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Case Report

Unintentional direct intraventricular injection of gadolinium with fatal outcome: report of a case

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ABSTRACT

Gadolinium diethylenetriamine penta-acetic acid (Gd-DTPA) is the main contrast agent used in MRI, known for its good tolerance and rare toxicity. Even intrathecal injection of limited doses of Gadolinium can be performed in some indications. To our knowledge, only 3cases of accidental intraventricular injection of Gadolinium have been yet reported in the literature. We report the case of a 40-year-old male patient, who presented with headaches and vomiting. Brain MRI showed a right parietal abscess. The patient underwent emergent surgery for drainage of the septic collection. Postoperative MRI showed the development of a hydrocephalus related to a ventriculitis. Another surgery was performed to set up an external ventricular shunt, which lead to an improvement of the neurological status. A control brain MRI was scheduled for the patient, which revealed extensive abnormal enhancement inside the right lateral ventricle, on the basal cisterns as well as a leptomeningeal enhancement. Shortly after Gadolinium injection, the patient presented a tonic-clonic seizure. This clinico-radiological context leads to discover of the inadvertent intraventricular administration. Afterward, the patient's condition quickly deteriorated. Two days after the MRI he presented a cardiorespiratory arrest followed by death. Direct administration of Gadolinium into a ventriculostomy mistaken for intravenous catheter is a rare but harmful situation. Despite their rarity, such cases prove the importance of tracing all lines to their insertion sites to be confident of their appropriateness for injection.

Introduction

Gadolinium diethylenetriamine penta-acetic acid (Gd-DTPA) is the main contrast agent used in MRI [1]. When administered through intravenous route or even within the intrathecal space at low doses, it has negligible systemic toxicity [2,3]. The main reported complications are nephrogenic systemic fibrosis in patients with renal failure [4]. More rarely, higher doses inside the intrathecal space, used in cases of spinal myelography, can lead to severe neurotoxicity.

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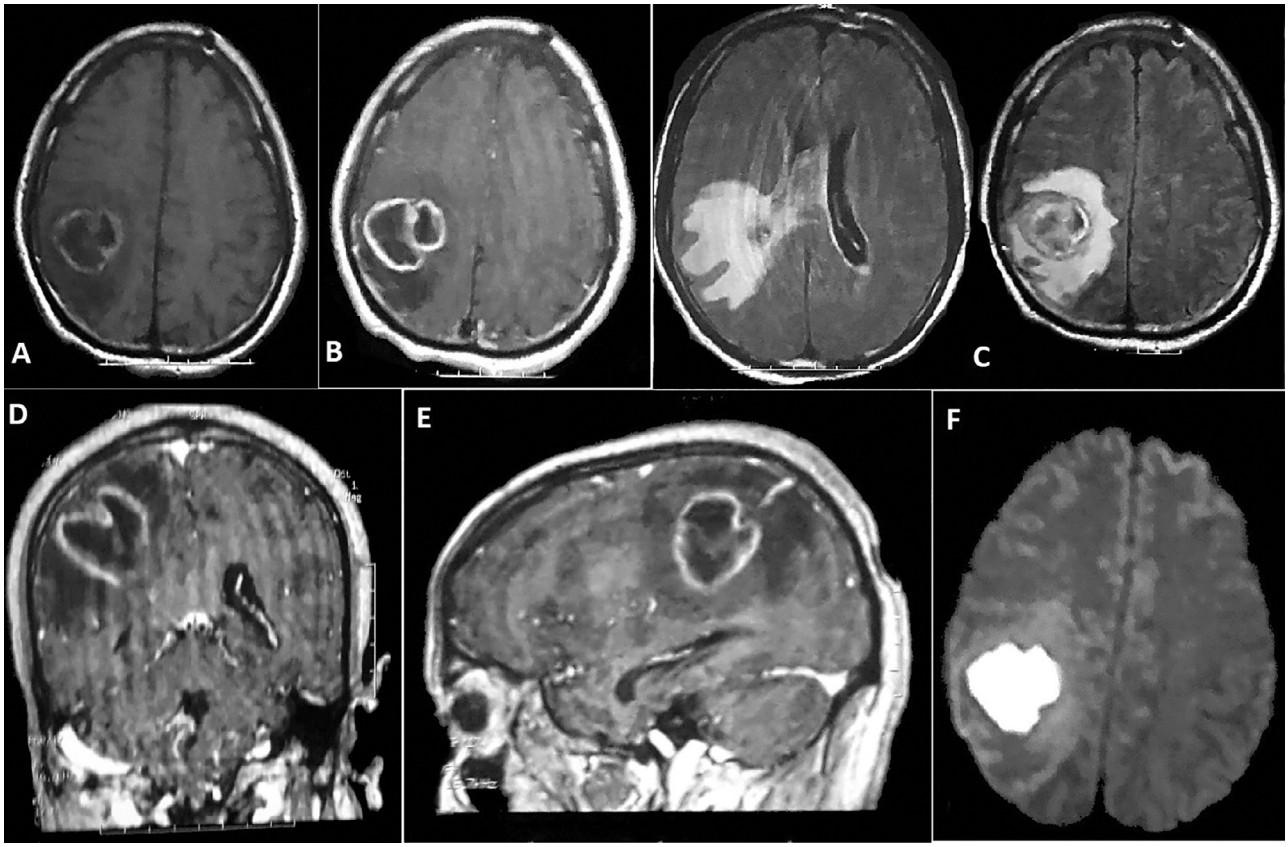

