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Short Communication

Gadolinium Deposition in all Human Tissues after Repeat MRI with GBCA Administration-In the Radiological and Neurological Community Accepted or Further Ignored?

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Abstract

The application of intravenous gadolinium-based contrast agents (GBCA) is a great relief in the diagnosis and characterization of pathologic processes and course control, especially in multiple sclerosis (MS), where they play a large role in the detection of disease activity. The contrast administration in spinal cord MRI is still under discussion, since compared with brain lesions, only a small fraction of spinal cord lesions show contrast enhancement, and when it is seen, it is commonly associated with new clinical symptoms.

Keywords Multiple sclerosis; Gadolinium deposition

Introduction

In December of 2013, Kanda et al. published the first paper to report the detection of Gd-deposition in the brains of patients with normal renal function- Free Gd 3+ ion is toxic [1]. However, the focus is now on the Gd accumulation in various tissues of patients, including brain, skin, liver, bone, immune system and kidneys, which do not have renal impairment [2]. Although the deposition of Gd is associated with all agents, the extent is much less with the macrocyclic (m)GBCA) The Gd concentration of the brain with repeat linear GBCA administration was 14 times greater than with repeat mGBCA [3].

Discussion

Semelka et al. informs us that Gd in humans can cause health issues – a family of disorders. The term Gd Deposition Disease (GDD) is proposed [4,5]. At present there is no long-term observation of Gd deposits, in particular over 10 to 20 years, in particular of extremely vulnerable groups of patients, children and adolescence with MS. Brain development begins during fetal life and continues throughout adolescence. During this critical period of development ("maturational changes in the human brain"), the brain is particularly vulnerable to toxin exposure. Gd deposition after repeated contrast -enhanced MR imaging can be found in Gd deposits in the bone. Pregnancy can lead to mobilization of Gd induced by transmetallation from the bone [6]. Released Gd can be the cause of health issues in the mother and fetus,

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because Gd penetrates through the placenta. Gd is released again and again through the kidneys of the foetus into the amniotic fluid, which is the fetus regularly swallows during gestation. A retrospective study by Ray et al. found that GBCA-enhanced MRI at any time during pregnancy is associated with an increased risk of a broad set of rheumatological, inflammatory or infiltrative skin conditions, and for stillbirth or neonatal death [6]. The potential clearly exists for biomolecular interferences with oxidative stress by deposition of Gd. Interestingly; one factor of the biomolecular mechanisms for underlying progression in MS is also chronic oxidative stress, which leads to mitochondrial injury. Remarkably, mitochondria and mitochondrial DNA are highly susceptible to oxidative damage [7]. GBCA administration has only been approved under the assumptions that the potential. The detection of disease activity (MS), as defined as new / enlarging MR imaging, has been proposed as a biomarker in MS and is also possible in principle without GBCA [8,9].

Conclusion

The investigation without GBCA, among other things, currently fails due to the time required to evaluate the MRI, which is increased by about 2.5 times. Furthermore the classification of new T2 lesions can be more difficult, indeed T2 signal alterations are a durable "footprint" of plaque formation and thus a relatively reliable means of ascertaining lesion accumulation [10,11]. Little attention is given to the fact that the detection of active herds with GBCA is very limited in the case of a 6-month routine control study in MS. New inflammatory lesions take up Gd for approximately 3-4 weeks after their development, there is no recommendation to make an interval between baseline and follow-up scans in 6 month with GBCA [11,12]. The contrast administration in spinal cord MRI is still under discussion, since compared with brain lesions, only a small fraction of spinal cord lesions show contrast enhancement, and when it is seen, it is commonly associated with new clinical symptoms [13,14].

Follow-up MR imaging must be directed individually after

- 1. The activity of the disease,
- 2. The different drug therapies with recognition of side effects,

3. Controls in children and pregnant patients and adverse effects such as opportunistic infections [15]. Individual patient care must be provided not only by the neurologist, but also by the radiologist. Many radiologists support the concept of communicating more directly with patients but they are constrained by time or workload [16].

For the patient with MS, it is therefore essential to maintain an MRI log that documents ("passport") each GBCA administration, with a risk-benefit assessment including clear documentation of date, dose, type of formulation (linear or mGBCA), and Magnetic field strength (e.g. 1.5 or 3T image acquisition). In addition, in the case of GBCA during pregnancy and breastfeeding should be included in the log. MRI CD-ROMs with covers should be provided to patients to ensure comparability in follow-up examinations.

