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Radiation-Induced Brain Calcification: Paradoxical High Signal Intensity in T1-Weighted MR Images

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Summary

Background. Irradiation to the central nervous system (CNS) in childhood is known to induce cerebral calcification after a latent period. Calcification has been generally found to show nil or a reduction in signal intensity in magnetic resonance (MR) images. However, we have studied three patients with radiation-induced brain calcification, who manifested increased signal intensity on T1-weighted MR images.

Method. Three girls had each been diagnosed as having a suprasellar germ cell tumour and were treated with conventional fractionated radiotherapy in their childhood. In one case, chemotherapy was given prior to the CNS irradiation.

Findings. All three patients survived their disease, and a follow-up CT scan revealed calcification in the brain, which has shown an increased signal intensity in the T1-weighted images of MR.

Interpretation. Cerebral calcification may be presented as a high signal intensity in the T1-weighted MR images. This may be explained by a surface-relaxation effect by the calcium salt particle, precipitated in the brain due to radiation-induced mineralising micro-angiopathy.

Keywords: Calcification; mineralising micro-angiopathy; MR; radiotherapy.

Introduction

Calcium deposition in the brain has been widely recognized as one of the radiological manifestations of the late effects of radiation and chemotherapy in treating childhood CNS neoplasms. Mineralising micro-angiopathy is believed to play a causative role in deposition of calcium salt in these patients [10]. The deposition of calcium has been clearly visible on CT scan. Recently, magnetic resonance (MR) has become the standard technique for following up patients with an intracranial tumour after therapeutic intervention. The effect of calcium deposition on signal intensity in MR images has generally been thought to be either no effect or a reduction in signal intensity [4, 5, 6, 8]. We have studied three patients in each of whom cranial MR has demonstrated the unusual characteristic of a hyper-intense signal present on T1-weighted images in the area that was clearly calcified on the CT scan.

Case Reports

Case 1

A 15-year-old girl was diagnosed as having a suprasellar germ cell tumour. She completed a therapeutic course of irradiation (2000 cGy to the whole brain followed by an additional local irradiation of 3000 cGy). After radiation, the tumour became shrunken, and hormonal supplementation therapy was administered as an out-patient. At the age of 32 years, a CT scan revealed symmetrical calcification in the basal ganglia. On MR, the areas of calcification demonstrated paradoxically increased signal intensity on the T1-weighted images and decreased signal intensity on the T2-weighted images. Her mental status was preserved within normal range, and she continues to work part-time in a publishing company. No extrapyramidal sign has been observed.

Case 2

An 11-year-old girl was diagnosed as having a suprasellar tumour. Obstructive hydrocephalus was treated by bilateral external ventricular drainage followed by a ventriculo-peritoneal shunt. The histological examination on the surgical specimens obtained at open biopsy revealed the tumour to be a germinoma with syncytiotrophoblastic giant cells. CNS irradiation with a dosage of 3000 cGy, 2000 cGy, and 3000 cGy was given to the whole brain, the local tumour region, and to the whole spine, respectively. The tumour shrunk and disappeared, and she was followed up as an out-patient. Calcification in the basal ganglia gradually developed becoming increasingly apparent on CT scans. At the age of 20 years, the areas of calcification on CT scan demonstrated a paradoxically increased signal intensity on T1-weighted MR images and a decreased signal intensity on T2-weighted images. Her intellectual performance has become slightly lower than normal, but no extrapyramidal sign has been observed.

