Radiation-induced telangiectasia after cranial irradiation: evaluation by susceptibility weighted imaging with 3.0 tesla MR

Poster No.: C-0753
Congress: ECR 2012
Type: Scientific Exhibit
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Keywords: Neuroradiology brain, MR, Radiation therapy / Oncology, Haemorrhage
DOI: 10.1594/ecr2012/C-0753

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Purpose

Radiation therapy is one of the efficacious treatments for brain neoplasm. However cranial irradiation can cause complications, not only benefits. Complications of cranial irradiation are known such as necrosis, diffuse white matter injury, central nervous system (CNS) atrophy, mineralizing, microangiopathy, telangiectasia, optic neuropathy, large vessel vasculopathy [1]. Although clinically important complications are infrequent with modern radiation therapy techniques, we often encounter asymptomatic complications following radiation therapy such as diffuse white matter injury, CNS atrophy, mineralizing microangiopathy, telangiectasia at follow-up MR imaging and CT. Histopathologically radiation-induced telangiectasia in the brain is the results of varying amounts of hemorrhage and parenchymal hematomas [2]. Although there are many reports in the past, the frequency, dose relation, and latency of radiation-induced telangiectasia remain still unclear.

MR imaging is useful for the diagnosis and evaluation of these cerebral complications following radiation therapy [3]. MR imaging is currently considered to be the best imaging technique for evaluation of cerebral injury following radiation therapy [4].

Susceptibility-weighted imaging (SWI) is a three-dimensional gradient echo MR imaging technique using the blood oxygen level dependent (BOLD) effect [5]. SWI is very sensitive to differences of the magnetic susceptibility properties between tissues, such as blood products including deoxyhemoglobin, methemoglobin and hemosiderin. T2*-weighted image is also considered high sensitive MR technique in the visualization of cerebral hemorrhage. However SWI is currently considered to be more sensitive than the other conventional MR imagings including T2*-weighted imaging in detecting hemorrhage [6,7].

Purpose of this study is to evaluate the frequency, latency, patient factor, dose relation and patient factor of radiation-induced telangiectasia after cranial irradiation using SWI at 3.0 tesla MR.
Methods and Materials

Patients

We retrospectively reviewed the MR imaging and clinical records of 34 patients (18 males, 16 females, aged 13-78 years, mean 48 years) who had undergone brain irradiation and undergone MR imaging including SWI with follow-up for at least 3 months. The average follow-up period was 29 months (3-169 months). We divided patients into two groups: low dose (LD) and high dose (HD) groups.

Eleven patients in the LD group received 24-30Gy of whole brain irradiation. Eight patients of this group had been diagnosed brain metastasis, one had been diagnosed germinoma by biopsy, and two had received prophylactic cranial irradiation (PCI) for lung small cell carcinoma. Twenty-three patients in the HD group received 44-60Gy of localized irradiation. All HD group patients had undergone surgical resection or biopsy and were proven their pathological diagnosis. The diagnoses included 17 high grade gliomas, 2 central neurocytomas, 1 medulloblastoma, 1 meningioma, 1 germinoma, 1 occult primary cancer. We also divided 34 patients by factors such as gender (male vs. female), age (over 60 vs. less than 60), hypertension (with vs. without), chemotherapy (underwent vs. did not undergo). Patient characteristics are summarized in Table1. The age means patient's age at the beginning of the irradiation. The patients who had received medication for hypertension were classified as hypertension group.

Brain Radiation Therapy

LD group patients were treated with total doses between 24-30 Gy, at 2.0-3.0 Gy dose per fraction. The treatment duration was 2-2.4 weeks. HD group patients were treated with total doses between 44-60 Gy, at 1.8-2.0 Gy dose per fraction. The treatment duration was 4.4-6 weeks. We used 6MV-Xray in all patients.

