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Case Report

Atheromatous plaque formation in a man with high-risk atherosclerosis after Gamma Knife stereotactic radiosurgery for trigeminal neuralgia

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ABSTRACT

We report a rare case of atheromatous plaque formation in the offending parent artery of a 39-year-old man 11 months after Gamma Knife stereotactic radiosurgery (GKSR) for trigeminal neuralgia (TN). Focal atheromatous changes to the parent vessel remote from the root entry zone (REZ) of the trigeminal nerve were discovered during rescue open surgery; this has seldom been reported. Our report suggests that younger male TN patients with hyperlipidemia who receive GKSR may have an increased risk of post-radiation atheromatous formation. A review of the literature is carried out together with a discussion of the possible mechanism by which this complication occurred.

1. Introduction

Gamma Knife stereotactic radiosurgery (GKSR) is regarded as the least invasive technique for the treatment of trigeminal neuralgia (TN). In the treatment of recurrent or residual TN after failed repeated GKSR, microvascular decompression (MVD) can be performed. However, some gross changes that are produced by radiation may be discovered during such open surgery; these can include trigeminal nerve atrophy, thickening of the arachnoid, adhesions between blood vessels and the trigeminal nerve, and even focal atheromatous changes in vessel segments adjacent to the trigeminal nerve. To our knowledge, this is the fourth patient worldwide to be reported to have such focal atheromatous changes.

2. Case Report

A 39-year-old man had developed typical trigeminal neuralgia on the left side of his face at the maxillary division for 6 months and was placed on carbamazepine; however, there were some intolerable adverse effects. He had suffered from hypertension for 3 years without regular medication control. A physical examination revealed his body weight was 107 kg and body height was 177 cm. His laboratory tests showed high-density lipoprotein cholesterol (HDL-C) 24 mg/dL, low-density lipoprotein cholesterol (LDL-C) 169 mg/dL, total cholesterol (CHO) 256 mg/dL, and triglycerides (TG) 278 mg/dL. His plasma glucose after overnight fasting was normal. Enhanced magnetic resonance angiography showed an ectatic and tortuous vertebrobasilar artery in the left cerebellopontine angle close to the trigeminal nerve (Fig. 1). After discussing the relative risks and benefits of MVD and GKSR, the patient chose radiosurgery.

2.1. GKSR and its efficacy

The patient underwent Gamma Knife (Elekta, Stockholm, Sweden) radiosurgery 6 months after there had been a failure of effective pain control by medication. A single 4-mm isocenter of radiation was used to target the root entry zone (REZ) of the trigeminal nerve (Fig. 2). The maximum radiation dose was 80 Gray (Gy). The patient tolerated the procedure without difficulty and was discharged from the hospital the following day. After radiosurgery, the patient found there had been some relief of his facial

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Fig. 1. Magnetic resonance angiography showing an ectatic and tortuous vertebrobasilar artery in the left cerebello-pontine angle.

pain, but he continued to require high doses of carbamazepine. One week prior to this admission, he began to have more frequent attacks of severe pain at levels that he had never experienced before. The patient chose MVD as a final remedy 11 months after the radiosurgery.

2.2. MVD and the findings during the operation

A routine retrosigmoid craniectomy and MVD was performed on the left side. There was no thickening or adherence of the arachnoid overlying the vessels and the trigeminal nerve. Sharp dissection of the arachnoid to free the underlying structures and coagulation and division of one of the tributaries of the superior petrosal vein were performed. The offending artery was noted to be one of the branches of the anterior inferior cerebellar artery (AICA) and had been pushed by the tortuous vertebral artery against the REZ of the trigeminal nerve. It was also noted that, at the bifurcation of the AICA remote from the REZ and adjacent to the nerve, there was an abnormal circular yellowish discoloration surrounding the vessel wall, which was consistent with atheromatous changes (Fig. 3). Inspection of the vessels proximally and distally showed a normal elasticity without other abnormalities or atherosclerotic changes. The MVD was accomplished by the inter-positioning of two Teflon felts between the arteries and the REZ. Immediately after recovery from the anesthesia, the patient reported no more facial pain and was discharged 4 days after the surgery. There has been no recurrence of pain after over 21 months of follow up.

Fig. 2. Axial magnetic resonance imaging (MRI) shows the radiation dose plan (Leksell GammaPlan Wizard 5.34). The 30% and 80% isodose lines are shown. Note that the vertebral artery and the bifurcation of the anterior inferior cerebellar artery (AICA) are outside the 30% isodose line.

3. Discussion

The pathological changes that occur with radiation-induced vasculopathy include fibrous thickening of the adventitia and exuberant loose connective tissue production with relative sparing of the media and intimal hyperplasia; these closely imitate those seen in atherosclerosis [1,2]. Vascular occlusion following conventional fractionated radiation therapy has been found to occur most often when the radiation dose exceeds 55 Gy, and is detected with a variable latency (mean 6.2 years) from the time of treatment [3].

