MRI of Carotid Angiopathy after Therapeutic Radiation

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Objective: Our goal was to assess whether significant secondary atherosclerotic changes from radiation can be detected on SE MR of the neck.

Materials and Methods: Pre- and postradiation MR scans of 16 patients with head and neck malignancies were studied randomly, independently, and blindly by two readers to determine the frequency of narrowing of the carotid arterial lumen and obliteration of the carotid space within the carotid sheath.

Results: Interval narrowing of either the common, internal, or external carotid artery lumen was seen in 108 of 192 (56%) of vessels evaluated on post-radiation MR scans compared with preradiation studies. The differences in the grades of vessel luminal diameter were statistically significant (p < 0.05 for one reader and p < 0.0001 for the other reader). Among the 16 patients, 3 patients had vessels with a critical degree of stenosis, newly appearing on postradiation scans. Seven of 16 patients had diffuse obliteration of the planes within the carotid space.

Conclusion: The incidence of accelerated atherosclerosis from therapeutic radiation may be greater than expected in nonirradiated patients. Magnetic resonance scans are an effective, noninvasive method for this type of follow-up.


Instances of radiation-related narrowing of the cervical portion of the internal carotid arteries are infrequently reported in the imaging literature. In the experimental literature, however, histopathological changes in irradiated vessels are well described (1-4). Nonetheless, there are relatively few case reports that link strokes or transient ischemic cerebrovascular episodes to prior radiation of the head and neck (5-14). These few cases use clinical information and angiography as the proof to suggest that radiation induces accelerated atherosclerosis in the cervical carotid branches.

Successful radiation therapy for head and neck cancers has increased the survival time of afflicted patients, but also puts them at risk for radiation-induced carotid atherosclerosis (13). The incidence and severity of radiation change in the carotid vessels of this population have been difficult to assess, in part because of the risks and invasiveness of carotid angiography used to evaluate the arteries.

Magnetic resonance imaging has the advantage of noninvasively evaluating the carotid vessels for atherosclerotic vascular disease. The absence of signal from the vascular lumen on SE MR allows excellent contrast between the "black blood" and lesions involving the vascular wall (15-17). Moreover, on T1-weighted scans, the fat in the neck has high signal intensity and allows easy evaluation of the vessel wall (15,18-21). Most studies of carotid vessels using MR angiography have relied upon distortion of the arterial lumen and have not tried to visualize directly the atheroma or plaque in the wall (22,23).

The aim of this study was to assess whether significant arterial narrowing and secondary atherosclerotic changes occur after radiation therapy as determined by MR findings. We compared pre- and postradiation SE MR scans of the carotid walls and lumina to gauge atherosclerotic changes without resorting to angiography.
MATERIALS AND METHODS

The pre- and postradiation MR scans of 16 consecutive patients who underwent radiation therapy for head and neck cancers were retrospectively reviewed. The postradiation MR scans were performed at least 6 months after the last radiation treatment, with the longest follow-up interval being 30 months and the median interval 17.5 months. The posttreatment scans in these 16 patients were performed to serve as a baseline for future surveillance. None of these patients had suspected residual or recurrent tumor around the carotid vessels. Postradiation MR scans obtained <6 months after radiotherapy were excluded.

Because 1 of the 16 patients had an incomplete record, dosages were available for 15 patients and 90 vessels (Table 1). The highest doses to the carotid arteries varied from 40 to 74 Gy, with a mean of 63 Gy, median of 64 Gy, and modal dose of 60 Gy. The 15 patients were all treated with a technique involving opposed lateral fields, with the dose prescribed to midline at the isocenter, with or without a supraclavicular field matched on. The supraclavicular field was either an anterior-only field prescribed to a depth of 3 cm or opposed anterior and posterior fields prescribed to midline. All supraclavicular fields were matched to the divergence of the lateral fields at the midline anteriorly to avoid overlap; however, there was some minimal divergence of the anterior-only supraclavicular field superiorly into the lateral fields. The anteroposterior supraclavicular fields were half beam blocked to avoid any divergence into the lateral fields. Spinal cord blocks were added to the photon fields at doses between 40 and 46 Gy, and the posterior necks were boosted with en face electrons.

After the carotid arteries were graded for degree of stenosis, the radiation portal films were reviewed to determine the approximate dosage to the distal common, proximal internal, and proximal external carotid arteries. The neuroradiologist drew in the carotid bifurcation on the radiation therapy portal films based on anatomic landmarks from posttreatment MR scans. The radiation oncologist was then able to calculate precise dosages for each vessel studied. The carotid arteries received varying doses along their lengths due to the employment of multiple coned-down fields to focus the highest doses only on areas of residual or resected disease. In all cases, however, at least a small segment of carotid artery received the highest dose given.

All of the MR studies were retrospectively reviewed independently and blindly by two senior neuroradiologists. The 32 studies were presented in random order with no clinical or radiation history provided.

