Cerebral fat embolism: Use of MR spectroscopy for accurate diagnosis

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Abstract

Cerebral fat embolism (CFE) is an uncommon but serious complication following orthopedic procedures. It usually presents with altered mental status, and can be a part of fat embolism syndrome (FES) if associated with cutaneous and respiratory manifestations. Because of the presence of other common factors affecting the mental status, particularly in the postoperative period, the diagnosis of CFE can be challenging. Magnetic resonance imaging (MRI) of brain typically shows multiple lesions distributed predominantly in the subcortical region, which appear as hyperintense lesions on T2 and diffusion weighted images. Although the location offers a clue, the MRI findings are not specific for CFE. Watershed infarcts, hypoxic encephalopathy, disseminated infections, demyelinating disorders, diffuse axonal injury can also show similar changes on MRI of brain. The presence of fat in these hyperintense lesions, identified by MR spectroscopy as raised lipid peaks will help in accurate diagnosis of CFE. Normal brain tissue or conditions producing similar MRI changes will not show any lipid peak on MR spectroscopy. We present a case of CFE initially misdiagnosed as brain stem stroke based on clinical presentation and cranial computed tomography (CT) scan, and later, MR spectroscopy elucidated the accurate diagnosis.

Key Words

Cerebral fat embolism, fat embolism syndrome, hip arthroplasty, lipid peak, MRI brain, MR spectroscopy, MRI of brain changes in cerebral fat embolism, MR spectroscopy in cerebral fat embolism

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Introduction

Unexpected neurological deterioration occurs in more than half of patients following orthopedic procedures. Medications with psychotropic effect used for pain control is responsible for most of these cases. Stroke is also very common in this vulnerable period, and seen in 22% of patients undergoing hip arthroplasty. The embolization of free fat from disruption of bone marrow is also very common, and can present as cerebral fat embolism (CFE) in up to 10% of patients. Fat embolism syndrome typically presents with triad of hypoxia, petechial rashes and neurological changes, and also known for varied presentation. Patients with predominate neurological manifestations can be of diagnostic challenge due to the presence of other factors affecting mental status especially following trauma or postoperative period. Cranial computed tomography (CT) scan is usually normal in most cases. MRI of the brain will show classical changes on the fluid-attenuated inversion recovery (FLAIR) and conventional T2-weighted (T2W) images as multiple diffuse foci of hyperintensity in the white matter of the subcortical, periventricular, and centrum semiovale regions. The changes seen on T2W images may require several days to develop and are associated with edema. Elderly patients undergoing major orthopedic surgery, particularly in the postoperative period, are prone for many unforeseen complications like Hypoxic encephalopathy, hypoglycemic encephalopathy, disseminated infections and diffuse axonal injury, which have similar magnetic resonance imaging (MRI) findings. MR spectroscopy will be advantageous in this scenario by detecting the fat in these lesions, not seen in other conditions producing similar MRI changes. We present a case of CFE following hip arthroplasty which showed typical changes on the MRI of the brain and the use of MR spectroscopy for accurate diagnosis.

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Case Report

A 65-year-old woman underwent elective left hip total arthroplasty for uncontrolled osteoarthritis. Her immediate postoperative period was uneventful and she was started on morphine patient-controlled analgesia pump. In the evening, she was found to be very drowsy which was attributed to