Fig. 1 – Preoperative brain MRI: (A) Axial section on T1-WI; (B) Axial section on T1-WI with injection of Gadolinium; (C) Axial sections on T2 FLAIR-WI; (D) Coronal section on T1-WI with injection of Gadolinium; (E) Sagittal section on T1-WI; (F) Axial section on diffusion-WI. They show a right parietal lesion, hypointense on T1-WI, hyperintense on T2-WI, with peripheral enhancement after injection of Gadolinium and perilesional oedema. This lesion seemed to erupt the ependymal wall and diffuse inside the right lateral ventricule.

This situation is seldom, and only few cases were reported [5,6]. Direct intraventricular injection of Gadolinium has been experimentally performed in animal models. But, in humans, this situation is anecdotal as to the best of our knowledge, only 3 cases of accidental intraventricular injection of Gadolinium were outlined in the literature [7]. We report a new case, the third worldwide, of intraventricular Gd-DTPA injection in a patient who underwent neurosurgery.

Case presentation

We report the case of a 40-year-old male patient, with no medical background, who presented with headaches and vomiting. These symptoms progressively occurred for a week. Physical exam found a conscious patient with no neurological deficit or fever. Brain MRI (Fig. 1) showed a right parietal lesion, hypointense on T1-WI, hyperintense on T2-WI with peripheral enhancement after Gadolinium injection. The lesion was extending to the lateral ventricle. Diffusion-WI showed a hyperintensity that orientated towards the diagnosis of an intracerebral abscess.

The patient underwent emergent surgery. Peroperative, an encapsulated abscess was found, whose medial part eroded the wall of the occipital horn of the right lateral ventricle, reflected by the issue of cerebrospinal fluid (CSF). The septic collection was drained in totality, and a sampling was sent for bacteriological investigations. Postoperative, the patient regained a perfect state of consciousness without any neurological deficit, but kept intense headaches. He received empiric antibiotics based on CEFOTAXIM and CIPROFLOXACIN. Postoperative brain CT scan (Fig. 2) showed an important oedema around the residual cavity. Progressively, both general and neurological status of the patient worsened: he became febrile, confused, and presented the progressive onset of a left hemiplegia. Bacteriological examination concluded to a multisensitive Streprococcus. This lead to a substitution of CIPROFLOXACIN with VANCOMYCIN. In order to look for an origin for the intracranial abscess, clinical, biological and radiological investigations were performed, but no evident

Fig. 2 – Axial section of a brain CT scan (performed 2 days after evacuation of the abscess and beginning of the antibiotherapy) showing the persistence of oedema around the residual cavity of the drained abscess.