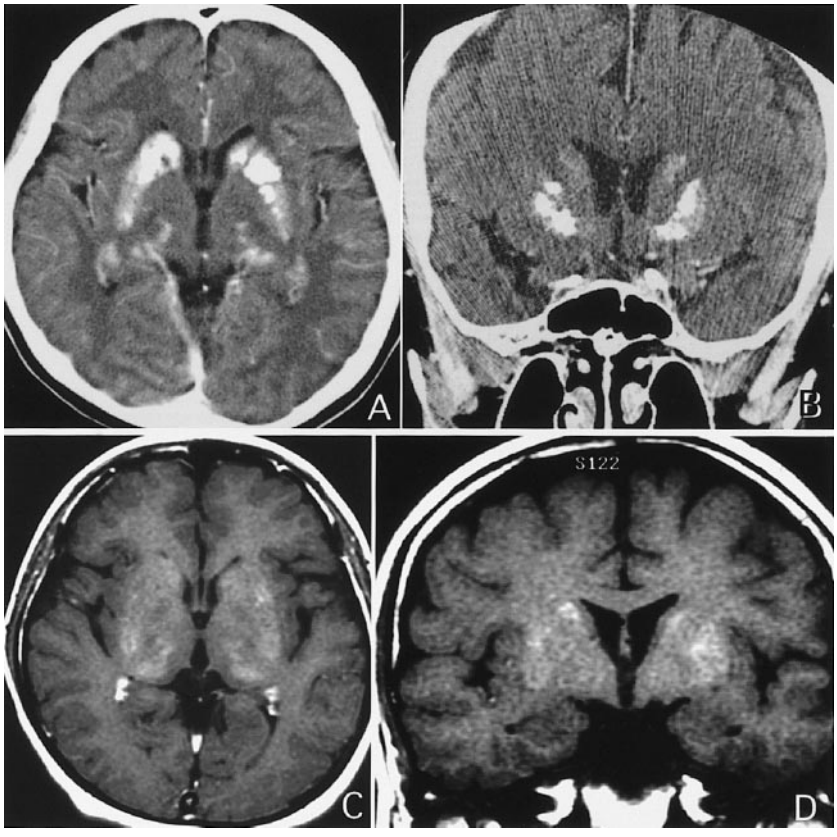

Fig. 1. Case 1. CT scan showing calcification of basal ganglia and thalami bilaterally. (A) axial section; (B) coronal section. T1-weighted images of MR showing paradoxical high signal intensity area in basal ganglia and thalami bilaterally (C) axial section; (D) coronal section

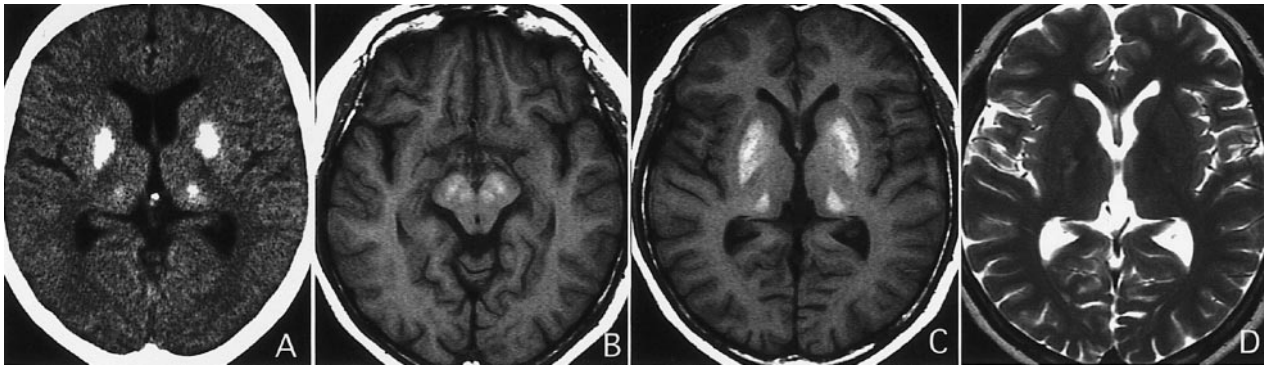

Fig. 2. Case 2. (A) CT scan showing calcification of bilateral basal ganglia and thalami bilaterally. T1-weighted images of MR showing paradoxical high signal intensity area on both sides in red nucleus, substantia nigra, basal ganglia and thalamus (B and C). Calcification in the midbrain was not visible on CT scan. T2-weighted image of MR showing slightly decreased signal intensity areas in basal ganglia and thalami bilaterally

