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Short report

Focal epileptic activity following intravenous contrast material injection in patients with metastatic brain disease

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SUMMARY Four patients with metastatic brain disease were referred for computed tomographic (CT) examination with contrast material injection. Within 2 to 4 minutes after the intravenous administration of water soluble contrast agent, focal epileptic activity occurred. The seizures became generalised in two of the patients who later died following status epilepticus. In the other two patients the focal seizures correlated with the localisation of the metastatic mass lesions. None of the patients had a previous history of epilepsy.

Adverse reactions to iodinated contrast agents have been reported extensively. Decreased haematocrit, increased osmolality, and an osmotic diuresis occur in almost all patients receiving intravenous contrast media. Idiosyncratic reactions ranging from nausea and vomiting to anaphylactic shock and death, have been well documented. Urticaria, chills, fever, and flushing are not uncommon. More serious complications include hypotension and cardiac dysrhythmias. Oral, lingual, and pharyngeal oedema may progress quickly to upper airway obstruction and bronchospasm. Changes in the mental status, including anxiety and restlessness, may also occur.[1-6]

Water soluble contrast media have been shown to penetrate the blood-brain barrier in a dose-dependent manner in doses similar to those used clinically.[7,8] Intracisternal injections are approximately 1000 times more lethal than intravenous injections.[9] In the past, water-soluble contrast media could not be injected intrathecally to diagnose central nervous system diseases above the lumbar region because of their severe neurotoxic effects, manifested primarily by epileptogenic activity. The possibility of epileptic complication is greater when large amounts of the contrast medium are introduced intrathecally.[10] Although the advent of non-ionic water soluble contrast agents into neuro-radiological practice has reduced the risk of complications, EEG changes such as dysrhythmia and spike activity have been reported following intrathecal injection.[11]

The side effects caused by intravenous injection of contrast agents have been explained on the basis of histamine releasing reactions, the neurotoxicity of the contrast material, and its osmolality.[1,12] Focal seizures due to fat soluble contrast material (iodophendylate) have been reported as a rare phenomenon. This patient's reaction occurred 4 months after the intrathecal injection and was associated with a permanent brain lesion.[13]

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Clinical material and methods

Four patients, one female and three males, aged from 32 to 71 years, with histologically verified malignant disease of various kinds, were subjected to CT examination of the brain, as part of the routine oncological follow-up, or because of clinical suspicion of brain metastases. No epileptic activity had been noted clinically in the patients prior to the administration of contrast material. Two different contrast agents were employed: Hexabrix and Urografin. In the three patients who received Urografin, the concentration differed (30%, 60%, and 75%). Two of the patients received a bolus injection (cases 1 and 2). The remaining two patients

were given drip infusion. The focal seizures began shortly (2-4 minutes) after the start of the drip infusion. The relation between the contrast material injection and the focal motor epileptic attacks were obvious in all patients. Two patients (cases 3 and 4) had focal seizures, contralateral to the mass lesions, and the focal activity responded to intravenous diazepam. In two other patients (cases 1 and 4) the metastatic mass lesions were bilaterally disseminated. These patients developed secondary generalised seizures after the injection of contrast material, and died in status epilepticus.

Case Reports

Case 1 A follow-up CT scan of the brain for a 32 year old male was requested by the oncology department. Two years earlier, the patient had undergone excision of a seminoma of his right testis. Eighteen months later, fine needle biopsy of a lung nodule disclosed metastatic seminoma. He underwent radiotherapy and chemotherapy. The patient had had his first brain CT scan 3 months prior to the present study, because of slowly progressing headache. Multiple metastases of both hemispheres, surrounded by oedema, were demonstrated at that time. On physical examination, the patient was somnolent. Neurological examination showed spastic quadriparesis and bilateral Babinski sign. Two minutes after bolus intravenous injection of 80 ml 60% Urografin, focal jerks of the left angle of the mouth appeared. Three minutes later, the jerking extended to the left upper extremity. The CT examination was stopped, and 10 mg diazepam were administered intravenously. Grand mal followed, and status epilepticus ensued. The patient received antiepileptic treatment, but slipped into a deep coma and died several hours later. No epileptic activity had been noted prior to the contrast material injection.

Case 2 A 62 year old male was referred for a CT scan of the brain. Three years earlier he had undergone surgery of the descending colon for adenocarcinoma. One month before the CT examination he developed a slowly progressive right hemiparesis and dysphasia. The non-enhanced CT scan showed low density areas in the left basal ganglia and left occipital lobe. Urografin 75%, 60 ml, was given via intravenous bolus injection. Approximately 3 minutes after the injection, epileptic contractions of the right lower extremity appeared, which responded to 5 mg diazepam intravenously, and the CT examination was completed. The enhanced scan demonstrated two mass lesions in the left hemisphere: one in the area of the basal ganglia, and one occipital. The masses were surrounded by low density areas (oedema) (fig, a). The findings were interpreted as secondary deposits. The patient had no prior history of epilepsy.

Case 3 A 71 year old male with inoperable squamous cell carcinoma of the lung, developed progressive right spastic hemiparesis. During the CT examination of the brain, Hexabrix 80% was administered via rapid drip infusion. Two minutes after the start of the infusion, right arm clonic jerks were observed. The injection of 3 mg diazepam was ineffective, but after additional 3 mg diazepam were injected the seizures subsided, and the examination was completed. The enhanced CT scan demonstrated two small lesions in the left hemisphere: one occipital and the other parietal, parasagittal. Low density areas (oedema) surrounded these lesions and were diagnosed as metastases (fig, b). No epilepsy was noted in the patient's history.