Maher and Pollock [4] first reported a patient who developed focal atheromatous disease of the loop of the superior cerebellar artery (SCA) and two veins adjacent to the trigeminal nerve 10 months after GKSR. Shetter et al [5] observed a single patient having a small atherosclerotic plaque in the SCA near its contact point with the trigeminal nerve. Huang et al [6] mentioned another patient who had atherosclerotic plaque in the SCA at the trigeminal REZ during MVD. Here, we reported the fourth TN patient with a focal atheromatous change in the AICA remote from the trigeminal REZ at the time of MVD, 11 months after GKSR. All of the patients reported above did not have any symptoms in terms of cerebral vascular ischemia or infarction at the time of MVD.

Radiation-induced vascular injury is well recognized in the literature. In a study of the role of irradiation in the atherosclerotic process in patients affected by Hodgkin and nonHodgkin lymphoma, Bilora et al [7] concluded that the irradiated cases had greater intima-media thickness in the carotid district, even after dividing them according to age and sex; they also indicated that younger males were affected more than younger females, probably because of the protective effect of estrogen in fertile women.

Having performed approximately 1200 MVD for the treatment of TN, hemifacial spasm (HFS), and vestibular neurectomy over a period of >20 years, the senior author (Li) has observed similar pathological changes in some of the offending arteries of many elderly patients who did not have any irradiation history. However, most of these atheromatous changes were diffuse (heterogeneous) rather than focal (homogeneous) and were distributed in the vessel wall as part of a generalized atherosclerotic process. In view of the serum lipid profiles and physical findings of our patient, he was considered to have hyperlipidemia, hypertension, and obesity with a body mass index >34.1 kg/m^2, all of which are regarded as risk factors for atherosclerosis according to the parameters established in the literature. Nevertheless, the focal atheromatous changes of this relatively young patient are distinct from a more generalized atherosclerotic process found in elderly patients, because the adjacent segments of the artery looked normal and showed a normal elasticity.

The number of patients who have had GKSR treatment for TN and then undergone MVD is relatively small; nevertheless, most of

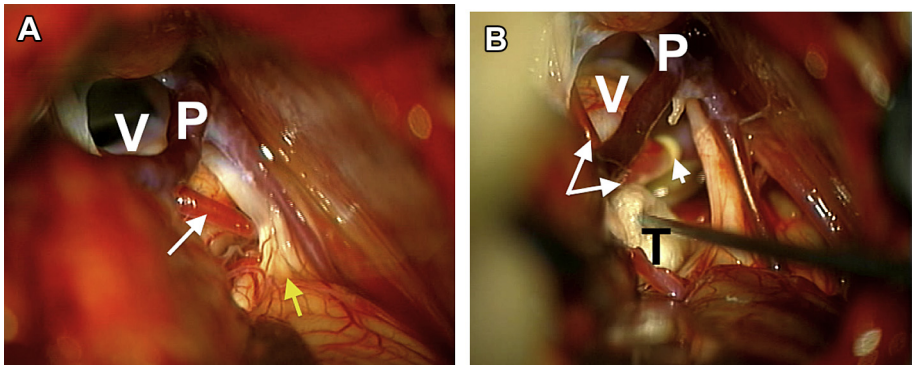

Fig. 3. (A) The original position of one branch (white arrow) of the AICA contacting the trigeminal nerve before dissection. The yellow arrow indicates the REZ. (B) A focal circular atheromatous plaque can be noted at the bifurcation of the AICA (white arrowhead). Two branches originate from the bifurcation of the AICA (double white arrows); one compresses the nerve root superiorly, another compresses the REZ inferiorly. AICA = anterior inferior cerebellar artery; P = petrosal veins; REZ = root entry zone; T = Teflon felt; V = vertebral artery.

the patients who have had a rescue MVD did not show any focal atheromatous changes at open surgery. From the anatomic findings of our patient during open surgery, the calculated radiation dose to the offending artery was estimated to range between 24 Gy and 64 Gy, which was lower than the 71–89 Gy range reported by Maher and Pollock [4].

The focal atheromatous plaque in our patient does not have the history or associated processes related to a vasculopathy. We suggest that patients with high-risk factors for the atherosclerosis process should be carefully evaluated before undergoing radiosurgery, especially younger male patients. Radiation might have been a direct inducing factor in terms of intimal injury and caused the subsequent atheromatous changes in this young hyperlipidemia patient. GKSR is still a safe and effective option for the treatment of TN among elderly patients who are refractory to medication or have failed to respond to other less invasive treatments. Generally, in younger patients with TN, it is accepted that the first choice of treatment should be MVD, whereas among elderly patients with comorbidities, the Gasserian ganglion percutaneous technique is to be recommended [8].

In conclusion, we report the fourth case of atheromatous formation discovered at a rescue MVD. Careful observation of future patients treated will be required to determine whether the vascular changes reported here are indeed related to the GKSR treatment and what kind of patients are the most likely to be affected. Further studies, including long-term follow up, will also be required to determine what the consequences are in patients who might have these atheromatous changes. Although this complication has been described previously in the literature, in these three cases no information was presented on the patients' lipid profiles. Our report seems to suggest that younger male TN patients with hyperlipidemia who receive GKSR may be at an increased risk of postradiation atheromatous formation.

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