MR imaging

At three or more months after completion of radiotherapy, all patients underwent MR imaging including SWI. All brain MR imaging was obtained with a 3.0 tesla MR system (Signa EXCITE HD, General Electric, Milwaukee, WI, USA) using an 8-channel phased-array coil (USA Instruments, Aurora, OH, USA). We acquired SWI using a 3D-spoiled gradient recalled acquisition in the steady state (SPGR) sequence with flow compensation using the following imaging parameters: TR/TE, 45/30 msec; FA, 20°; FOV, 21 cm; matrix, 512 ‘ 192; section thickness, 1.5 mm, acquisition time, 7 min 40-50 sec. All images were obtained in the axial plane. We post-processed the SWI using a high-pass filter and then converted the images into negative phase masks that were multiplied four times into the corresponding magnitude images using research
software (PSIRecon: GE Yokogawa Medical Systems, Tokyo, Japan). A minimum
intensity projection was used to display the processed data using contiguous 10.5-mm-

thick sections with 7 mm overlap in the transverse plane (Advantage workstation ver. 4.1,
General Electric, Milwaukee, WI, USA). Follow-up interval of MR imaging was dependent
on clinical course, and serial MR images were obtained in 21 patients.

Image Evaluation

The presence of telangiectasia was determined if small focus of very low-signal-intensity
area was recognized on SWI. The presence of telangiectasia on SWI was evaluated by
two neuroradiologists. We excluded the areas of surgical intervention and mineralizing by
reviewing surgical records and subsequent CT. We also excluded regions of metastasis
or residual tumor by the combined inspection of T1WI and contrast enhanced-T1WI.
The final decision regarding the presence of telangiectasia on MR imaging was made
by means of mutual consent between the two neuroradiologists. The number of these
telangiectasias was counted. In HD group, irradiation dose of each region was evaluated
by two radiation oncologists using dose distribution map.

Statistical Analyses

For comparison between the LD and HD groups, between the patients with and those
without telangiectasia, we used the Fisher exact test. We also used the Fisher exact
test for comparisons between the groups which were divided by several factors such
as gender, age, hypertension, and chemotherapy. P<0.5 was considered to indicate
statistical significance.
### Table 1: Patient characteristics

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**Results**

Sixteen (47%) of the 34 patients developed telangiectatic lesions. A typical case of telangiectasia is shown in Figures 1 and 2. Five patients had one focus; other 11 patients had two or more foci. There were 45 foci in 15 patients except one patient who had too many foci to count. None of telangiectatic foci disappeared in observation period.

In this study the latency period for radiation-induced telangiectasia is 3 months to 9 years. Telangiectasia was observed in 6 patients (17%) within one year. The mean and median latency period that telangiectasia was observed for the first time is 33 months and 19 months, respectively.

Four (36%) of the 11 patients in the LD group developed telangiectasia, whereas twelve (52%) of the 23 patients in HD group developed telangiectasia; this difference was not statistically significant. (p=.47, Fisher exact test). We observed 38 foci in HD group except one patient who had too many foci to count and evaluated the dose value of each region of telangiectasia. Twenty-six foci were observed in over 40 Gy dose regions. There were no foci that were observed in less than 20Gy irradiation area. Result of dose value for telangiectasia is summarized in Table 2.

There was no statistically significant difference in the frequency of telangiectasia between the groups which were divided by gender (p=.74), age (p=.29), hypertension (p=1), chemotherapy (p=.60). Results of comparison of each group are summarized in Table 3.

**Discussion**

Radiation-induced alterations of vasculature are important for the development of CNS alterations. The pathologic findings of radiation-induced vascular alteration consist of endothelial proliferation, fibrinoid necrosis, vascular ectasia [8-10]. These alterations lead inflammatory perivascular infiltration, low grade hemorrhage, dystrophic calcifications, malformation-aggregates of dilated blood vessels, and telangiectasia [11]. Gaensler reported that histopathologically radiation-induced telangiectasia in the brain is the results of varying amounts of hemorrhage and parenchymal hematomas [2]. Radiation-induced vascular alterations occasionally induce intracerebral hemorrhage as delayed complication [12-13]. Therefore, radiation-induced vascular alterations represented by telangiectasia must be evaluated to know the severity of brain injury.