Case 4 An enhanced CT scan of the brain was requested for a 57 year old female, who had undergone excision of histologically proven malignant melanoma of the left leg 3 years previously. The patient had been uncooperative for several days. She had a right Babinski sign and general hyper-reflexia. Four minutes after the start of a rapid drip intravenous injection of 30% Urografin, after 90 ml had been administered, the patient had a contracture in her left arm and left leg. The contrast material infusion was immediately stopped, and 10 mg diazepam were injected intravenously, without effect. Within 5 minues the jerks became generalised and a prolonged grand mal seizure followed. An additional 10 mg of diazepam were given intravenously. The convulsions subsided, but the patient remained in deep coma. Despite anti-convulsive treatment the patient died the next day. The requested CT scan was not completed. Post mortem examination revealed multiple disseminated metastases of malignant melanoma to the brain, surrounded by extensive oedema. This patient had no prior history of epilepsy.

Discussion

Focal motor epileptic activity following intravenous contrast material injection has not yet been reported. We have never observed this phenomenon in patients with normal CT examination of the brain, nor in patients with other brain lesions, such as intracranial

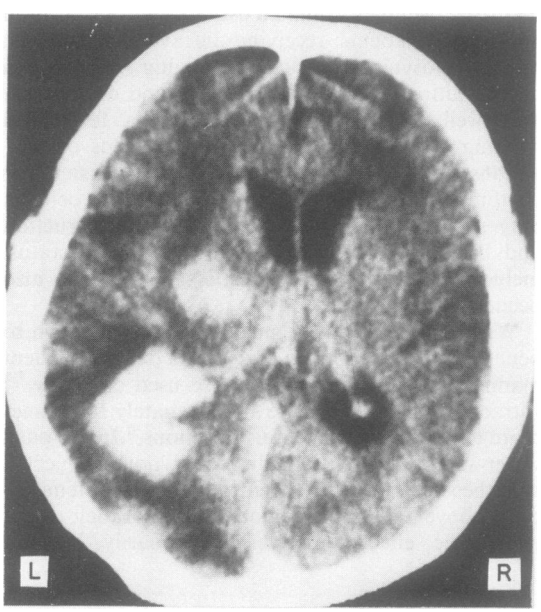

Fig *(a) Case 2. Two large enhanced mass lesions surrounded by oedema: one in the area of the left basal ganglia, and the other left occipital. The left occipital horn is collapsed, and there is a midline shift to the right with right hydrocephalus.*

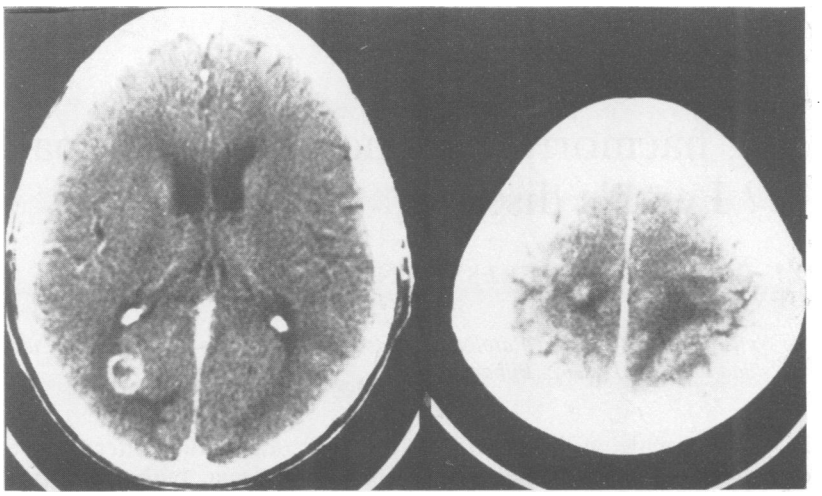

Fig *(b) Case 3. Two small enhanced mass lesions in the left hemisphere, surrounded by oedema. Left occipital lesion showing ring enhancement (left slice) and small left parietal mass lesion (right slice). The low density area demonstrated in the right parietal region (right slice) was also suggestive of a small additional metastasis, but no mass lesion could be demonstrated.*

haematomas, brain infection, or primary brain tumours.

The focal motor activity in our patients, who had metastatic brain disease, occurred 2–4 minutes after the administration of the contrast agent. These patients had never demonstrated such activity previously. The seizures were independent of the specific agent used, the manner of injection (bolus or drip infusion) and the histology of the primary tumour. In two patients (cases 2 and 3) the focal activity was contralateral to the CT findings. This fact, as well as the rapid onset of the seizures following the injections, lead us to believe that the jerks were due to the injection of contrast material.

It is likely that the extensive oedema surrounding the metastatic lesions (as seen at necropsy or on CT scans) is related to the severe breakdown of the blood–brain barrier. As a result of the oedema, there is direct contact of the high osmolality contrast material with the brain substance, resulting in impaired electric activity of these neurons. On the other hand, metastatic lesions can be the reason for focal epileptic activity; and the contrast agent penetrated the blood–brain barrier, so probably playing the role of a trigger for the first clinical onset of the focal epileptic activity.

It is possible that metastatic brain disease could be diagnosed incidentally following any contrast examination, such as urography or angiography, before the performance of a CT scan of the brain. The phenomenon of focal epileptic activity, after intravenous administration of contrast material, should be taken into consideration by physicians requesting enhanced CT scans, as well as those performing it in patients who are suspected for brain metastases.

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