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Case Report

Rapid Progression of Early Delayed Radiation Effect in Pleomorphic Xanthoastrocytoma

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Early delayed radiation effects are known to occur within several months after completing radiotherapy for brain tumors. We present marked changes of magnetic resonance imaging (MRI) scan that occurred one month after radiotherapy in a patient with a pleomorphic xanthoastrocytoma, which was eventually diagnosed as an early delayed radiation effect. Such an early development of dramatic MRI change has not been reported in patients treated with radiotherapy for pleomorphic xanthoastrocytomas.

KEY WORDS : Blood brain barrier · Delayed radiation effect · Low grade glioma · Magnetic resonance imaging · Pleomorphic xanthoastrocytoma · Radiation therapy.

INTRODUCTION

When there are unanticipated changes in imaging studies obtained during the post-irradiation period in a patient with a low grade glioma, it is very important to discriminate between radiation-induced benign changes and tumor progression so as to choose an appropriate treatment modality[22]. The interpretation of early post-treatment images continues to be a clinically challenging problem, although diverse techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), 2-fluoro-2-D-deoxyglucose positron emission tomography (FDG-PET) and thallium-201 single-photon emission computerized tomography (TI-201 SPECT), have been used to evaluate these conditions[2,8,13,17]. The present case involved marked MRI changes only one month after radiotherapy in a patient with a pleomorphic xanthoastrocytoma, which was eventually diagnosed as secondary irradiation changes. To the best of our knowledge, such an early development of dramatic MRI changes has not been reported in patients treated with radiotherapy for pleomorphic xanthoastrocytomas.

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CASE REPORT

A 49-year-old man presented with headache and nausea for 2 weeks. He had a history of a pleomorphic xanthoastrocytoma, and had undergone stereotactic biopsy and completed radiotherapy, 54 Gy in divided doses, one month prior to admission. When the imaging studies and pathologic specimens of the patient were reviewed, the tumor was consistent with a pleomorphic xanthoastrocytoma (Fig. 1, 2). MRI obtained at the time of the second admission revealed a heterogeneously enhanced lesion with marked edema and a midline shift to the right side. TI-201 SPECT showed an area of increased uptake and the thallium index was increased relative to the time of the initial diagnosis (Fig. 3). A second biopsy was performed to differentiate between malignant transformation of the tumor and secondary radiation effects. It was targeted at three points : two points of the enhanced portion and the other was the center of the tumor. We have obtained four to six specimens from each point. Histological examination showed reactive gliosis with edema surrounding neuronal cells and did not reveal any malignant components in multiple specimens (Fig. 4). The patient was treated conservatively with steroids. The follow-up MRI was obtained after 3 weeks and it showed a significant decrease in both the enhanced lesion and edema (Fig. 5). The patient recovered without any neurologic deficits and was discharged.

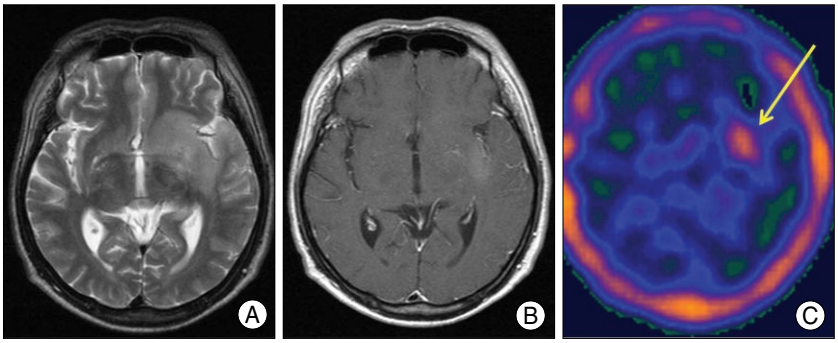

Fig. 1. T2-weighted (A) and enhanced T1-weighted (B) magnetic resonance image scans show a tumor in the left insular cortex without surrounding edema or a mass effect. The Tl-201 scan (C) demonstrates elevated uptake in the tumor (arrow). The tumor's activity ratio divided by the contralateral normal area's activity (the thallium-index) was 1.7.

