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Rapid contrast-induced encephalopathy after a small dose of contrast agent: illustrative case

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BACKGROUND Contrast-induced encephalopathy is a rare complication of cerebral angiography with only few cases reported to date. This paper reports on contrast-induced encephalopathy mimicking meningoencephalitis following cerebral angiography with iopromide, a subhypertonic nonionic contrast agent.

OBSERVATIONS A 50-year-old woman underwent cerebral angiography for assessment of recurrent nasopharyngeal carcinoma with invasion of internal carotid artery. The patient experienced symptoms including a disturbance of consciousness, seizures, frequent blinking, and stiffness in the extremities immediately after angiography of the left common carotid artery using iopromide (4 ml/s, total 6 ml). Computed tomography scans of the brain showed no obvious abnormalities, whereas brain magnetic resonance imaging showed swelling of the left cerebral cortex without signs of ischemia or hemorrhage. The patient was treated with intravenous rehydration, mannitol dehydration, and other supportive treatment. With this treatment, neurological status progressively improved, with complete resolution of symptoms at day 10.

LESSONS This observation highlights that even a small dose of subhypertonic nonionic contrast agent can rapidly induce contrast encephalopathy.

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KEYWORDS cerebral angiography; contrast-induced encephalopathy; neurotoxicity

Contrast-induced encephalopathy (CIE) is a rare, acute, reversible neurological disorder that occurs after contrast agent injection.[1] Its clinical manifestations are diverse but the prognosis is good. CIE can occur following the use of various types of osmotic contrast agents, including ionic, nonionic, hyperosmolar, subhyperosmolar, and isoosmolar, but it has been proposed to occur most frequently with the use of hyperosmotic contrast agents. The exact mechanisms and causes of contrast-agent neurotoxicity are still controversial but have been linked to a temporary disruption of the blood–brain barrier (BBB).[2] Here, we report a case of CIE that occurred rapidly with a small-dose contrast agent.

Illustrative Case

A 50-year-old woman with recurrent nasopharyngeal carcinoma (NPC) with no other confirmed diseases was scheduled for cerebral angiography. The patient developed a disturbance of consciousness, seizures, frequent blinking, and stiffness in the extremities immediately following angiography using iopromide (300 mg, Bayer Healthcare, 4 ml/s, total 6 ml), which is a subhypertonic, nonionic contrast agent. Several hours later, she developed a fever with temperatures up to 38.5°C. Noncontrast brain computed tomography (CT) showed no obvious abnormalities (Fig. 1A). To exclude cerebral stroke, we performed magnetic resonance imaging (MRI). No obvious abnormal intensity was found in T2-weighted MRI and magnetic resonance angiography (MRA) (Fig. 1B and C). However, a T2-weighted fluid-attenuated inversion recovery (FLAIR) image revealed cortical hyperintensities of the left temporal lobe and insular lobe (Fig. 1D). The diffusion-weighted image (DWI) revealed hyperintensities in the cortices of the left frontal, temporal, and insular lobes (Fig. 1F), whereas the apparent diffusion coefficient (ADC) showed no alteration (Fig. 1E). The following day, the gaze of the patient was shifted to the left, and the muscle strength of the left upper limb was grade 3/5 while the remaining limbs had a muscle strength of grade 0/5. Concurrently, the patient developed a twilight state. The patient was unable to cooperate and a lumbar puncture was therefore unsuccessful. As other potential causes for the patient's condition, such as ischemic complications and meningitis, were ruled out, CIE was considered. The patient was treated with large amounts of intravenous fluid infusion and dehydration, and symptoms resolved by day 10.

ABBREVIATIONS ADC = apparent diffusion coefficient; BBB = blood–brain barrier; CIE = contrast-induced encephalopathy; CT = computed tomography; DWI = diffusion-weighted image; FLAIR = fluid-attenuated inversion recovery; MRA = magnetic resonance angiography; MRI = magnetic resonance imaging; NPC = nasopharyngeal carcinoma.