Conventional SE images employed a TR of 700–800 ms, TEs of 11–20 ms, one to two excitations, and FOV of 20–24 cm. The image matrix used was 192 × 256. Interslice gaps were not routinely used and the slice thickness was 5 mm. Contiguous MR sections included the common, internal, and external carotid arteries. The T1-weighted axial images of the head and neck MR were used predominantly for defining arterial stenosis, the relationship between the arterial system and primary tumor, and obliteration of the carotid space presumed to be due to postradiation fibrosis of arterial adventitia.

All scans were performed on a 1.5 T Signa scanner (General Electric Medical Systems, Milwaukee, WI, U.S.A.) typically employing a Medical Advances anteroposterior volume neck surface coil.

The arterial lumina of both common, internal, and external carotid arteries (total 96 arteries in 16 patients × 2 readers) were evaluated based on a six point grading system (Table 2). After review of all of the films, we compared the postradiation luminal narrowing with preradiation vascular lumina and classified the arteries into those with narrowing of luminal diameter, no change in luminal diameter, and luminal enlargement (Table 3). A comparison of the pre- and postradiation luminal diameters defined by our grading system was analyzed statistically using the Student t test of independent pairs of data with two tails and 98 df for each reviewer.

The patients’ records were reviewed in an effort to analyze additional confounding factors leading to stenosis of arteries in the head and neck, such as smoking, alcohol consumption, serum cholesterol, hypertension, combined chemotherapy, previous surgery, and radiation fields and dosage. The relationship between the proximity of primary tumors to vessels, malignant invasion, and postradiation stenosis of arteries was also scrutinized. Charts were also analyzed to determine whether the patients had neurologic symptoms referable to carotid artery ischemic disease.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Degree of stenosis</th>
<th>% stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No stenosis</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>Mild</td>
<td>1–39</td>
</tr>
<tr>
<td>2</td>
<td>Moderate</td>
<td>40–59</td>
</tr>
<tr>
<td>3</td>
<td>Severe</td>
<td>60–79</td>
</tr>
<tr>
<td>4</td>
<td>Critical</td>
<td>80–99</td>
</tr>
<tr>
<td>5</td>
<td>Occluded</td>
<td>100</td>
</tr>
</tbody>
</table>

**TABLE 1. Radiation dosage to vessels in neck**

<table>
<thead>
<tr>
<th>Dosage (Gy)</th>
<th>No. of vessels receiving dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;70</td>
<td>18</td>
</tr>
<tr>
<td>65–69.99</td>
<td>9</td>
</tr>
<tr>
<td>60–64.99</td>
<td>45</td>
</tr>
<tr>
<td>50–59.99</td>
<td>8</td>
</tr>
<tr>
<td>&lt;50</td>
<td>10</td>
</tr>
</tbody>
</table>

**TABLE 2. Grading scale for carotid arterial stenosis**

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TABLE 3. Changes of stenosis between pre- and postradiation in 16 patients (96 arteries x 2 reviewers)

<table>
<thead>
<tr>
<th>Grades on preradiation therapy</th>
<th>Grades on postradiation therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

The decrease in the vessel’s luminal diameter is statistically significant by Student t test (p < 0.05 reader 1, p < 0.001 reader 2).

RESULTS

Postradiation MR scans of 12 (reader 1) and 16 (reader 2) of the 16 patients showed narrowing of either the common, internal, or external carotid arteries compared with the preradiation MR study. There were no significant stenotic changes in two patients and apparent enlargement of lumina in two patients according to reader 1. Looking at internal carotid arteries alone, 57% (reader 1) and 59% (reader 2) showed increased narrowing on the postradiation scan and 81% of patients had worsening in one or the other internal carotid artery.

Among the 192 (96 x 2 readers) individual carotid (right and left common, external, and internal carotid) arteries evaluated in the 16 patients, 108 arteries (56%) showed a higher grade of stenotic changes (51/96 by reader 1 and 57/96 by reader 2). Sixty-one (32%) arteries showed no significant change in luminal diameter (25/96 by reader 1 and 36/96 by reader 2), and 23 (12%) arteries appeared to have a wider postradiation lumen (20/96 by reader 1 and 3/96 by reader 2). The mean increase in grade (worsening stenosis) was 1.42. Forty cases changed by two or more grades. Among these five cases, three patients showed a new critical degree of stenosis (80-99%) on the postradiation scan (Fig. 1). The Student t test of all arteries of the blinded study also suggested a significant increase in the degree of carotid stenosis on the postradiation scan (p < 0.05 for reader 1 and p < 0.0001 for reader 2). Nineteen of the 23 arteries called more open (lower grade) by the two readers differed by only one grade (Table 3). Reevaluation of these 23 instances, in an unblinded consensus reading of pre- and postradiation MR scans, showed no significant changes in 20 of the 23 arteries called more open on the blinded reading.

