Physiopathology and radiological presentation of contrast-induced encephalopathy

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Disclosures:
Dr. Louis Deprez: Nothing to disclose
Mr. Martin Laurent Philippe Moïse: Nothing to disclose

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Purpose or Learning Objective:

- To identify imaging features that are suggestive of contrast-induced encephalopathy (CIE) in patients presenting with acute neurological symptoms after endovascular procedures.

- To understand the physiopathology of CIE and its main risk factors.

- To better differentiate CIE from other post-procedural related complications

Methods or Background:

Contrast-induced encephalopathy (CIE) is a rare acute complication of intravascular injection of iodinated contrast media (ICM), mostly seen after direct first-pass intra-arterial injection (mainly during cardiointerventional and neurointerventional procedures), manifesting with acute neurological symptoms1. Cases following intravenous injections are reported2. CIE has been reported with any type ICM but seems more frequent with hyperosmolar ionic contrast agents, that are less frequently used nowadays compared to modern iso-osmolar non-ionic contrast agents. As of today, no direct relationship between contrast media volume and CIE has been proven.

The incidence of contrast-induced encephalopathy following cerebral angiography ranges from 0,3 to 2%3 and peaks at about 3% in posterior circulation aneurysm embolization4.

Usual clinical manifestations of CIE are encephalopathy, cortical blindness5, focal sensitivo-motor neurological deficit, aphasia and seizures.

Its main differential diagnosis are procedure-related ischemic, hemorrhagic and hemodynamic complications, whose treatment is very different and represents an absolute emergency.

As an exclusion diagnosis, emergency imaging is required to rule out these complications and, if possible, confirm the clinical suspicion of CIE as specific radiological findings can be found on both computed tomography (CT) and magnetic resonance imaging (MRI). Clinical outcome is spontaneously favorable in most cases with complete neurological resolution within days, even though cases of persistent neurological deficit6 or death7 have been reported.

Main predictive factors include hypertension, chronic renal failure and past history of intracranial hemorrhage. Per-operative or post-operative hypertension relative to patient's baseline seems to be associated with contrast-induced encephalopathy1.

Our experience matches data from the scientific literature reported here. Out of 1557 neurointerventional procedures over 5 years, we retrospectively found 16 cases of CIE (roughly 1%), with either classical clinical features (cortical blindness) or typical imaging features. Clinical outcome was favorable in all cases after a few days (median time of 2 days). Most common clinical presentations were cortical blindness (31,25%) and hemiparesia (62,5%). Most common concomitant risk factors were hypertension (93,75%), tabagic intoxication (81,25%) and previous subarachnoid hemorrhage (50%). Roughly -half of the patients exhibited MRI (8/16) and/or CT (7/16) signs of CIE.

Results or Findings:

1. Physiopathology of CIE

The physiopathological pathways of CIE remains controversial. CIE is thought to be a consequence of the direct toxicity of ICMs on the neural cortex after its leakage in the subarachnoïd spaces (and sometimes the brain parenchyma itself) through a blood-brain barrier deficiency and endothelial dysfunction. In a sense, its physiopathology is similar to posterior reversible encephalopathy syndrome (PRES)8. It is no surprise that pre-existing conditions that chronically alter the vascular autoregulation of brain vessels and the endothelial function (such as arterial hypertension and previous subarachnoid hemorrhage) will be more frequently found in patients with CIE.

Some studies1 have also shown the presence of blood pressure variation during the procedure. Whether the acute endothelial dysfunction is caused by the toxicity of the contrast agent itself or by blood pressure variations during the procedure is not entirely clear.

2. Imaging features

Unsurprisingly, most imaging findings will concern the cerebral cortex or the subarachnoid space. Contrast extravasation is classically depicted ipsilateral to symptoms. Cortical findings may be more subtle, and easily missed if not looked for thoroughly. Meningeal reaction can occur, with thickening and enhancement of the meninges. Follow-up imaging will show disapperance of those features after a few days.