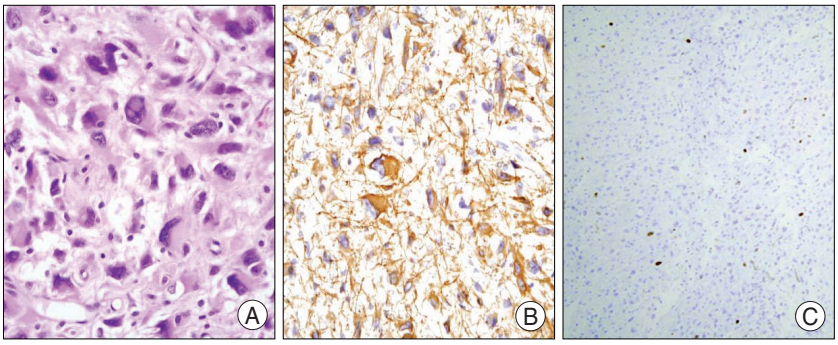

Fig. 2. A : Photomicrograph of the tumor showing marked nuclear and cytoplasmic pleomorphism with xanthomatous change. Some cells exhibit a large intranuclear cytoplasmic inclusion, but endothelial proliferation, mitoses and necrosis are absent (hematoxylin and eosin; original magnification, ×200). B : Immunostaining for glial fibrillary acidic protein (GFAP). Many neoplastic cells are positive for GFAP (GFAP; original magnification, ×200). C : Approximately 1% of tumor cells are positive for Ki-67 (Ki-67; original magnification, ×100).

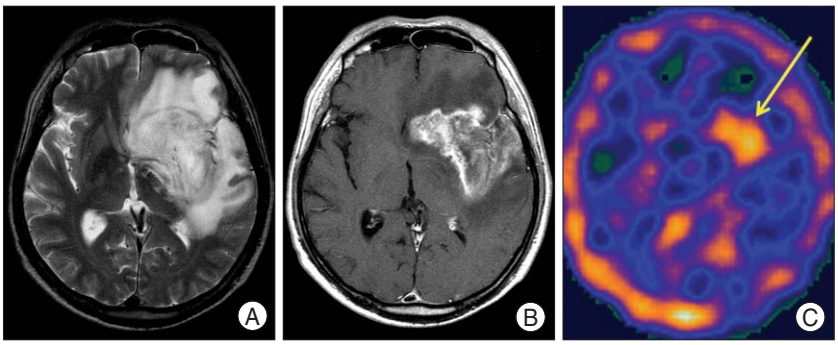

Fig. 3. A and B : Markedly increased hyperintensities around the tumor in the T2-weighted magnetic resonance image (MRI) scan and the contrast enhancement of the T1-weighted MRI scans appear one month after the end of radiotherapy. C : The area of thallium uptake (arrow) is shown and the thallium-index is slightly increased (thallium-index was 2.1).

DISCUSSION

Radiation-induced changes have been divided into three different types on the basis of the time of occurrence : acute (during radiation), early delayed (up to months postradiation), and late (several months to years postradiation)[3]. It is particularly difficult to distinguish between the early delayed reaction of irradiation and tumor progression as the clinical signs and symptoms are not specific to detect the difference. Similarly, CT and MRI give only minimal information[7,13,22]. This lack of specificity has prompted investigation into diverse imaging techniques such as PET scans and TI-201 SPECT, however, the efficacy and usefulness of these studies have questioned because of their high false positivity[11,14,17].

The thallium index was slightly increased at the time of MRI changes compared with that of pre-radiation state in our case although no evidence of tumor progression or malignant change were not detected in multiple biopsy specimens. The mechanism of the discordance between histological characteristics and scintigraphic findings has been proposed that the reactive astrocytes and lymphocytes, induced by radiation, can cause accumulation of thallium-201 due to the Na^+/K^+ adenosine triphosphatase on their cell membrane[9,24]. In addition, regional blood flow in the area of blood brain barrier (BBB) impairment may play some role in uptake of TI-201[19]. To date, therefore, it is not recommended that only one imaging modality be used as the sole indicator for additional treatment.

Clinical symptom and signs of early delayed radiation effect include headache, nausea, vomiting, somnolence, fatigue and lethargy[5,20]. Because these symptom and signs resolve spontaneously with only conservative management within a few weeks, it is important to suspect the early delayed reaction to irradiation[13,23]. Failure to recognize this may lead to administering adjuvant treatments such as chemotherapy, further irradiation, or recraniotomy that can aggravate the symptoms and cause neurological deficits. On the imaging study, the radiation effect in the early delayed period is also reversible and this may or may not be enhanced with contrast administration[2,23]. Watne et al.[23] reported on six patients with early delayed effects of radiation. They observed that the CT scan changes were seen at 4 to 8