aetiology could be found. 14 days after surgery, the neurological status of the patient was more a subject of concern, as he became aphasic and presented an epileptic seizure. Another brain CT scan (Fig. 3) showed a biventricular hydrocephalus associated to a cerebral edema. The patient was then reoperated in order to set up an external ventricular shunt (EVD). The latter consisted on tubing that exit the head and then attached to a bag. The CSF collected from the EVD was purulent. Following this surgery, the patient presented a slight improvement of his neurological status. He could open his eyes to verbal command, move his right limbs to localize the pain, but did not still have any verbal response. Another MRI was performed, showing radiological features corresponding to a ventriculitis (Fig. 4). But, 25 days after the first surgery, and 15 days after the EVD, the patient presented another deterioration of his state of consciousness. The brain CT scan (Fig. 5) showed a left ventricular dilatation, despite the presence of the external shunt on the right ventricle. This imaging showed the existence of different abscesses developing separately inside of each of the ventricles, without any communication between these structures. Another surgery was performed to set up an EVD on the left lateral ventricle (Fig. 6). The neurological status reimproved following this surgery, but the patient remained septic (oscillating fever, disturbed biological inflammatory parameters) after 33 days of CEFOTAXIM and 20 days of VANCOMYCIN. VANCOMYCIN was then resubtituted with RIFAMPYCIN (all antibiotics were administrated intravenously). Following this switch, both general and neurologic statuses of the patient improved. He regained a perfect state of consciousness, had no more aphasia and could progressively mobilize his left limbs. Biological assessments on the CSF found 4 elements/mm^3. A control brain MRI was scheduled in order to

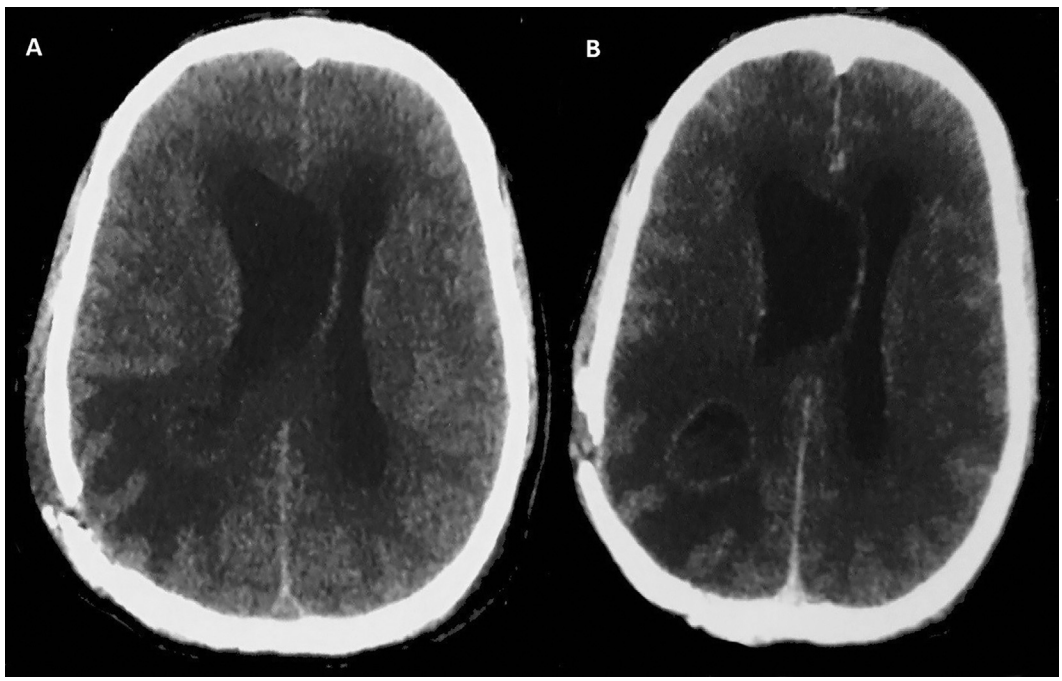

Fig. 3 – Axial sections of brain CT sections (performed 9 days after the previous imaging) before (A) and after (B) injection of contrast agent showing a biventricular hydrocephalus associated to a cerebral swelling.

