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CLINICAL ARTICLE - BRAIN INJURY

Transient disappearance of microbleeds in the subacute period based on T2*-weighted gradient echo imaging in traumatic brain injury

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Abstract We report three cases of traumatic microbleeds evaluated by sequential observation. Hypo-intensities on T2* gradient echo imaging (T2*GEI) appeared just 2–3 h after the injury (the hyper-acute period). However, these hypo-intensities on T2*GEI disappeared or became obscure 2–6 days after the injury (the subacute period). A follow-up MRI again revealed clear hypo-intensities on T2*GEI 1–3 months after the injury (the chronic period). Our cases indicate that hypo-intensities on T2*GEI might change dynamically from the hyper-acute to the chronic period. The differences of susceptibility effects by hematoma age might be the cause of this dynamic change.

Keywords Diffuse axonal injury · T2*-weighted gradient echo imaging · Magnetic resonance imaging · Microbleeds · Traumatic brain injury

Introduction

Neuropathological studies have demonstrated that diffuse axonal injury (DAI) typically collapses the axons as well as the surrounding small vessels [1]. Thus, traumatic microbleeds (TMBs) are regarded as a radiological marker of a DAI. In patients with a DAI, computed tomography (CT) and conventional sequences of magnetic resonance imaging (MRI) may fail to detect any associated traumatic brain damage. T2* gradient echo imaging (T2*GEI) is known to be sensitive for the detection of TMBs in the chronic period [2, 3]. TMBs are associated with cognitive sequelae [4, 5] and their detection is important for the diagnosis of a DAI. However, there are only a few reports on an early MRI after a head injury, and little is known about the temporal changes in hypo-intensities detected by T2*GEI [6].

To the best of our knowledge, this is the first report of patients demonstrating dynamic changes in T2*GEI from the hyper-acute to the chronic period. We report three cases with TMBs, which showed dynamic T2*GEI changes based on sequential evaluations.

Case reports

All cases used the same MRI 1.5-T scanner (Gyroscan Intera; Philips Medical Systems, Best, The Netherlands). We obtained T2*GEI in the axial plane with the following parameters; 431–435/13/18/1 (TR/TE/flip angle/excitations), field of view 23 cm, acquisition matrix 256 × 205, and 5-mm slice thickness with a 1-mm gap.

Case 1

A 15-year-old boy suffered a closed injury by falling down eight stairs. On admission, he was unconscious with the Glasgow Coma Scale (GCS) score of 10. A CT scan revealed a small left parietal contusion. However, his clinical status was poor given the minor abnormalities detected by the CT scan, so an MRI was performed 3 h after the injury. Multiple hypo-intensities on the T2*GEI were observed at the bilateral parietal lobe and corpus callosum (Fig. 1a). Diffusion-weighted

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imaging (DWI) revealed no abnormalities (Fig. 1b). He was diagnosed with a DAI and treated conservatively. He gradually recovered and his GCS score increased to 15. Six days after the injury, a subsequent MRI revealed that the hypo-intensities on T2*GEI had become obscure (Fig. 1c), while the hyper-intensity of the DWI was clear (Fig. 1d). He was discharged with mild cognitive impairment. A month later, he returned to school and a follow-up MRI again revealed clear hypo-intensities on the T2*GEI (Fig. 1e).

Case 2

A 15-year-old boy suffered a severe closed injury in a traffic accident. On admission, he demonstrated the GCS score of 9. A CT scan revealed no abnormal findings, and an MRI was performed 2 h after the injury. Multiple hypo-intensities on T2*GEI were observed at the superficial left parietal cortex and corpus callosum (Fig. 2a). He was also treated conservatively. Five days after the injury, a subsequent MRI revealed that the hypo-intensities on the T2*GEI had disappeared (Fig. 2b). He was discharged with mild memory disturbance. A month later, a follow-up MRI again revealed clear hypo-intensities on the T2*GEI (Fig. 2c).

Case 3

A 12-year-old girl suffered a severe closed injury in a traffic accident. On admission, she demonstrated a GCS score of 10. A CT scan revealed a small right parietal contusion (Fig. 3a), and an MRI was performed 36 h after the injury. T2*GEI revealed very small hypo-intensities at the right parietal cortex (Fig. 3b). She recovered with no abnormal findings. Three months later, a follow-up MRI revealed clear hypo-intensities on the T2*GEI (Fig. 3c).

