are critical for proper and effective therapy.

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