2.1 Computed tomography **(CT) features**

- **spontaneous hyperdensity** in the **subarachnoïd space** (SA) (leaked ICM in the SA through blood-brain barrier deficiency) (Fig. 1). A density higher than blood (>80 Hounsfield Units) is highly suggestive of iodinated contrast. Dual-energy CT is useful to differentiate subarachnoid hemorrhage from contrast extravasation9.
- abnormal **cortical enhancement** and **edema**, with cortical thickening (Fig. 2)
- Those features are often combined, as shown in Fig. 3 and 4.

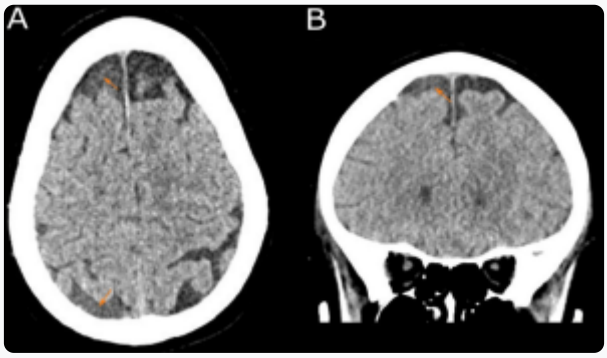
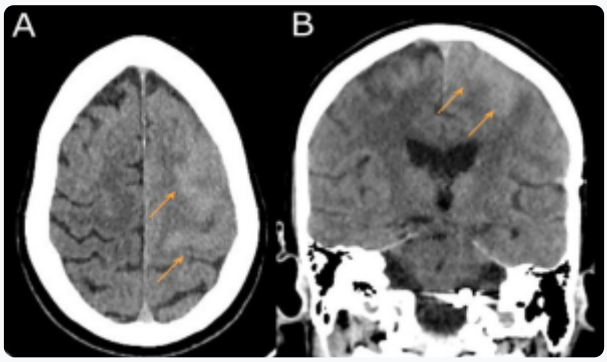


Fig 1: Sub-arachnoid space hyperdensity in the left cerebral convexity (orange arrows), following cerebral aneurysm embolization, corresponding to iodinated contrast media extravasation, shown in axial (A) et coronal (B) planes. Patient suffered from transitory right hemiparesia.



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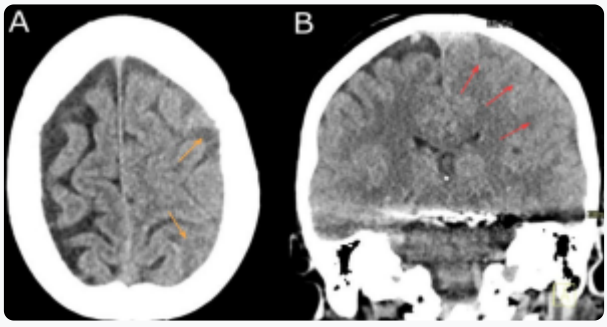


Fig 3: Sub-arachnoid space hyperdensity in the left cerebral convexity (orange arrows), corresponding to iodinated contrast media extravasation, and cortical oedema with cortex enlargement (red arrows), shown in axial (A) et coronal (B) planes.

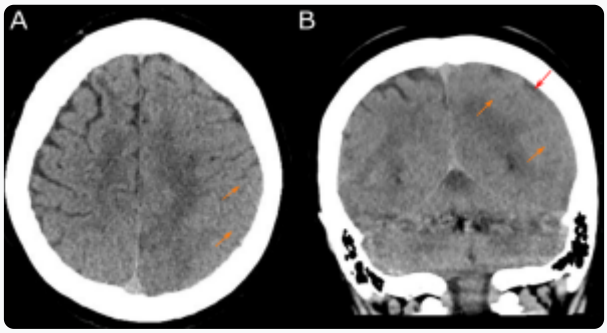
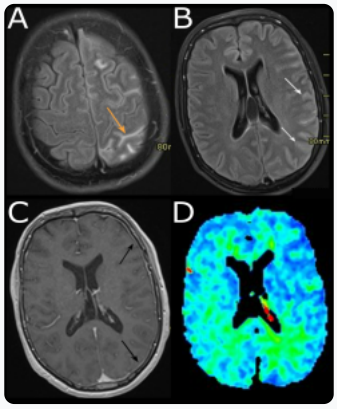


