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Contrast-induced Encephalopathy: A Review

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ABSTRACT

Contrast-induced encephalopathy is a very rare complication following percutaneous coronary intervention that requires a high index of suspicion. We hereby discuss the underlying pathophysiology, diagnosis and management of this condition.

1. INTRODUCTION

Contrast agents are commonly used as a diagnostic tool in several imaging techniques nowadays. They make an important contribution to reaching a diagnosis; however, their use also carries multiple risks. One of these is contrast-induced encephalopathy, a rare but serious complication with significant morbidity, which is most commonly seen in cerebral interventions, both diagnostic and therapeutic, but may also occur following coronary angiography. The aim of the following review is to understand the underlying pathophysiology, the currently available diagnostic tools, therapeutic measures as well as the prognosis of this rare condition.

2. PATHOPHYSIOLOGY

The underlying pathophysiology is not completely understood; however it is thought to be caused by a combination of neurotoxicity of the contrast media, which causes osmotic disruption of the blood-brain barrier, resulting in oedema, particularly in the occipital cortex, and chemotoxicity resulting from contrast hyperosmolality (Yu et al., 2011; Min-Tsun et al., 2013). This leads to hyperosmolality of plasma with consequent cerebral vasodilation, reduction of the intracellular space and resultant widening of gap junctions, thus causing increased permeability of the blood brain barrier, and arterial spasm. Contrast material that crosses the blood-brain barrier causes changes in oncotic pressure and results in cerebral oedema. Neural electrophysiology may also be affected due to the ionic

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properties of contrast (Yu et al., 2011). Different types of contrast media have been found to cause contrast-induced encephalopathy, including ionic, non-ionic, hyperosmolar and isosmolar (Min-Tsun et al., 2013). Since almost all contrast agents are primarily filtered and excreted by the kidneys, patients with compromised renal function, especially those with end-stage renal disease, are at significantly higher risk of contrast-induced encephalopathy due to accumulation of contrast agents in the blood (Muruve et al., 1996). This risk is further increased with increasing doses of contrast administered (Law et al., 2012).

3. EPIDEMIOLOGY

Contrast-induced encephalopathy was first reported in 1970, presenting as transient cortical blindness, following a coronary angiogram. The incidence of contrast-induced encephalopathy is between 0.3 to 1% with non-ionic contrast agents, but may reach as high as 4% with the use of hyperosmolar iodinated contrast agents (Min-Tsun et al., 2013). The reported incidence in patients undergoing coronary angiography is 0.06%, those undergoing vertebral angiography is 0.3-1%, and those undergoing endovascular coil treatment of posterior circulation aneurysms is 2.9% (Leong et al., 2012).

4. PRESENTATION

The condition may present with encephalopathy, transient cortical blindness, seizures and focal neurological deficits. Neurological signs usually develop within hours to days of exposure and, even with severe cases, including coma, prognosis is usually favourable, with spontaneous recovery of neurological deficits, usually over a period of a few days. Interestingly, there have been case reports, such as that by Nagamine et al. (2014), in which the patient had a sub-acute onset of disease, presenting at a later stage, with a much more protracted clinical course. The onset in such cases may be insidious and may hardly be noticed by the patient. Mode of presentation of this entity varies and may include localized cortical and subcortical deficits, such as hemiparesis, hemianopia, cortical blindness, speech disturbances, Parkinsonism, as well as global deficits, like confusion, memory loss, seizures, and coma (Yu et al., 2011). When neuroimaging with CT or MRI reveals changes, there is usually a close correlation to the region affected and the clinical syndrome present. However, this is not always the case. Menna et al. (2013) described a patient with mild aphasia, while Sawaya et al. (2007) described another one with a global encephalopathic syndrome; both had normal CT findings.

5. DIAGNOSIS

Diagnosis is mainly based on clinical presentation and imaging, i.e. CT and MRI. Changes on computed tomographic imaging may reveal abnormal cortical contrast enhancement and oedema, subarachnoid contrast enhancement (which may be comparable to the image obtained in subarachnoid haemorrhage), and striatal contrast enhancement (Leong et al., 2012). High intensity signals measuring 80 to 160 Hounsfield units are characteristic of this condition and may be considered to be pathognomonic (Yu et al., 2011). Magnetic resonance imaging changes include hyper-intensity on T2-weighted images, FLAIR (fluid-attenuated inversion recovery) images, and diffusion-weighted imaging. ADC (apparent diffusion coefficient) maps remain unchanged; this helps to differentiate contrast-induced encephalopathy from cerebral ischaemia (Yu et al., 2011). Since the abnormal findings present on MRI are consistent with vasogenic oedema, contrast-induced encephalopathy has occasionally been compared to posterior reversible encephalopathy syndrome (PRES), as mentioned by Suri et al. (2011) and Nagamine et al. (2014) in their case reports. As with PRES, clinical sequelae are minimal or absent, and radiological changes are reversible in most patients. Neuro-electrophysiological studies further add to the weight of the possible diagnosis. Electroencephalography shows diffuse slowing of cerebral activity (Yu et al., 2011).