Case 3

A 9-year-old girl was diagnosed as having a suprasellar tumour. The serum and CSF levels of human chorionic gonadotropin (HCG) and of alpha fetoprotein (AFP) were markedly elevated. The tumour consisted of fine calcification in an irregularly-shaped gadolinium-enhanced component on MR. Malignant mixed germ cell tumour was suspected, and chemotherapy with ifosphamide, cisplatinum, and etoposide was administered three times before CNS irradiation. The tumour markedly decreased in size, and both the serum and the CSF levels of HCG and AFP have decreased to below detectable levels. CNS irradiation was followed with a dosage of 3000 cGy to the whole brain, 2400 cGy to the spine, and 3000 cGy to the local area, in this order. After the irradiation, chemotherapy was again administered two times with the same regimen. At three years after the treatment, a CT scan showed a high density area in the basal

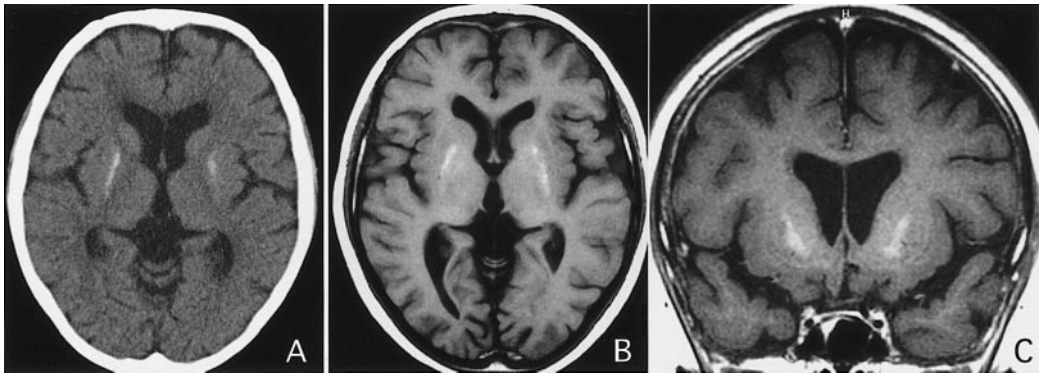

Fig. 3. Case 3. (A) CT scan showing calcification of basal ganglia bilaterally. T1-weighted images of MR also showing paradoxical high signal intensity area in both basal ganglia (B) axial section; (C) coronal section

ganglia, and MR showed a high signal intensity in the same area on T1-weighted images.

Discussion

The neurotoxic effects of radiation and chemotherapy have long been a major concern in the treatment of childhood CNS neoplasms [9, 11]. Calcification is known to be one of the most common radiological manifestations of radiation-related injury to the brain, since the first report of radiation-induced calcification in the basal ganglia by Harwood–Nash *et al.* [5, 12]. While calcification within the basal ganglia is unusual before 40 years of age, and is considered to be part of the normal aging process of the brain [2], after irradiation, mineralising micro-angiopathy is considered to play a pivotal role in the early development of calcification [3]. It has been reported that calcification by mineralising micro-angiopathy was present within the walls of precapillaries, venules, and smaller arteries such as the lenticulostriate artery. Early dystrophic calcification also developed in the perivascular brain tissue secondary to the leakage of plasma fluid from damaged vessels, and regional ischemia has resulted from the consequent impairment in microcirculation [10]. Such calcification has been easily detected on CT scans as marked high density areas. Recently, MR has become the standard technique for following up a patient with CNS neoplasms due to its high resolution. Areas of calcification commonly demonstrate a decreased signal on T1-weighted and T2-weighted images, due to a paucity of mobile protons [4, 5, 6, 8]. However, in our series, calcification demonstrated an increased signal on T1-weighted sequences. Boyko *et al.*, who performed histological examination on lesions which showed hyperattenuation on CT, and at the same time, a hyperintense signal on MR [1], demonstrated that these lesions all showed a strong positive stain for calcium and a focal weak positive stain by Perl's iron stain.