The frequency of radiation-induced telangiectasia is about 20% in the past reports [14]. The frequency in this study was higher than that of the previous reports despite of short follow-up period. As SWI was obtained only once in several patients in LD group, there is a possibility that we observed previously existing microbleeding. However, even though we consider such possibility, the frequency is still higher than that of the previous reports. This is because SWI is high sensitive MR technique in the visualization of cerebral
hemorrhage. SWI is currently considered to be more sensitive than the other conventional MR imagings in detecting hemorrhage [6]. In many previous reports telangiectasias were detected in mainly T2WI. Therefore, so many foci might have been over looked. We can easily suspect that radiation-induced telangiectasia occurs more frequently than in previously known.

The latency period of radiation-induced telangiectasia is reported in several literatures. The range is wide between 5 months to 22 years [1]. In this study the latency period is 3 months to 9 years. Telangiectasia was observed in 6 patients (17%) within one year. The mean latency period that telangiectasia was observed for the first time is 33 months. The latency period in this study is almost similar to previous reports, but in this study telangiectasia appears relatively in early time. It may be related to the high sensitivity of SWI. SWI may be able to reveal the telangiectasia that cannot be detected on the other MR techniques. SWI is considered to be useful technique for evaluation of hemorrhage at radiation injury regions [15].

In general, the complications of radiation therapy to the brain relate to the total dose, patient age, underlying disease and concomitant therapy [3]. In this study there was no statistically significant difference between LD and HD groups. However, there was a trend that telangiectasia appeared in the high dose region. In the previous report, there was same trend that higher radiation dose was associated with higher frequency of telangiectasia [14]. Dose escalation could be the risk factor for development of telangiectasia. Research of large number of patient is desired. On the other hand, there were no foci that were observed in less than 20 Gy radiation region. The radiation dose threshold for development of telangiectasia is not clear. In the previous reports, telangiectasias have developed in patients who received radiation doses ranging from 18Gy to 78Gy [2,16]. To our knowledge, there is no report of radiation-induced telangiectasia with a dose lower than 18Gy. In a low radiation dose, telangiectasia may be less likely to develop.

The other factors such as gender, age, hypertension and chemotherapy seem to be unrelated to appearance of telangiectasia. However, it is known that the immature brain is more sensitive to radiation than the adult brain [17]. Koike et al reported that radiation-induced telangiectasia occurs more frequent in younger patient [14]. In this study there were only three patients whose age was under 20. If there are more pediatric patients, significant difference might have been seen.

There are several limitations in this study. First, this study lacks of histopathologic confirmation in all cases. Second, SWI before irradiation is not available. However, we tried to exclude mineralizing and microbleeding before irradiation comparing previous MR imaging and subsequent CT. Lastly, this study includes small number of patients and short follow-up period.
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Table 1: Patient characteristics

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Fig. 1: Figure 1. a 31-year-old man with surgical resection for high-grade glioma in the left parietal lobe, followed by localized irradiation to a dose of 60 Gy (case 4). A. SWI obtained 17 months after completion of radiation therapy. B. SWI obtained 33 months after completion of radiation therapy. Hypointense focus that cannot be detected in image A appears in the left parietal white matter image B (arrow).

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Fig. 2: A 53-year-old-man with surgical resection for high-grade glioma in left frontal lobe, followed by localized irradiation to a dose of 60 Gy (case 7). A, B. SWIs obtained 169 months after completion of radiation therapy. Many hypointense foci can be detected mainly in the cerebral white matter.

Table 2: Dose value of each telangiectasia in HD group. (One patient who had too many foci to count, is excluded)

Table 3: Results of comparison between groups divided by several factors
Conclusion

Radiation-induced telangiectasia occurs more frequently than previously suspected. SWI is useful for the evaluation including early detection of radiation-induced telangiectasia. In this research, although there was no significant difference, dose escalation could be a risk factor of telangiectasia.
References