Fig 4: Sub-arachnoid space hyperdensity in the left cerebral convexity (red arrow), corresponding to iodinated contrast media extravasation, and cortical oedema with cortex enlargement (orrange arrows), shown in axial (A) et coronal (B) planes.

2.2 Magnetic resonance imaging **(MRI) features**

- **FLAIR hyperintensity in the subarachnoid space** (Fig. 5, 6), as the leaked subarachnoïd ICM is responsible of incomplete cerebro-spinal fluid's signal suppression. Probably due to the mechanism of impaired brain-blood barrier and endothelial function, **post-gadolinium FLAIR** is more sensitive (Fig. 7).
- T2 and **FLAIR hyperintensity of the cortex**, relative to cortical vasogenic oedema (Fig. 5, 8, 9 10, 11).
- **Cortical and leptomeningeal enhancement** after gadolinium enhancement (Fig. 10,11)
- **Dural thickening** and hypersignal after gadolinium injection (Fig. 5, 11)
- **No diffusion restriction**, due to the lack of cytotoxic oedema
- MRI imaging seems to be more sensitive at day one after the procedure than immediatly after. Negative emergent imaging should not rule out CIE, and MR imaging should be repeated after 24h.



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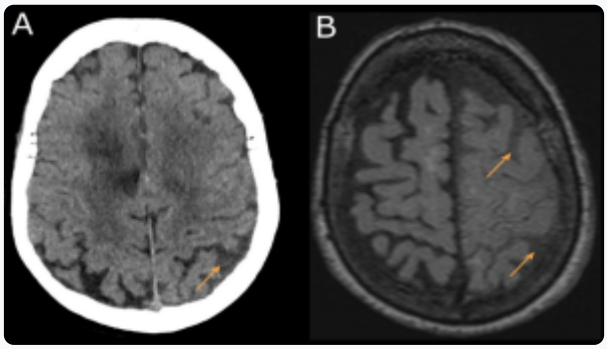

Fig 6: Comparison between CT and MRI. CT (A) showing (orange arrow) hyperdensity in the subarachnoid spaces of the parietal convexity. MRI (B) showing FLAIR hyperintensity (orange arrows) in the same area.

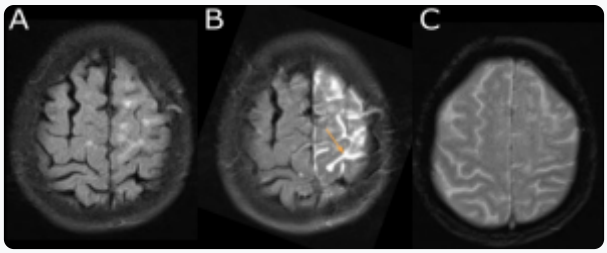

Fig 7: Pre-interventional FLAIR sequence (A). Post-gadolinium injection FLAIR sequence (B) with apparition of FLAIR hyperintensity in the subarachnoid spaces of the left cerebral convexity. (C) Normal T2 gradient echo sequence, showing no blood products.

