Neuro-imaging is essential for making a diagnosis of the central nervous system diseases. Although intrinsic tissue contrast is present in the CT/MR images, neuro-imaging also relies heavily on contrast media to improve lesion detection (sensitivity) and to aid in lesion characterisation (specificity). Furthermore, contrast could be used for functional assessment of physiologic processes including perfusion/blood flow and vascular status. During the cerebral angiography, contrast is injected via the catheter to opacify the intracranial arteries. Contrast agents are essential for contemporary neuro-diagnosis. Although rare, contrast reactions do occur and one must be aware of this. Adverse reactions are more common with CT contrast agents (‘iodinated’ contrast) than with MR contrast agents (‘gadolinium’ contrast).

CT Scan

Since the contrast could not pass through the blood-brain barrier (BBB), only vascular structures and areas of the brain that have no BBB (such as choroid plexus, pineal and anterior lobe of pituitary gland) enhance normally. Three pathologic (abnormal) enhancements occur.1 1) Abnormal enhancement within enlarged vessels without breakdown of BBB, including AVM or neoplasm with enlarged vascular spaces. 2) Breakdown of BBB with leakage of contrast e.g. neoplasm, infarction and inflammation. 3) Lesions with no BBB such as meningioma, acoustic schwannoma.

Adverse reactions happen after contrast administration. They are more common with the ‘iodinated’ contrast than with ‘gadolinium’ contrast. Most adverse effects after iodinated contrast are mild or moderate, which do not require treatment. Approximately 3% of patients undergoing contrast examination will have some types of reaction, usually mild vasomotor symptoms. About 0.03% will require hospitalisation and 1.6% requires treatment.1 Reactions leading to death are rare and occur in about 1:250,000 patients.

The contrast reaction is classified into:2
1) **Mild Reaction** (no need for treatment): Nausea/vomiting, urticaria.
2) **Moderate Reaction** (not immediately life threatening but often requires treatment): Vasovagal reaction, mild bronchospasm or hypotension.
3) **Severe Reaction** (potentially or immediately life threatening): severe vasovagal reactions, hypotension or bronchospasm, laryngeal oedema and cardiac arrest.

4) **Organ-specific Effect**: pulmonary oedema or seizure
5) **Delayed** (0.5% to 9%): headaches, muscle pains and flu-like symptoms up to 48 hours after contrast media. Delayed cutaneous reactions ranging from 3 hours to 7 days after contrast injection, most often with exanthem (self-limited).

Prior sensitisation to the contrast agent is not required for an adverse reaction to occur. There is no reliable screening test to predict which patients will have a severe reaction. Most reaction occurs within a few minutes of injection. High-risk patients (those with a history of allergy or asthma) should be pre-treated with steroids but it does not guarantee an absence of reactions. Patients with a history of documented iodinated contrast reaction should not be injected with iodinated contrast. It is better to consider alternative examinations such as MRI with gadolinium contrast. The iodinated contrast media can damage the kidneys (contrast nephrotoxicity). Patients with renal dysfunction taking Metformin could have risks of lactic acidosis and therefore, Metformin should be suspended at the time of contrast injection.

MR Imaging

In the presence of intact BBB, most of the normal neuronal structures will not enhance as in CT scan. Any pathology that disrupts the BBB will enhance after IV contrast injection. In order to avoid erroneous interpretation of the contrast enhancing lesion, unenhanced images must be available for comparison.3

Gadolinium chelates are extremely well tolerated by the vast majority of patients. The frequency of all acute events after an injection of 0.1 or 0.2 mmol/kg of gadolinium chelate ranges from 0.07% to 2.4%. The vast majority of these reactions are mild. 'Allergic' responses are unusual (0.004% to 0.7%), including urticaria and very rarely bronchospasm. Severe life-threatening reactions are exceedingly rare (0.001% to 0.01%). Persons with asthma and various allergies are also at greater risks (up to 3.7%).2

Gadolinium agents are considered to have no nephrotoxicity at approved dosages. However, they can result in nephrogenic systemic fibrosis (NSF) for patients with actual renal failure or severe chronic kidney disease. NSF is a fibrosing disease, which will primarily be identified in skin and subcutaneous tissues but will also involve other organs including the lung, oesophagus, heart and skeletal muscles. It is estimated that patients with severe chronic kidney disease...
(GFR<30) have a 1% to 7% chance of developing NSF after exposure to gadolinium agents, especially high doses or multiple doses. There has been no report of NSF in patients with normal renal function. Therefore, estimated GFR is recommended to be obtained within six weeks of a Gadolinium-enhanced study in patients with renal disease, over 60 years of age, with hypertension, DM, or severe liver disease. In patients with GFR<15 ml/min/1.73m2, the risk of NSF is greatest and there therefore should be absolute avoidance of contrast MRI. Alternative examinations should be suggested. For patients with GFR that is abnormal but greater than 15ml/min/1.73m2, judicious use of the lowest possible doses of selected macrocyclic agents are recommended.

The intra-thecal contrast (MR cisternography) is used for the diagnosis of Cerebrospinal fluid (CSF) rhinorrhea and spontaneous intracranial hypotension (SIH), which imply an abnormal communication between the subarachnoid space and nasal cavity or spinal canal. For these patients, confirmation, localisation and characteristics of the actual site/sites of CSF leak are challenging but important for treatment planning. Conventional myelography is now obsolete. Radiouclide cisternography (RC) has radiation hazards and poor spatial resolution. CT scan is sensitive for bony lesions but impossible to confirm the site of active CSF leak. Non-enhanced MR imaging has some use in demonstrating CSF fistulae but with relative high frequency of false positive findings of up to 42% and also false negatives. CT cisternography is more reliable. It can identify the spinal level of a CSF leak in 67% of patients compared with 50% and 55% with spinal MRI and RC respectively but requires scanning of the whole spine and skull base. The patients will receive a considerable dose of radiation. The bony structures may also partially obscure the subtle site of CSF leakage.

MR cisternography can demonstrate the site of CSF leakage but with no radiation or bone artifacts. It requires a lumbar puncture and followed by a single low-dose gadolinium injection into the lumbar subarachnoid space. Many studies showed the relative safety and feasibility of low-dose gadolinium-enhanced MR cisternography in confirming and determining the focus of active CSF leaks. The results of initial human studies also revealed that the procedure do not manifest clinical evidence of gross physical or neurologic abnormalities, CSF changes, or electroencephalographic alterations. The adverse reactions are rare, including nausea/vomiting, headache, anaphylactoid reaction and seizure.

Conclusion

Contrast agents used for CT, MRI scan and cerebral angiography play an important role in neuro-imaging. Although they are safe for use, adverse reactions may happen and therefore any contrast should be used judiciously. Recently, MR cisternography is more often used for the investigation of SIH and CSF rhinorrhea.

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References