Result

In order to assess the harmful of GBCAs, the focus is almost exclusively on Gd deposition in the brain. Up-to-date –July 2017, in a Personal View in The Lancet, Neurology, Gulani et al., on behalf the International Society for Magnetic Resonance in Medicine (ISMRM),



summaries the evidence on the Gd deposition phenomenon in the Brain and offer guidelines for clinicians and researcher. One of many recommendations of the ISMRM is:" The ISMRM urges caution in the use of any medical compound, including GBCAs. Per standard practice, use of GBCAs should be avoided when not necessary. The evidence on Gd deposition emphasizes but does not alter this practice, and GBCAs should not be withheld from patients with a clinical indication for Gd-enhanced MRI. The physician responsible for the administration of a contrast agent should understand the benefits and risks of the agent" [17]. A problematic fact is the lack of knowledge of the practicing radiologists, neurologists and assigning physicians in the indication position to the MRI. In a survey of 5390 physicians in various pediatric professional societies, Radiologist had more aware of brain Gd deposition (87%) than non-radiologist physicians (26%). The number of MRIs requested by referring pediatric physicians correlated among others with their knowledge of brain Gd deposition. The survey did not include any knowledge about Gd deposition in other organs [18]. Terashima et al. Reich demand: Clinicians and researchers should be prepared to discuss the potential risk of Gd deposition in the brain with patients who require GBCAs [19]. However, if the scientific community currently has unsecured knowledge, how is the patient to make the decision for himself? The patient is extremely overburdened here, especially when parents have to make the decision for the children. The doctor is only legally protected. Uncertainty remains.

References

- Kanda E (2016) Gadolinium based contrast agents (GBCA): Safety overview after 3 decades of clinical experience. Magn Reson Imaging 34: 1341-1345.
- 2. Rogosnitzky M, Branch S (2016) Gadolinium-based contrast agent toxicity: a review of known and proposed mechanisms. BioMetals 29: 365-376.
- 3. Robert P, Lehericy S, Grand S, Violas Z, Fretellier N (2015) T1weighted hypersignal in the deep cerebellar nuclei after repeated administrations of gadolinium-based contrast agents in health rats: difference between linear and macrocylclic agents. Invest Radiol 50: 473-480.
- 4. Semelka RC, Ramalho J, AIObaidy M (2016) Gadolinium deposition disease: Initial description of a disease that has been around for a while. Magn Reson Imaging 34: 1383-1390.
- 5. Semelka RC, Ramalho M, AIObaidy M (2016) Gadolinium in Humans: A Family of Disorders. AJR 207: W1-W5.
- 6. Ray JG, Vermeulen MJ, Bharatha A (2016) Association between MRI exposure during pregnancy and fetal and childhood outcomes. JAMA 316: 952-961.

- Feng X, Xia Q, Yuan L (2010) Impaired mitochondrial function and oxidative stress in rat cortical neurons: Implications for gadolinium-induced neurotoxicity. Neurotoxicology 31: 391-398.
- 8. Cabezas M, Corral JF, Oliver A (2016) Improved automataic detection of new T2 lesions in multiple sclerosis using deformation fields. AJNR Am J Neuroradiol.
- 9. Zhang Y, Gauthier SA, Gupta A (2016) Magnetic Susceptibility from Quantitative Susceptibility mapping Can Differentiate new Enhancing from Nonenhancing Multiple Sclerosis Lesions without Gadolinium injection. AJNR 37: 1794-1799.
- 10. Sormani M, Rio J, Tintore M (2013) Scoring treatment response in patients with relapsing multiple sclerosis. Mult Scler 19: 605-612.
- 11. McNamara C, Sugrue G, Murray B (2017) Current and Emerging Therapies in Multiple Sclerosis: Implications for the Radiologist, Part 2-Surveillance for Treatment Complications and Disease Progression. Am J Neuroradiol.
- 12. Cotton F, Weiner HL, Jolesz FA (2003) MRI contrast uptake in new lesions in relapsing-remitting MS followed at weekly intervals. Neurology 60: 640-646.
- 13. Gass A, Rocca MA, Agosta A (2015) MAGNIMS Study Group. MRI monitoring of pathological changes in the spinal cord in patients with multiple sclerosis. Lancet Neurol 14: 443-454.
- 14. Wattjes MP, Steenwijk MD, Stangel M (2015) MRI in the Diagnosis and Monitoring of Multiple Sclerosis: An Update. Clinical Neuroradiol S2: 157-165.
- 15. McNamara C, Sugrue G, Murray B (2017) Current and Emerging Therapies in Multiple Sclerosis: Implications for the Radiologist, Part1-Mechanisms, Efficacy, and Safety. Am J Neuroradiol.
- 16. Kemp JL, Mahoney MC, Mathews VP (2017) Patient-centered Radiology: Where Are We, Where Do We Want to Be, and how Do We Get There? Radiology.
- 17. Gulani V, Calamante F, Shellock FG, Kanal E, Reeder SB (2017) Gadolinium deposition in the brain: summary of evidence and recommendations. Lancet Neurol 16: 564-570.
- Mithal LB, Patel PS, Mithal D, Palac HL, Rozenfeld MN Use of gadolinium-based magnetic resonance imaging contrast agents and awareness of brain gadolinium deposition among pediatric providers in North America. Pediatr Radiol 46: 657-664.
- 19. Terashima K, Reich DS (2017) Gadolinium deposition: practical guidelines in the face of uncertainty. Lancet Neurol 16: 495-497.