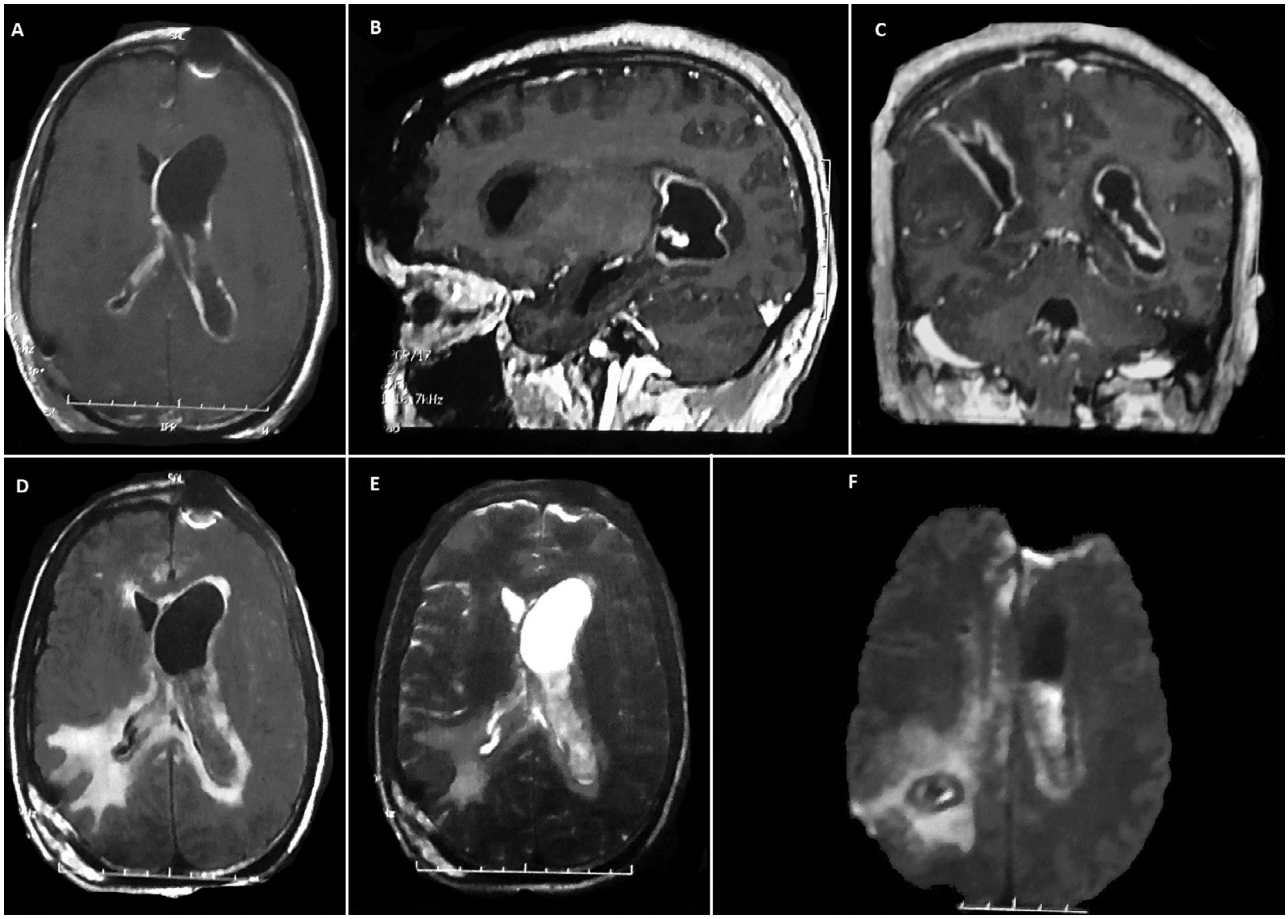

Fig. 4 – Brain MRI (performed 27 days after the first surgery, and 17 days after the placement of the right EVD): Axial (A), Sagittal (B) and Coronal (C) sections on T1-WI with Gadolinium injection; Axial sections on T2 FLAIR-WI (D), T2*-WI (E) and diffusion-WI (E). They show an enhancement of the ventricular wall suggestive of an intraventricular diffusion of the infection with ventriculitis.

check the evolution of the cerebral infection in preview for a ventriculoperitoneal shunt. This examination (Fig. 7) revealed extensive abnormal enhancement inside the right lateral ventricle, on the basal cisterns as well as a leptomeningeal enhancement. Viewing these features, and as the patient presented shortly after Gadolinium (Magnevist was used as contrast agent) injection a tonic-clonic seizure, the inadvertent intraventricular administration was discovered (after an approximate injection of 10 mL of Gd-DTPA through the ventricular catheter, which was thought to be a venous tube located in the right forearm). Afterward, the patient's condition further deteriorated, as he could only open the eyes to pain, without any motor or verbal responses. Another head CT scan performed 24 hours after the last MRI (Fig. 8) demonstrated a diffuse cerebral edema with crowding of the basal cisterns. No hyperdensity related to the gadolinium was observed probably. The pressure valve on the ventriculostomy was set to zero, but the patient presented several status epilepticus with persistant postictal coma, as well as labile blood pressure varying between systolic of 17 and 6. Two days after the MRI he presented a brutal cardiorespiratory arrest followed by death.