narcotics and morphine pump was discontinued. Cranial CT scan showed right caudate and left thalamus hypodensity suggestive of stoke. The following day, patient's condition deteriorated with the development of hypotension and respiratory distress. CT scan of the chest showed ground-glass opacities in both lung fields without any evidence of pulmonary thromboembolism. Brain natriuretic peptide was elevated at 4963 pg/mL (normal <100 pg/mL) and troponins were elevated at 2.45 mg/ml (normal <0.04 mg/ml). She was treated with diuretics for congestive heart failure and raised troponins were considered to be due to Type II myocardial infarction. Her mental status continued to deteriorate requiring emergency intubation for airway protection and later transferred to our medical center for further management of postoperative stoke and congestive heart failure. Her blood pressure improved with a norepinephrine drip and respiratory status was stabilized with mechanical ventilation and diuretics. Neurological examination showed the patient to be comatose with decerebrate posturing of the left upper extremity on sternal rub. Deep tendon reflexes showed clonus on the right ride. Eye examination showed skew deviation of eyeballs to the left side and pupils were anisocoric with right pupil 3 mm and left pupil 7 mm in size, both reacting to light. Cough and gag reflexes were intact. Vertical oculocephalic reflex was absent. A cold caloric test showed deviation of eye balls to same side without any corrective nystagmus. Clinically, acute stoke in the dorsal midbrain and thalamus was suspected and MRI of the brain with stroke protocol along with MR angiogram (MRA) were performed on the fourth day of surgery. MRI of brain showed hyperintense signals in the cortical and subcortical regions on diffusion (DWI) images [Figure 1]. Basal ganglia and cerebellum showed similar changes with less brain stem involvement [Figure 1]. Most of these lesions did not show any restricted diffusion with apparent diffusion coefficient (ADC) mapping. These lesions were hyperintense on FLAIR and T2W images. MRA was normal. These MRI brain findings were not consistent with stoke. In view of hypotension, hypoxic encephalopathy was considered, and the location of the lesions also raised possibility for disseminated fungal infections. The absence of contrast enhancement on these lesions on the contrast MRI of brain, on fifth postoperative day made disseminate infections less likely. However, on ADC mapping most of the subcortical lesions showed diffusion restriction making cytotoxic edema the physiological basis for these subcortical lesions [Figure 1]. Hypoxic encephalopathy can produce similar changes but tends to involve more cortical regions particularly the occipitoparietal region, with predilection for caudate and putamen due to their increased susceptibility for hypoxia. The history of hip arthroplasty and typical anatomical distribution of lesions in the subcortical areas was indicative, but not diagnostic of CFE. To clarify the diagnosis, MR spectroscopy was done on the sixth postoperative day. MR spectroscopy was obtained with multivoxel 3D chemical shift technique in both short and long TE period. Raised lipid peak was noted at 0.9 ppm and 1.4 ppm in the both short TE and long TE sequence confirming the presence of fat in the voxel corresponding to the subcortical hyperintense lesions seen on T2 and Diffusion weighted images on MRI [Figure 2]. As fat is normally not seen in the cerebral tissue, the presence of lipid peak strongly suggests that, fat is being embolized from bone marrow following the orthopedic procedure. Confident diagnosis of CFE was made in the light of clinical presentation, MRI brain and MR spectroscopy findings. MR spectroscopy also showed raised lactate peak in these lesions suggesting anaerobic metabolism due to fat embolization leading to terminal hypoxia. The presence of raised lactate peak along with lipid peak suggests cerebral infarction and carries unfavorable prognosis.

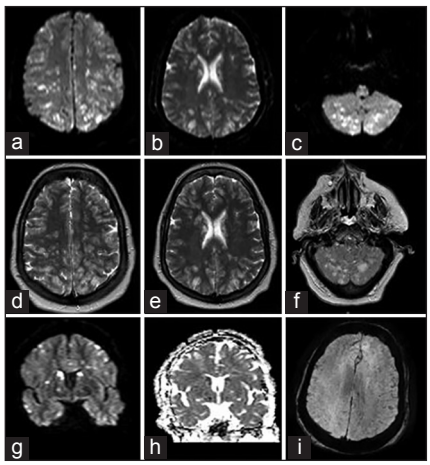

Figure 1: Diffusion images showing hyper intense signal in the centrum semiovale (Image a), basal ganglia and thalamus (Image b) and cerebellum (Image c). T2 images in the corresponding area showing bright signals (Image d, e and f) consistent with starfield pattern. Coronal images showing hyperintense signal in the basal ganglia on diffusion images and restriction in the ADC images (Image g and h). Diffuse punctate hemorrhages seen in Ven sequence (Image i)

She did not show any skin changes consistent with fat embolism syndrome (FES). Echocardiogram showed normal ventricular function without any thrombus or patent foramen ovale. The patient was continued on supportive management and unfortunately did not show any significant change in her neurological condition. MRI of the brain performed two weeks later showed continued restricted diffusion of these predominate subcortical lesions along with the development of diffuse punctate microhemorrages observed throughout the cerebral hemispheres on Susceptibility Weighted Imaging (SWI)

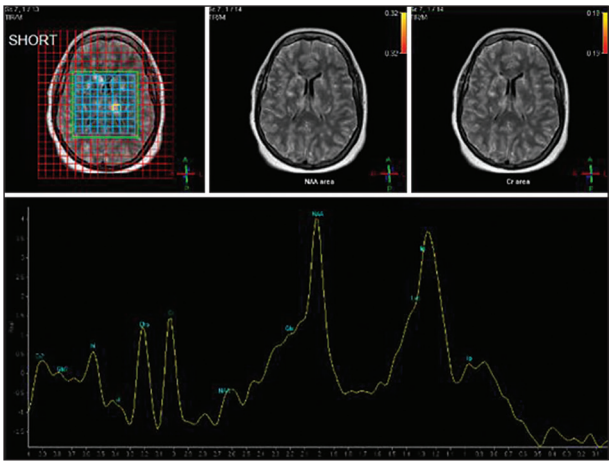

Figure 2: MR spectroscopy showing elevated Lactate and lipid peak in the short TE

[Figure 2]. Post contrast, diffuse heterogeneous enhancement was seen in cortical, subcortical, infratentorial, and cerebellar regions consistent with subacute infarcts. Since there was no improvement in the mental status, elective tracheostomy and feeding tube placement were performed and she was discharged to long term acute care facility in stable condition.