When the changes in stenoses were evaluated by radiation dosage, it was found that 46% of patients receiving ≥70 Gy, 56% of patients receiving 65–69.99 Gy, 59% of patients receiving 60–64.99 Gy, 31% of patients receiving 50–59.99 Gy, and 55% of patients receiving <50 Gy had a worsening of their carotid stenoses. Comparing the higher dose ranges (≥65 Gy) with the lower dose range (<60 Gy) showed an insignificant (49% vs. 44%) difference in the chance of stenoses getting worse. One patient had different dosages applied to the carotid vessels on the right side (66.74, 62.28, 62.28 Gy to the common, internal, and external carotid artery) compared with the left side (60 Gy to all vessels) because of electron beams applied. This individual had two readings of no change, three readings of one grade worse, and one reading of two grades worse on the low dose side (mean score of 0.833). On the high dose side, there were three readings of two grades worse, two readings of one grade worse, and one reading of no change (mean score of 1.33). In this single example of intraindividual variation, the higher dose applied correlated with worsening stenoses ipsilaterally.

Although nine patients showed a critical degree of stenosis in the internal carotid arteries (one unilateral and eight bilateral), no patients had neuro-
logical problems documented in their medical records during the follow-up period of our study. There were no brain MR angiograms performed, so we could not evaluate the status of the intracranial vessels to assess for collateral circulation in these patients.

The T1-weighted axial images of the head and neck were subjectively felt to be the most useful sequences to evaluate the common, internal, and external carotid arteries for thickening of the vessel wall in all 16 cases.

Among the 16 patients, 7 (11/32 carotid spaces) showed diffuse obliteration of the carotid space with thickening of the vessel wall on the postradiation scan (Fig. 2). Evaluation of MR scans from 10 control patients with atherosclerosis who had no history of the radiation therapy did not reveal obliteration of the carotid space.

Complete information about additional risk factors in the test patients was not available. However, we found that all of the patients except one had a history of smoking and heavy alcohol intake, so it was impossible to control for these factors. Clinical data in the 16 patients were insufficient to examine the effects of hypertension, diabetes, and serum cholesterol. Two patients who had their primary tumor plastered to the carotid arteries showed two grades higher narrowing of vessel lumina on postradiation MR scans.

In a study of interobserver agreement, it was found that the reviewers agreed on the direction of change in grade of stenoses in 73% of cases.

**DISCUSSION**

Acute endothelial changes of postradiation angiopathy are nonspecific and similar to those produced by perfusion of sclerogenic solutions. The media shows decreased muscularcellularity beginning only a few weeks following radiation. Later the media develops fibrosis (4). Pathologically stenotic changes of vessels are mainly related to this late fibrosis of the vessel wall rather than to acute changes. The adventitia of the irradiated vessels also shows the same pattern of pathological changes (7). Radiation can also induce premature atherosclerosis by degeneration and fragmentation of the internal elastic membrane followed by regeneration and formation of one or more new layers of elastic material (1). The breakdown of elastic lamina of the arteries parallels the development of arteriosclerosis. Radiation also inhibits capillary sprouting and vascular remodeling. Therefore, the small vessels such as the vasa vasorum are more susceptible vessels to irradiation damage (4). Occlusion of the vasa vasorum may also be important in the late development of fibrotic and degenerative changes in irradiated vessels (11,14).

Radiation angiopathy is thought to be both time and dose dependent, so one would expect that the larger the dose, the greater the effect; the longer the time after exposure, the more severe the lesion (3). Injury of large vessels can be produced by doses over 5 Gy and consists of endothelial swelling, elastic fiber degeneration, and vacuolar degeneration of muscle fibers (1). Radiotherapy of head and neck malignancies generally requires doses of >50 Gy; therefore, many patients who have received radiotherapy have a chance of developing radiation angiopathy. Since all 16 of our patients received >40 Gy of radiation in our studies, we did not find a relationship between dosage and luminal narrowing. Anecdotally we had one patient with a difference in doses applied to the right and left carotid arteries. This one case demonstrated a greater degree of narrowing on the higher dose side.

The latency between irradiation and subsequent neurological symptoms has been studied in one report with ranges from 6 months to >30 years (11). With time, luminal narrowing increases, but separating the effects of normal aging from radiation ef-

**FIG. 2.** A 53-year-old man with right supraglottic carcinoma. a: Bulky low intensity mass lesion is demonstrated at right supraglottic area with near obstruction of the supraglottic air column on axial T1-weighted MR scan (800/20). Both walls of the carotid arteries (arrows) and the carotid space are well identified without thickening or obliteration. b: Six months after radiation (54 Gy) and total laryngectomy, there is diffuse thickening of both walls of the carotid arteries with luminal narrowing (arrows).
MR of Carotid Angiopathy Post-XRT

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