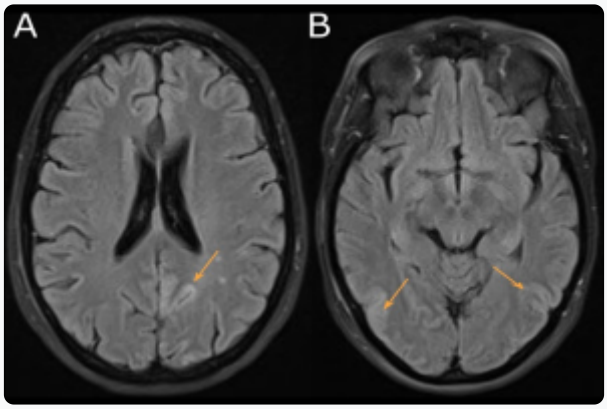

Fig 8: Cortical oedema with enlargement and FLAIR hyperintensity of the cortex (orrange arrows) of the occipital and temporal lobes.

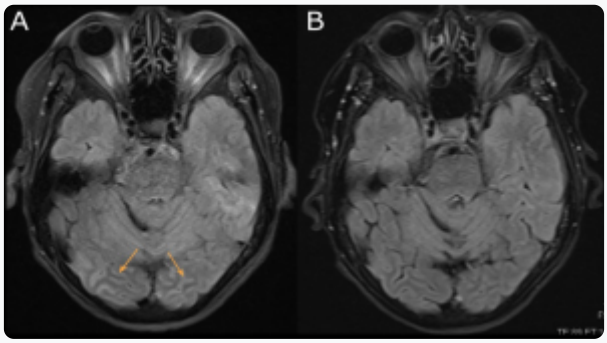

Fig 9: Cortical oedema and contrast extravasation in FLAIR hyperintensity (orange arrows, A). Regression of those features at day +7 (B).

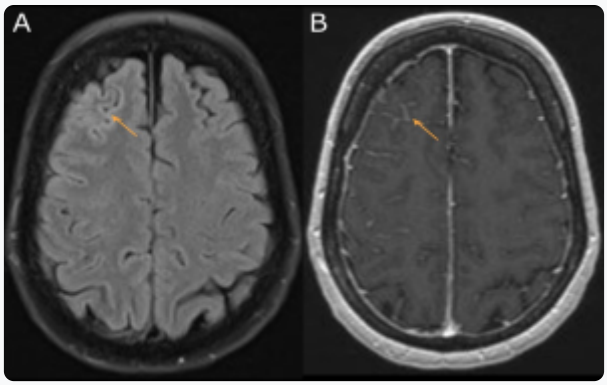

Fig 10: Cortical oedema in FLAIR hyperintensity (A, orange arrow). Leptomeningeal enhancement in T1 post-gadolinium injection sequence (B, orange arrow).

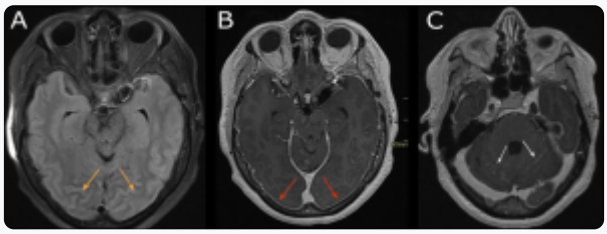

Fig 11: Bilateral occipital cortical oedema in FLAIR hyperintensity (orange arrows, A) in a patient with cortical blindess at wake-up after aneurysm embolisation. Dural (B, red arrows) and leptomeningeal (C, white arrows) enhancement on T1 after gadolinium.

3. Differential diagnosis

The main differential diagnosis of CIE are either ischemic, hemorrhagic or hemodynamic-related (PRES) lesions. PRES's physiopathology seems somehow closely related to CIE's and, as such, may be difficult to differentiate from CIE. These phenomenon can be associated.

3.1 Ischemic lesions

Ischemic lesions are easily differentiated from CIE features based on the restriction of diffusion of the water molecules within the parenchyma. Note that small asymptomatic ischemic infarcts can often be seen after cardio and

neurointerventional procedures, and that CIE shouldn't be excluded based on the presence of small ischemic lesions alone, if there are associated typical clinical or radiological CIE features.