Discussion

FES is a consequence of embolization of free fat. It usually follows fracture or manipulation of long bones, which leads to disruption of the integrity of bone marrow resulting in escape of bone marrow fat into the circulation. Up to 10% of patients with long bone fractures and up to 40% of patients with internal fixation of femur fracture can present with FES.[1,2] Hip arthroplasty procedures can also predispose to CFE and in a recent review article from Robert *et al*., they accounted for less than 5% of total reported cases but carry worse prognosis.[3] Patients can present with triad of varying severity of neurological, respiratory, and cutaneous manifestations, depending on the embolic burden in the respective vasculature. Neurological manifestations are seen in 80% of patients with FES, presenting as altered mental status with nonfocal signs, and can quickly progress to coma.[3] Unexpected neurological deterioration after major surgeries can be diagnostically challenging. The hemodynamic fluctuation during the perioperative period can precipitate ischemic stroke, seen in 22% of patients with elective hip replacement.[4] Many medications used in the perioperative period have mind-altering properties can cause hypoactive delirium. The nonspecific neurological changes seen in CFE, makes the diagnosis challenging, particularly, if the FES is lacking cutaneous and respiratory manifestation.

In our case, the absence of cutaneous manifestation did not fulfill any of the criteria used for the diagnosis of FES.[5] Moreover, the initial cranial CT scan finding of hypodense of lacunar lesion pointed towards stroke being the cause of neurological deterioration. The decline in respiratory and cardiac status was attributed to possible brain stem stroke or infections. This anchoring effect along with availability bias lead to misdiagnosis of stroke initially, and atypical presentation of CFE was undermined.

MRI of the brain is a sensitive test for detection of CFE, and shows changes typical of, but not specific to CFE. The constellation of findings seen in MRI of brain and can be grouped into three patterns as described by Kuo *et al*.[6] Type 1 pattern includes multiple nonterritorial foci of high signal intensity in white matter along with involvement of gray matter of basal ganglia and thalami [Figure 1]. Unlike other causes, in CFE the changes are more prominent in the centrum semiovale and appear as white spots on a dark background of the white matter on the T2W or diffusion weighted images described as Starfield pattern by Parizel *et al*.[7] They are seen in 84.6% patients in acute stage and only 18% of patients in late stage. Type 2A pattern consists of a confluent cytotoxic edema in the white matter seen as diffusion restricted lesions in the periventricular and subcortical white matter symmetrically.[6] This finding is seen in 81% of subacute cases but seen less often in acute stage. Type 2B pattern is seen less often and include contrast enhancement of these lesions seen in Type 2A pattern and DWI images may show increased diffusion. Type 2C pattern is the presence of extensive tiny petechial hemorrhages in the perivascular space.[6] It is seen in 60% of acute stages and 80% of late stages. Microhemorrhages are also seen in diffuse axonal damage but they are more distributed in grey-white matter interface and corpus callosum. The microhemorrhages in CFE are located predominately in the white matter and share the same distribution of the confluent white matter edema. Our patient showed a Type 1 and Type 2A pattern in the initial MRI done within one week of presentation and Type 2C pattern on the MRI done two weeks later. These changes are not specific to fat emboli and may be seen after systemic embolization, disseminated infections, hypoxic leukoencephalopathy, toxic leukoencephalopathy, hypoglycemic encephalopathy and diffuse axonal injuries.[6] MR spectroscopy will help in accurate diagnosis by identifying the extra cerebral fat in these corresponding lesions. The lipid peak, particularly in the short TE images, confirms the presence of fat in the circulation and the lactate peak suggests the anaerobic metabolism due to blockage of circulation by fat globules.[8,9]

At present there is no specific treatment for CFE, steroids and high dose statins have been tried with limited success. With supportive management the prognosis is excellent and complete neurological recovery has been reported, even if the patient presented with deep coma initially.[10]

Conclusion

Patients undergoing operative procedures of long bones and joints, or traumatic fractures of long bone are prone for fat embolism syndrome. The classical presentation with triad of cutaneous, respiratory and neurological manifestations is not seen in all patients, and the absence of one of the features can pose diagnostic challenge. Physicians should be mindful of CFE in patient with neurological deterioration following these procedures. Cranial CT is not helpful for diagnosis and is normal in most cases. MRI of the brain, in acute stages will show predominant subcortical, periventricular lesions on diffusion weighted and FLAIR images. The starfield pattern is not specific to CFE. When diagnosis is in doubt, MR spectroscopy will help in accurate diagnosis by identifying the embolized fat in the lesions seen on MRI of brain and is specific for CFE.

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