Discussion

The magnetic susceptibility differences resulting from the presence of paramagnetic blood breakdown products create local magnetic field inhomogeneities [7], which revealed marked hypo-intensities in T2*GEI. Morphological changes in acute hematomas might affect the T2*GEI findings. Ezaki et al. [6] reported that hypo-intensities identified by T2*GEI were resolved in less than 10 days in two patients with a DAI. In an experimental intracranial hematoma study in rabbits, Alemany et al. also demonstrated a clear increase in the

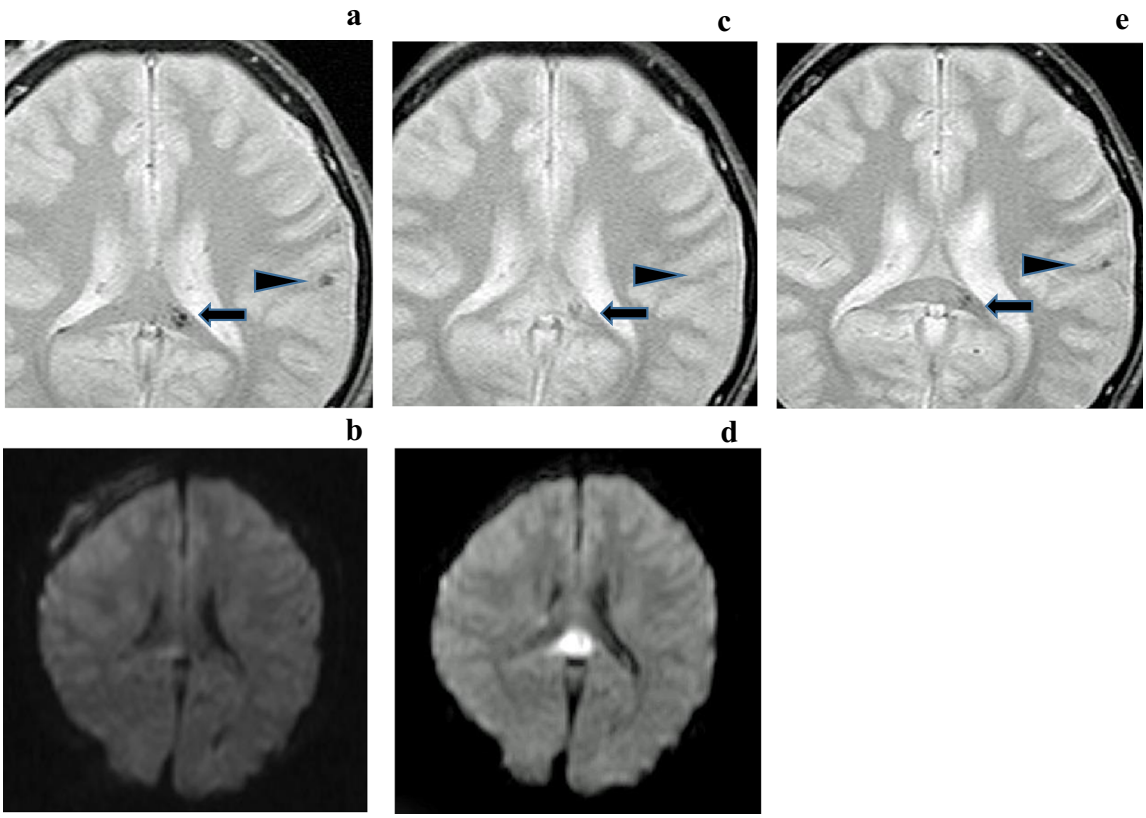

Fig. 1 Magnetic resonance images of a 15-year-old boy who was injured in a falling accident. **a** On admission 2 h after the injury, multiple small hypo-intensities on the T2*-weighted gradient echo imaging (T2*GEI) are seen at the corpus callosum and left parietal lobe. **b** Diffusion-weighted imaging (DWI) reveals no abnormalities on admission. **c** Hypo-intensities on the T2*GEI became substantially obscure 6 days after the injury. **d** DWI reveals hyper-intensity at the corpus callosum 6 days after the injury. **e** Hypo-intensities on the T2*GEI are clear again 30 days after the injury