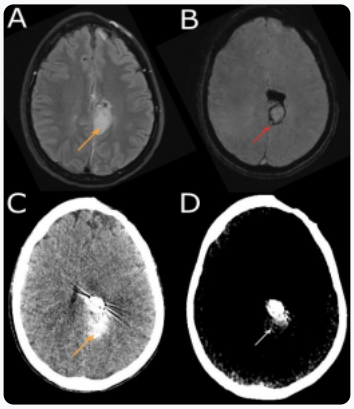

Fig 12: B1000 (A) and ADC (B), showing restricted diffusion in the left occipito-temporal regions (orange and red arrows). FLAIR (C) showing associated CIE features (cortical oedema (white arrow) and contrast extravasation (purple arrow).

3.2 Hemorrhagic lesions

Bleeding can happen after some endovascular procedures, mainly due do aneurysm perforation, arterio-veinous malformation or fistula rupture, or anti-platelet therapy in the setting of arterial stenting. Dual-energy CT is useful to differentiate hemorrhage from contrast extravasation.

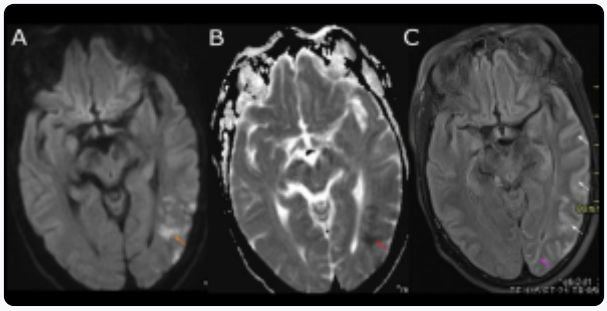

Fig 13: Bleeding after arterio-veinous malformation embolisation with liquid agent. FLAIR (A) showing nodular hyperintensity (orange arrow), with a rim in hypointensity on suspeptibilty weighted imaging (B, red arrow), and hyperdensity on CT (C, orange arrow), with persisting hyperdensity after virtual iodine suppression (dual-energy CT, white arrow, D).

3.3 Hemodynamic lesions

Posterior reversible encephalopathy syndrome (PRES) can rarely be seen after cerebral procedures. Its physiopathology seems to be closely related to CIE, and it may be difficult to separate the two entities. Fig. 14 illustrates a case of PRES following anterior cerebral artery stent implantation.

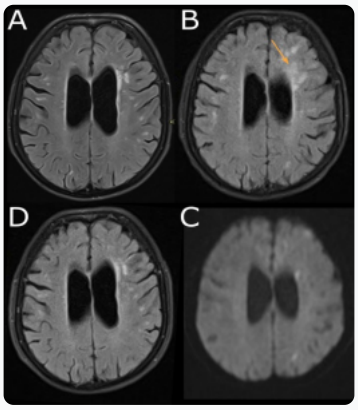

Fig 14: (A) Pre-interventional FLAIR. (B) Apparition of white matter FLAIR hyperintensity (arrow) at imaging after wake-up, with right hemiparesia. (C) diffusion showing small spots of high signal, without massive restricted diffusion. (D) One month follow-up showing regression of the signal abnormalities.

Conclusion:

CIE is a rare complication of intravascular ICM injection, with various clinical presentations, some typical imaging findings and favorable clinical outcome. It seems to be associated with pre-existing injuries of the blood-brain barrier. Acute imaging is mandatory to rule out other less-favorable complications and might help to assess the diagnosis of CIE.