6. PREDISPOSING FACTORS

Various risk factors have been associated with the development of contrast-induced encephalopathy (Min-Tsun et al., 2013) (table 1). Technically challenging revascularisation procedures during cardiac catheterisation play an important role in view of the significant amount of contrast medium utilised, as described in the case by Law et al. (2012), whereby the patient developed symptoms 12 hours following catheterization; these resolved within 24 hours, with resolution of MRI changes (mainly oedema) at 32 hours. Consequently, precautions should be taken (table 2).

7. MANAGEMENT

There is no definitive treatment for contrast-induced encephalopathy. Management is usually supportive, with eventual spontaneous recovery of neurological function in the majority of cases. Patients undergo adequate hydration with intravenous crystalloids. Anticonvulsants, usually benzodiazepines (Law et al., 2012), are used for control of seizures. Intravenous steroids and mannitol have been used in the treatment of patients in a few cases, in

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an attempt to reduce oedema. These have not been shown to be detrimental (Yu et al., 2011). A case report by Nagamine et al. (2014) presents a patient with transient cortical blindness following coiling of an unruptured internal carotid artery aneurysm. A three day course of pulsed intravenous methylprednisolone at a dose of 1,000mg daily was commenced on day 46 post-coiling. Imaging following intravenous steroids showed improvement both in terms of positron emission tomography (PET) on day 53, showing no areas of abnormal uptake, and also with reduction in lesion size on MRI on day 58, with almost complete resolution of lesions by day 90.

Another case report, by Pineda et al. (2013), claimed favourable results following craniectomy, with reduction in cerebral oedema. In this case report, one patient underwent craniectomy and faired better, both in terms of quality of life, and survival, compared to the two other patients who were treated conservatively. The rationale behind this technique was that craniectomy allowed for expansion of brain parenchyma and so resulted in less morbidity. However, this is only one case report and so one cannot draw any conclusions. Haemodialysis has been used in the treatment of contrast-induced encephalopathy in patients with chronic renal insufficiency, as reported by Muruve et al. (1996) and Yan et al. (2013), with positive results. Whilst there is no evidence favouring one treatment regime over another, the strict control of risk factors that may make patients susceptible to the development of this condition, may prove useful.

8. PROGNOSIS

Prognosis is usually favourable, with the condition being self-limiting and most patients returning to baseline neurological function within a few days of onset. However, onset is sometimes more insidious and resolution of symptoms may be more protracted (Nagamine et al., 2014). Rarely, the condition may result in permanent neurological deficits, and even death, as described by Leong et al. (2012). Ophthalmic involvement was found to have a higher propensity for permanent deficit (Kocabay et al., 2013).

9. CONCLUSION

Due to the unpredictability of this condition, with multiple presentations, clinical outcomes and causes, and with no definitive treatment yet known, prevention of its development is essential. Identification and minimisation of the risk factors predisposing patients to the development of contrast-induced encephalopathy, is thus imperative. Though a rare complication of intravenous contrast injection, contrast-induced encephalopathy is recognized as a cause of neurological deficit, with the potential to cause significant morbidity and rarely mortality. One must therefore keep this possibility in mind when neurological deterioration is noted in patients who have undergone procedures such as coronary angiogram, percutaneous coronary intervention, coil embolization, and other procedures involving contrast injection, even in a sub-acute setting. One must also be wary of misdiagnosis of this condition as cerebrovascular accident or subarachnoid haemorrhage, as may be suggested by CT and MR images. Since the safety of use of contrast following contrast-induced encephalopathy has not been studied widely, repeat studies must be considered seriously and with extreme caution, before being performed (Ting et al., 2013).

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Table 1

Risk Factors for Contrast-Induced Encephalopathy
Advanced age
Male gender
End-stage renal failure and impaired renal function
Chronic hypertension
Impaired cerebral auto-regulation
Infection, sepsis and shock (particularly by gram-positive organisms) (Sawaya et al., 2007)
Autoimmune disorders (Sawaya et al., 2007)
Transient ischaemic attack
Large doses of contrast used
Increased hydrostatic forces transmitted from carotid, cerebral and arch injections
Selective vertebral-basilar arteriography

Table 2

Recommended Precautions
Use of as minimal a dose of contrast as possible
Proper hydration prior to procedure
Use of low osmolality contrast in patients with several predisposing factors
Identify risk factors and optimize the patient's general condition

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