Discussion

Gadolinium is a paramagnetic material, which shortens the T1 relaxation time in tissues with hypervascularity or blood-brain barrier breakdown [8]. However, the increase of signal in a T1-WI is not related to the paramagnetic agent itself, but to the effect on neighbouring protons [9]. Thus, the increase of the dose of Gadolinium may lead to a negative enhancement. This was the fact we noticed in our case, when concentrated Gadolinium was instilled directly into the ventricles. Furthermore, there is marked enhancement at the level of the basal cisterns. This is related to a leakage of Gadolinium from the ventricles, consequence of a pressure gradient between these 2 sectors [10]. This was also the fact in our case, as marked darkening of the CSF in the ventricles and marked T1 hyperintensity of the CSF in the basal cisterns. Areas of enhancement along the ependyma and within the basal cisterns are not related to an authentic disruption of the blood-brain barrier, but are regions where there was a moderate dilution of the contrast with CSF [2].

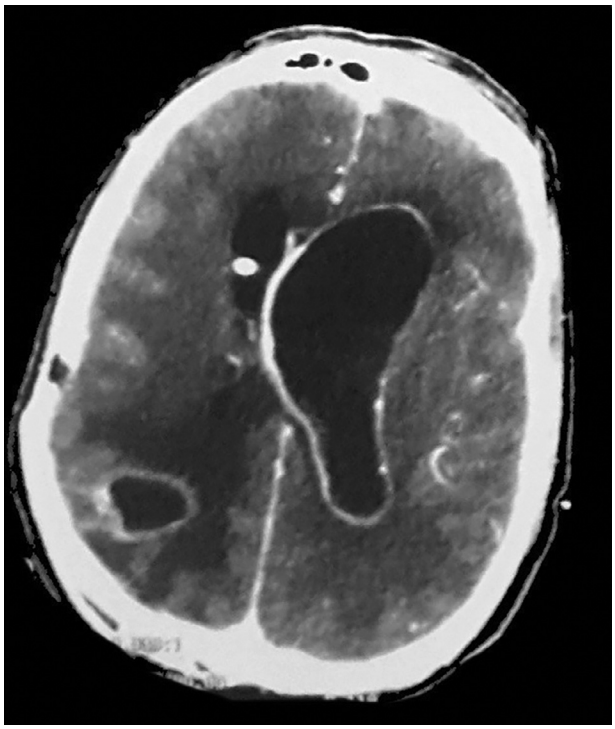

Fig. 5 – Axial section of a brain CT scan (performed 31 days after the first surgery) with contrast agent injection showing a hydrocephalus developing on the left lateral ventricle, despite of the presence of a ventricular catheter on the right lateral ventricle.