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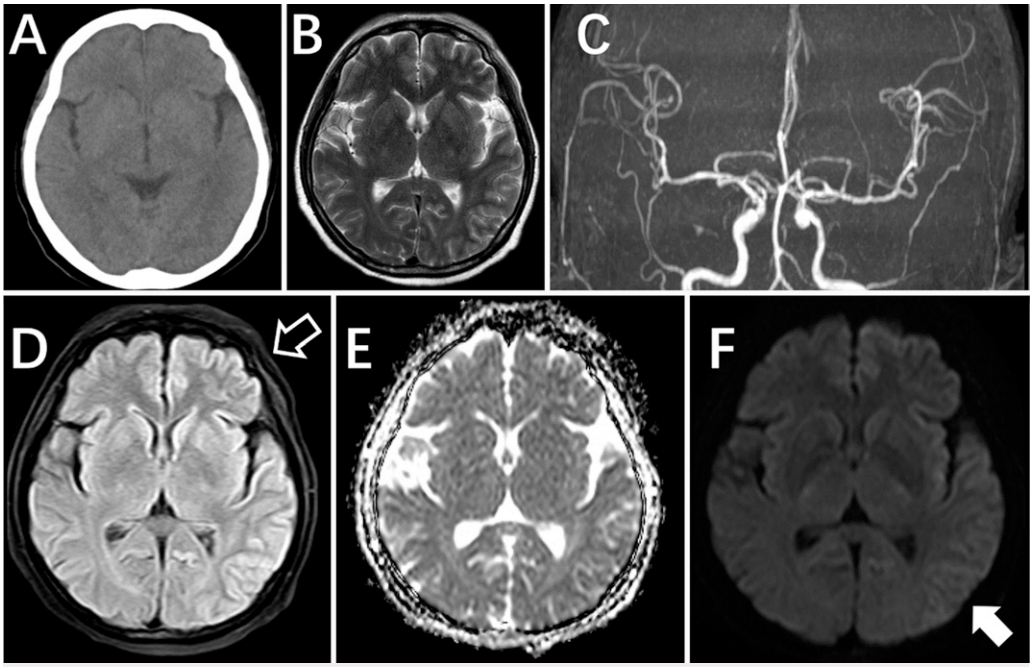

FIG. 1. Head CT and head MRI findings after onset. **A:** CT revealed no obvious abnormality. **B:** No obvious abnormality was found on T2-weighted MRI. **C:** MRA was normal. **D:** FLAIR revealed a hyperintensity in the left cerebral hemisphere (*white hollow arrow*). **E:** ADC was normal. **F:** DWI revealed hyperintensities in the cortices of the left frontal, temporal, and insular lobes (*solid white arrow*).

Discussion

CIE was first reported by M. Fischer-Williams et al. in 1970,[3] but the underlying pathomechanisms remain unclear to this day. Spina et al. have characterized contrast-induced neurological dysfunction as follows: 1) manifests within minutes to hours after injection of iodinated contrast agent; 2) short duration of symptoms, which generally disappear in 48 to 72 hours; and 3) symptoms cannot be attributed to other pathological processes, such as cerebral ischemia or hemorrhage, epilepsy, arterial dissection, and air embolism.[4] Although the literature indicates that the risk of adverse reactions of hypertonic contrast agent is higher than for other contrast agents, some reviews have suggested that CIE can occur with all types of contrast agents, including subhypertonic and isotonic contrast agents. Although the mechanisms leading to contrast agent–induced encephalopathy remain to be elucidated, it has been proposed that the hyperosmolarity of contrast agents results in a disruption of the BBB, leading to direct neurotoxicity and brain edema.[5] This is supported by findings in animal studies that have shown that ionic contrast media can cause BBB damage.[6] Hypertonic contrast agents may furthermore have chemical toxicity, promote the endocytosis and exocytosis of endothelial cells, and lead to endothelial cell contraction, and therefore interfere with the integrity of tight junction.[7] Factors predisposing to CIE included the use of large volumes of contrast agent (80–400 ml), chronic hypertension, transient ischemic attack, impaired brain autoregulation, impaired renal function, male sex, and previous adverse reactions to contrast agent.[8,9] The treatment of CIE is currently mainly supportive and usually includes intravenous rehydration; however, anticonvulsant drugs are also used in epileptic cases.[10] Furthermore, systemic corticosteroids and osmotic diuretics have previously been used. Symptoms and neurological deficits typically occur shortly after administration of the contrast agent and usually disappear within 24 to 48 hours.[11] Patients may not necessarily experience CIE if they are exposed to the contrast agent again but recurrence CIE has been reported.[12] Precautions include rehydration before administration and the use of the minimum amount of contrast agent required.[13] CIE should be considered when more common and potentially dangerous causes that may have fatal complications, such as intraventricular hemorrhage or subarachnoid hemorrhage, have been excluded. In our case, the diagnosis of CIE was based on clinical syndromes, brain CT, and brain MRI. Clinical symptoms appeared immediately after left common carotid angiography (4 ml/s, total 6 ml).

Observations

After angiography of the left common carotid artery using iopromide (300 mg, Bayer Healthcare, a subhypertonic nonionic contrast agent, 4 ml/s, total 6 ml), the patient immediately developed disturbance of consciousness, seizures, frequent blinking, and stiffness in the extremities. This report suggests that CIE may occur rapidly even with low-dose subhyperosmolar nonionic contrast agent injected in the carotid arteries. We propose that the cerebral autoregulatory capacity of this patient with recurrent NPC was compromised due to radiation therapy. To our knowledge, this is the first case of rapid CIE induced by a low dose of contrast agent.

Lessons

CIE can occur even with very low doses of subhyperosmolar nonionic contrast agent injected in the carotid arteries. It can also cause clinical symptoms immediately after the initial injection, not only after angiography has been completed.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Zhao, Chen, Zhu. Acquisition of data: Zhao. Analysis and interpretation of data: all authors. Drafting the article: Huang, Zhao, Zhu. Approved the final version of the manuscript on behalf of all authors: Huang. Statistical analysis: Chen. Administrative/technical/material support: Huang, Chen, Zhu. Study supervision: Zhu.

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