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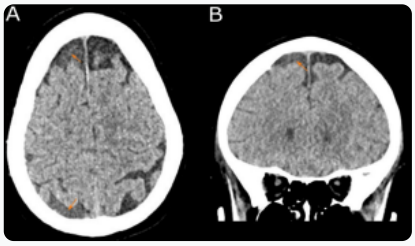

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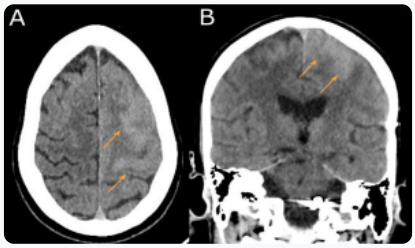

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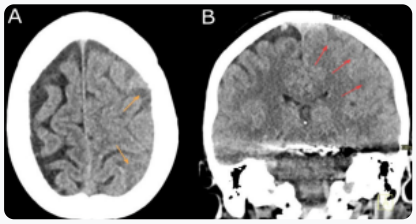

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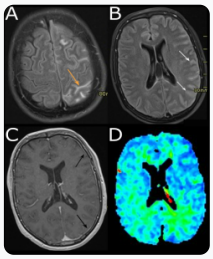

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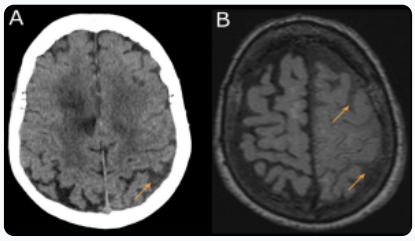

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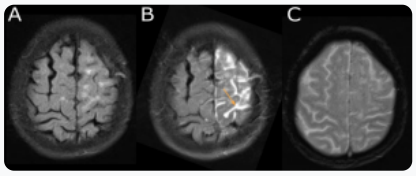

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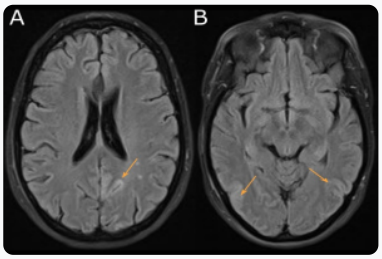

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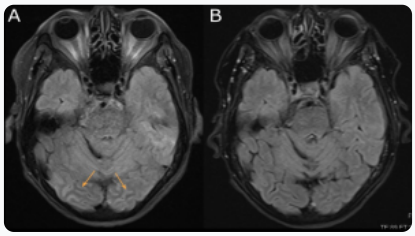

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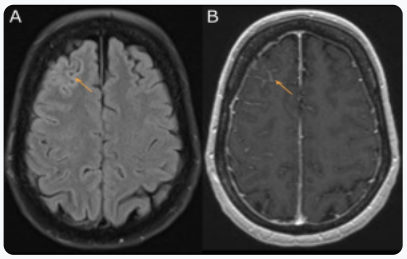

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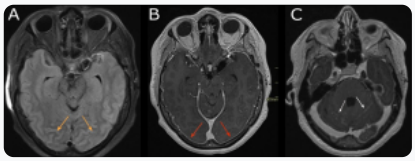

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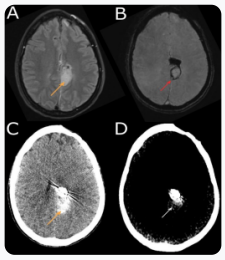

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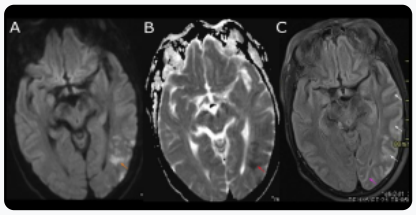

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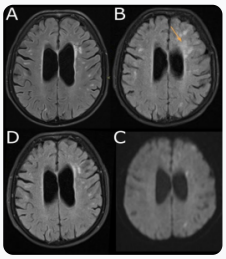

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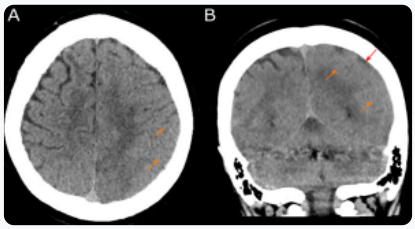

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