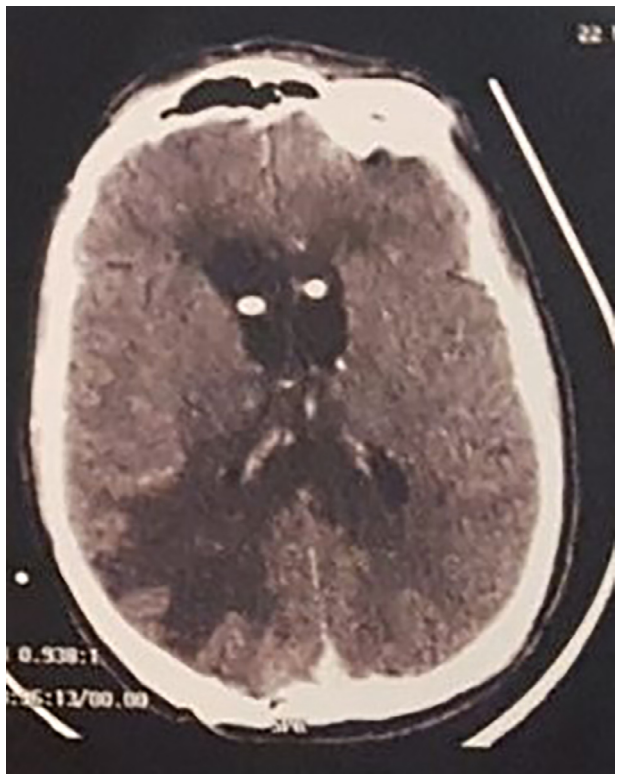

Fig. 6 – Axial section of a brain CT scan (performed one week after the previous) showing the regression of the hydrocephalus with presence of ventricular catheters on both lateral ventricles.

Gd-DTPA is usually administered intravenously at doses up to 0.1 mM/kg. These measures were proven to be safe with seldom side effects [11]. Higher doses that may reach 1 mL can be used for MR angiography and brain perfusion studies. Intrathecal injection of Gadolinium can also be used on myelography. We found that 2 patients who received intrathecal Gd-DTPA in doses higher than standard, presented an altered mentation (seizures, aphasia) [5,6].

Direct intraventricular injection of Gadolinium has been subject to trialsonly in animal models. To the best of our knowledge, only 2 patients had an inadvertent direct injection of Gd-DTPA [2].

Clinical presentations in these patients were different: the first, who basically suffered of a large tentorial meningioma, presented shortly after MRI an agitation and blood pressure drop. Then, his condition further deteriorated as he became increasingly altered and gradually developed aphasia, a depressed mentation, a right facial droop, and increased urine output suggesting diabetes insipidus. Thereafter, he required a tracheotomy and a long-term ventilator support, the he was lost from sight as his family requested his transfer to a facility closer to home.

The second patient, who underwent surgery for a cerebellar metastasis of a lung carcinoma, developed 1 day after the MRI an altered mental status and severe headache. This patient recovered her baseline neurological status on the day after MRI.

In our case, clinical manifestations and outcome appeared quicker and were heavier than those cited above. This may be related to the underlying pathology, as our patient suffered from ventriculitis before the incident occurred. This situation would have been source for a more severe neurotoxicity, explained by a more intense diffusion of the Gadolinium through the ependyme. .

Radiologic features were nearly similar. The first patient had an extensive abnormal enhancement within the surgical cavity, along the leptomeninges, and throughout the basal cisterns. The ventricular cavities appeared exceptionally hypointense on T1-weighted postcontrast images and a susceptibility artefact was observed along the ependymal margins. The second patient's MRI showed an enhancement within the basal cisterns as well as leptomeningeal enhancement, with a susceptibility artifact observed along the ependymal margins of the ventricles. Findings in ours patient's MRI were almost similar to those cited above.

Viewing that this situation is seldom, there is no randomized approach to treat such unfortunate accident. The best solution would be to prevent the occurrence of such inadvertences. The EVD should be systematically locked when a MRI is to be performed. Whenever this situation happens, it is obvious to provide antiepileptic to limit the risk of seizures. The