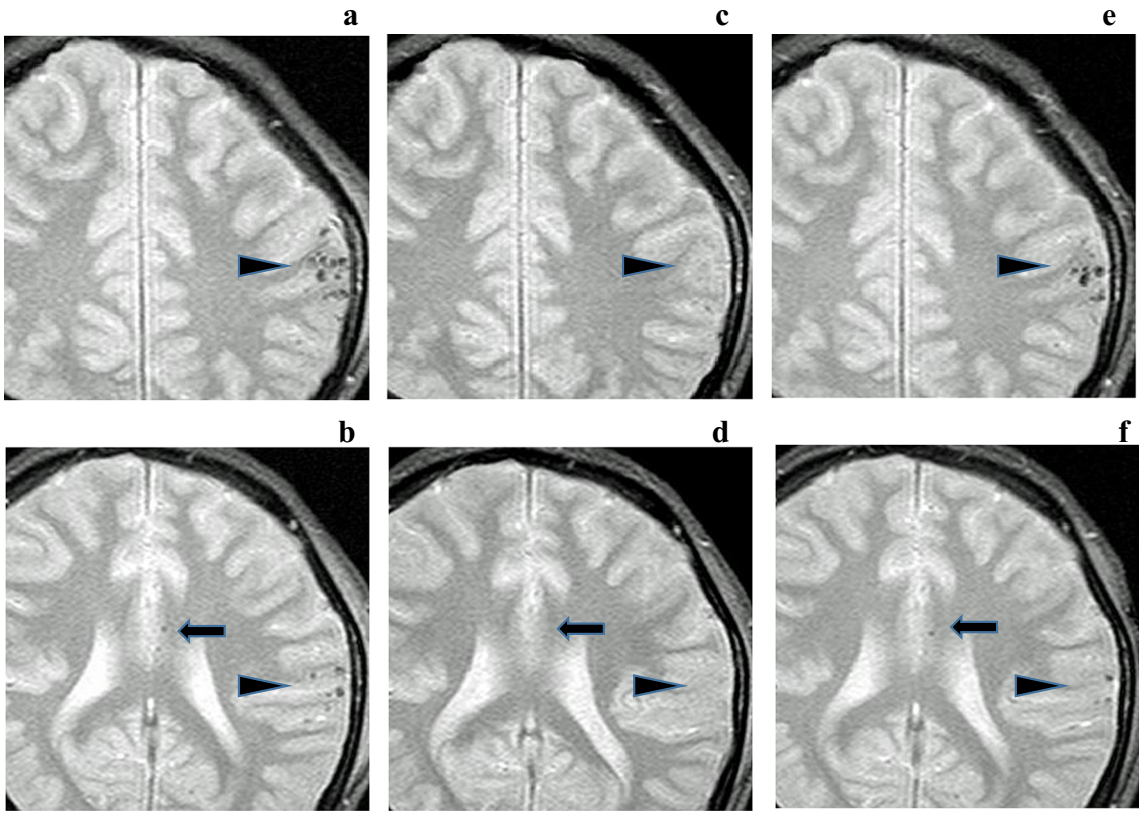

Fig. 2 Magnetic resonance images of a 15-year-old boy who was injured in a traffic accident. **a**, **b** On admission 3 h after the injury, multiple small hypo-intensities on the T2*-weighted gradient echo imaging (T2*GEI) are seen at the left parietal lobe and corpus callosum (*arrow*). **c**, **d** Hypo-intensities on the T2*GEI disappear 5 days after the injury. **e**, **f** Hypo-intensities on the T2*GEI again became clear 27 days after the injury

number of undetected hematomas from the hyper-acute to the subacute period [8]. However, they only mentioned changes in the signal intensity from the hyper-acute to the subacute period. Our cases also demonstrated that hypo-intensities identified by T2*GEI became obscure from the hyper-acute to the subacute period. Interestingly, hypo-intensities in the chronic period were again clear in all of our cases.

We speculate that susceptibility difference is the main cause of T2*GEI signal changes over time. As a hematoma ages, hemoglobin passes through the four main forms of oxyhemoglobin, deoxyhemoglobin, methemoglobin, and hemosiderin. Deoxyhemoglobin, intracellular methemoglobin, and hemosiderin have a magnetic susceptibility effect; however, oxyhemoglobin and extracellular methemoglobin have little susceptibility effect [9].