The paradoxically increased signal on T1-weighted images has been attributed to a surface-relaxation mechanism associated with particulate calcium, resulting in shortening of both T1 and T2 relaxation times. Dell *et al.* have reported that calcium salt shortened the T1-relaxation time of surrounding water [2]. Henkelman *et al.* have experimentally demonstrated that calcium hydroxy-apatite suspended in agarose gel had caused shortening in the T1-relaxation time under appropriate conditions [4], and considered that T1-shortening was directly related to the surface area of the calcium crystals in the gel. Only in those cases in whom the surface area of crystals was very large, were they able to demonstrate that the T1 effect predominated, yielding a net increase in MR signal intensity. Even then, they reported, as the calcium concentration rose above 30–40%, the decrease in proton density and reduced T2 negated the signal intensity increase from T1 shortening. The decreased proton density is believed to be the dominant factor. It is well known that liquids interact with solids at their interfaces. The presence of a solid particle in a liquid usually results in a layer, or layers, of the liquid adhering to the surface of the solid. In this configuration, the motion of the liquid molecules is restricted compared with the motion of free liquid molecules in the ambient solvent. The rotational and translational frequencies of the bound layer(s) of water are closer to the Larmor frequency, and therefore the water protons can relax more quickly than those remote from the crystal sur-

face. This hypothesis is essentially the same as has been accepted for the enhanced relativity induced by large proteins and other macromolecules. In this manner, brain calcification can cause high signal intensity on T1-weighted MR images.

All of our cases were girls with a suprasellar germinoma. Germinoma is usually seen in childhood, and radiation with or without chemotherapy has been the standard treatment. In this type of tumour, whole brain radiation is usually performed to prevent intracranial dissemination and boost irradiation will be added to the local brain. This may increase the possibility of micro-angiopathy in the fine arteries such as the lenticulostriate artery and the thalamoperforating arteries. Furthermore, long-term survival after CNS irradiation is a very important factor for the development of calcification. The survival rate of germ cell tumours is relatively high compared with other intracranial neoplasms which are treated with irradiation. The 20-year-survival rate for patients with pure germinoma has been reported to be 80.6% [7]. It is particularly important to recognize that lesions that are hyperintense on T1-weighted MR images and high density on CT are not necessarily areas of haemorrhage.

References

1. Boyko OB, Burger PC, Shelburne JD, Ingram P (1992) Non-heme mechanisms for T1 shortening: pathologic, CT, and MR elucidation. AJNR 13: 1439–1445
2. Dell LA, Brown MS, Orrison WW, Eckel CG, Matwiyoff NA (1988) Physiological intracranial calcification with hyperintensity on MR imaging: case report and experimental model. AJNR 9: 1145–1148
3. Flament-Durand J, Ketelbant-Balasse P, Maurus R, Regnier R, Spehl M (1975) Intracerebral calcifications appearing during the course of acute lymphocytic leukemia treated with methotrexate and x rays. Cancer 35: 319–325
4. Henkelman RM, Watts JF, Kucharczyk W (1991) High signal intensity in MR images of calcified brain tissue. Neueroradiology 179: 199–206
5. Harwood-Nash DCF, Reilly BJ (1969) Calcification of the basal ganglia following radiation therapy. Am J Roetgenol 105: 43–62
6. Holland BA, Kucharczyk W, Brant-Zawadzki M, Norman D, Hass DK, Harper PS (1985) MR imaging of calcified intracranial lesions. Radiology 157: 353–356
7. Matsutani M, Sano K, Takakura K, Fujimaki T, Nakamura O, Funata N, Seto T (1997) Primary intracranial germ cell tumors: a clinical analysis of 153 histologically verified cases. J Neurosurg 86: 446–455
8. Oot RF, New PFJ, Pile-Spellman J, Rosen BR, Shoukimas GM, Davis KR (1986) The detection of intracranial calcifications by MR. AJNR 7: 801–809
9. Pääkko E, Talvensaari K, Pythinen J, Lanning M (1994) Late cranial MRI after cranial irradiation in survivors of childhood cancer. Neuroradiology 36: 652–655
10. Shanley, DJ (1995) Mineralizing microangiopathy: CT and MRI. Neuroradiology 37: 331–333
11. Valk PE, Dillon WP (1991) Radiation injury of the brain. AJNR 156: 689–706
12. Yamashita J, Handa H, Munemitsu H, Nakano Y (1978) Bilateral basal ganglia calcification following radiation therapy for brain tumors. Neurol Med Chir (Tokyo) Part II, 18: 851–856

Comments

This triple case-report has illustrations of very good quality. Although the report in itself is not original, it reminds us about hitherto less well known MR-changes after irradiation, occurring in children, this is a less frequent phenomenon.

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