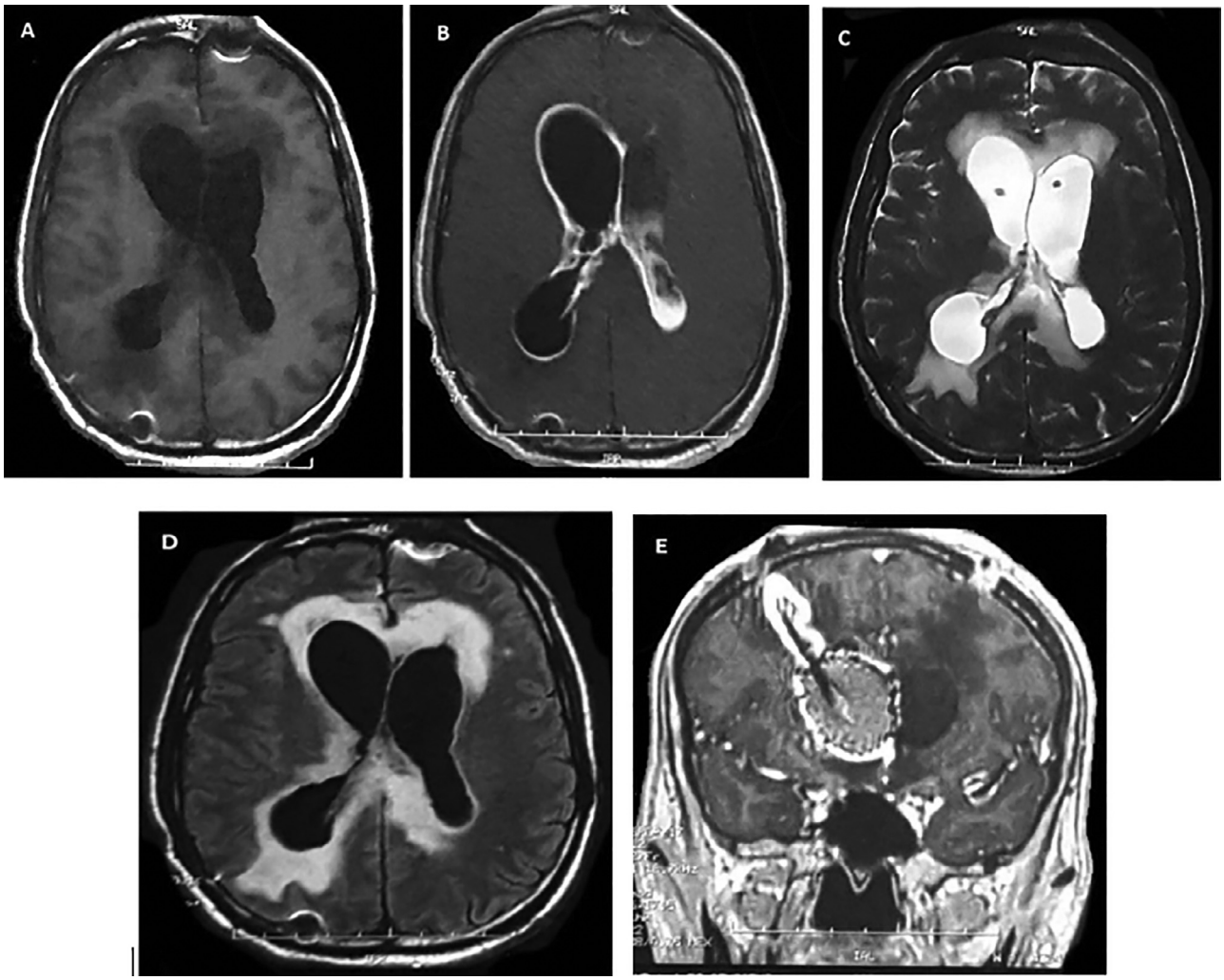

Fig. 7 – Brain MRI (performed 62 days after first surgery, during which occurred the incident) (A) Axial section on T1-WI; (B) Axial section on T1-WI with injection of Gadolinium; (C) Axial section on T2*-WI; (D) Axial section on T2 FLAIR-WI; (E) Coronal section on T1-WI with Gadolinium injection; (F) Sagittal section on T1-WI with Gadolinium injection and (G) Axial section on diffusion-WI. They show extensive abnormal enhancement inside the right lateral ventricle, on the basal cisterns as well as a leptomeningeal enhancement. The ventricular cavities appeared exceptionally hypointense on T1-WI.

pressure valve has to be set at the lowest possible in order to drain off the most of the contrast agent (while keeping in mind the risk of over drainage). A lumbar drain can also be placed to facilitate CSF drainage. Intubation can be discussed in order to anticipate increased intracranial pressure. Several control imaging have to be scheduled in order to overview the evolution of the induced intracerebral damage [2,12].

Fig. 8 – Axial section of a brain CT scan (performed on the day after the incident) showing a diffuse cerebral swelling.

Conclusions

The direct administration of Gadolinium into a ventriculostomy mistaken for intravenous catheter is a rare but harmful situation. The appearance of profound T1 hypointensity within the ventricles and diffuse susceptibility artefact along the ependyma is pathognomonic of intraventricular Gd-DTPA. Gadolinium is profoundly neurotoxic. Despite their rarity, such cases prove the importance of tracing all lines to their insertion sites to be confident of their appropriateness for injection.

Patient consent statement

A consent have been obtained from the patient's wife.

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