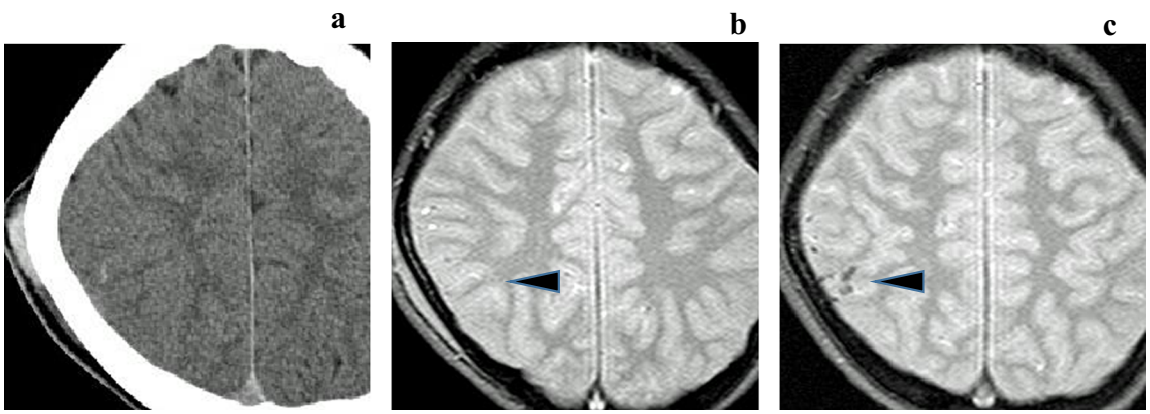

Fig. 3 Computed tomography (CT) and magnetic resonance images of a 13-year-old girl who was injured in a traffic accident. **a** On admission, a CT scan reveals a right parietal small contusion. **b** T2*-weighted gradient echo imaging (T2*GEI) reveals very faint hypo-intensities at the right parietal cortex 2 days after the injury. **c** Hypo-intensities on the T2*GEI became clear 90 days after the injury

In our cases, hypo-intensities on T2*GEI appeared only 2 h after the injury when even DWI could not detect any abnormal signal intensities. These hypo-intensities on T2*GEI in the hyper-acute period might correspond to deoxyhemoglobin. T2*GEI have the ability to capture the earliest and most minor traumatic changes. In addition, hypo-intensities on T2*GEI became obscure in the subacute phase 2–6 days after the injury. This so-called "negative period" corresponds to a period of chemical change from deoxyhemoglobin to extracellular methemoglobin. With chemical changes from methemoglobin to hemosiderin, the hypo-intensities on T2*GEI would again become clear.

This knowledge is very important for the correct diagnosis of DAI and the proper treatment of a head injury. Patients with moderate or severe head injury are often restless and require careful observation, so performing an MRI in this hyper-acute period is difficult and risky. Therefore, an MRI is usually performed when patients become more stable. This subacute period often corresponds to a negative period, leading to the possibility of under diagnosis if the MRI is performed during this time.

However, our study has some limitations, which require careful consideration in clinical use. First, our sample of cases was small. Second, the correlation between the hypo-intensities on T2*GEI and histopathological findings of TMBs was not absolute. Numerous reports have documented changes in the appearance of non-traumatic intracranial hemorrhage by MRI. TMBs are very small, so not only morphological changes in hemoglobin but also its various oxidation products, red blood cell membrane integrity, hematocrit, clot structure, molecular diffusion, pH, temperature, field strength, voxel size, previous contrast material use, and blood flow may affect the MRI [7, 9–11]. Third, we used an MRI at 1.5 T and T2*GEI. Currently, an MRI at 3T or susceptibility weighted imaging are reported as superior at detecting TMBs [2, 12]. In addition, we used a low range of both flip angle and echo time at 1.5 T. However, Alemany et al. reported that a higher number of bleeds were identified with the longer echo time (30 ms) as compared 14 ms in the early phase but became negative in the later phase [8]. If we used a high range of echo time, transient disappearance of microbleeds might become clearer. We need to pay attention to the gradient echo setting.

In conclusion, we report three cases of traumatic brain injury in which the hypo-intensities on T2*GEI changed dynamically over time. Hypo-intensities on T2*GEI may be clearest in the hyper-acute period and result in negative findings in the subacute period. We should be aware of how much time has elapsed when an MRI is performed following a traumatic brain injury.

Compliance with ethical standards

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Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed for the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. "For this type of study, formal consent is not required."

Informed consent Informed consent was obtained from all individual participants included in the study.

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