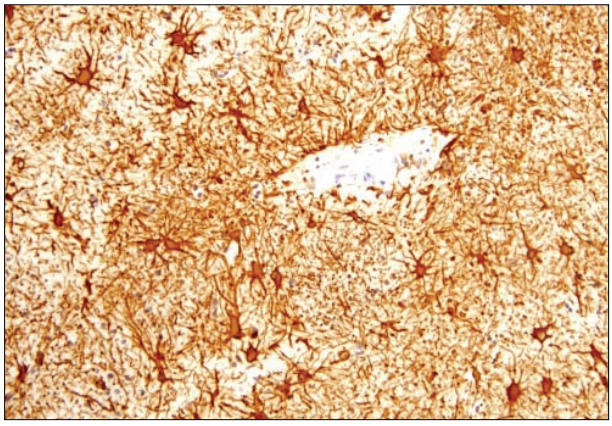

Fig. 4. Photomicrograph obtained at the second biopsy. Reactive gliosis demonstrating the abundance of glial intermediate filament is shown (GFAP; original magnification, x 200).

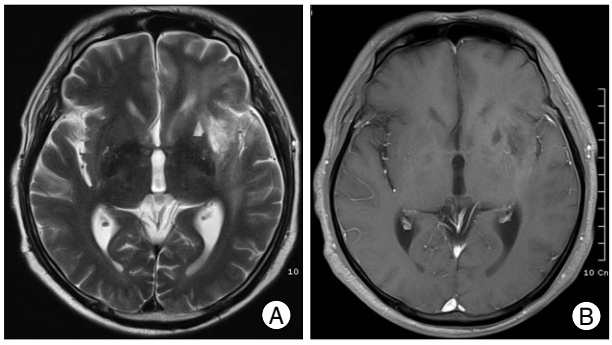

Fig. 5. Abnormal hyperintensities on the T2-weighted magnetic resonance image (MRI) scan (A) and the enhancement on the post-contrast T1-weighted MRI scan (B) have disappeared three weeks after conservative management. Multiple biopsy sites are also seen.

months after irradiation, followed by regression about 3 months later. They found that early delayed effects consisted of pronounced peritumoral edema without any contrast enhancement. Two cases involving patients with low-grade astrocytomas were presented in another report in which the patients exhibited peritumoral contrast enhancement without edema on MRI about 3 months after irradiation[2]. In the present case, the MRI changes involving both edema and contrast enhancement occurred only one month after irradiation. This is unique since the early delayed effects reported previously were observed at least three months after completing radiotherapy[2,23]. In addition, there was a possibility that initial diagnosis determined after initial biopsy was incorrect, for example, undergrading of high grade tumor, since such an early progression of low grade tumor is unusual, and these made us perform the second biopsy for differential diagnosis. In fact, the diagnostic error of stereotactic biopsy has been reported in 3-49% of cases[2,6,10,12,15,23].

One recent study documented that there was no evidence of hyperintensities on MRI, as might be expected from the radiation therapy during the months after its completion[1]. That study demonstrated that other non-radiation factors, such as surgical effects and malignant tumor progression, should be more strongly considered when white matter changes occur in the tumor environment during the early delayed period after radiation therapy. However, that report was limited to an analysis of the signal intensities of the white matter and there was no analysis of the enhancement patterns. Therefore, it is difficult to completely rule out the possibility that secondary irradiation changes actually occurred during the early period after radiation when new or increased contrast enhancement combined with increased hyperintensities are observed on T2-weighted MRI scans.

The exact mechanisms underlying early delayed changes after radiotherapy in brain tumors remain unclear. The pathology suggest that the primary locus of radiation injury is either the vascular endothelial cells, with resultant effects on the integrity of the BBB[19], or the oligodendrocytes with resultant axonal demyelination[16]. Impairment of the BBB leads to contrast enhancement[18], and demyelination causes an increase in the tissue water content, which develops increased intensity on the T2-weighted and proton-density images[22]. Both the turnover of myelin and sufficient endothelial cell replacement after initial radiation injury may confine their effects to a transient period, but the true mechanism regarding reversibility and the time difference of onset between the cases has not been clearly established.

The extent of radiation injury has been shown to depend not only on the delivered doses but also on the variation in individual cellular radiosensitivity, largely determined by genetic factors[4,21]. Thus, considering the dose delivered to the patient was in the therapeutic ranges, a factor such as low tolerance of brain tissue to radiation was thought to have a role in this rather early and intensive radiation injury.

CONCLUSION

An early delayed radiation effect widely known to arise within several months of completing radiotherapy can occur as early as one month after irradiation. Even though the changes shown by imaging studies parallel the malignant transformation in the patients with low-grade tumors during the early period after irradiation, it is reasonable to regard this phenomenon as early delayed radiation effects and to manage these patients conservatively during a brief period before considering a new surgical procedure or chemotherapeutic drugs.

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