Progressive Cerebral Occlusive Disease After Hypothalamic Astrocytoma Radiation Therapy

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Abstract

An 18 year-old woman received radiation therapy for hypothalamic astrocytoma at the age of 11 years. She developed progressive cerebral occlusive vascular disease with moyamoya vessels formation in both carotid systems. Apart from diabetes mellitus, she had no other risk factors for occlusive cerebrovascular disease. The site of occlusion was confined to the field of radiation and the development of moyamoya vessels strongly suggestive of a radiation-induced cause. Radiation therapy around the sella and parasellar region appears to be the most common risk factor for this vasculopathy. Progressive irradiation-induced cerebral vasculopathy is due to accelerated atherosclerosis.

Radiation therapy can cause delayed vascular complications. Small-vessel disease which causes obliterative vasculopathy is an important cause of radiation necrosis of the brain and spinal cord[1,2]. Radiation induced microscopic vascular anomalies or telangectasia may cause brain and spinal cord hemorrhages in long-term survivors[3]. Radiation-induced large vessel disease may manifest as occlusive cerebrovascular disease[2,4-7] or cause intracranial fusiform aneurysms[8]. In chronic occlusive large vessel disease of arteries of the circle of Willis due to radiation therapy, an abnormal capillary network (moyamoya) vessels may develop at the base of the brain[6,7]. This is a very rare entity. We report a case of radiation-associated chronic pregressive occlusive vascular disease with moyamoya vessels which occurred 7 years after the radiation of a hypothalamic astrocytoma.

CASE REPORT

A partial resection of a hypothalamic astrocytoma and ventriculoperitoneal shunt for obstructive hydrocephalus was performed on an 11 year-old girl in 1987. The neurological status was normal after surgery and the girl received radiation therapy of 46 Gy (1 Gy = 100 rad) in 23 fractions as limited field radiation. Transient diabetes insipidus occurred after the radiation. Three years later, she developed diabetes mellitus which was fairly well controlled with insulin therapy and later with oral

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hypoglycemic drugs. Apart from diabetes mellitus, the girl had normal growth and development and developed no long term complications of diabetes mellitus. The girl's mother had late onset diabetes mellitus.

In January 1995, at the age of 18 years (7 years after the radiation therapy), she developed subacute progressive right extremity weakness over a four day period. Neurological examination revealed right hemiparesis. Systemic examination showed no evidence of generalized vascular disease. CT-scan of the brain on admission showed calcifications in both basal ganglia and midpons. Lumbar puncture revealed normal CSF. Apart from diabetes mellitus, a search for other stroke risk factors included lipid profiles, 2 D echocardiogram, electrocardiogram, VDRL, ESR, LE preparation, antinuclear factor, rheumatoid factor, lupus anticoagulant and thyroid function tests. All were unremarkable. After 4 days of hospitalization and supportive therapy, she recovered completely. In spite of the recovery, MRI two weeks later revealed an ischemic lesion in the distribution of the left middle cerebral artery with neovascularized enhancement (Fig. 1).

In April 1995, she developed acute onset of alteration of consciousness and generalized weakness. On examination she was drowsy, did not respond to verbal command but responded to painful stimuli (more on the right side). Quadriparesis, bilateral facial weakness and bilateral pyramidal tract signs were detected. No brainstem signs were observed.

Cerebral angiograms using Seldenger's techinque *via* the right femoral artery were performed. The study showed long segmental narrowing of the right internal carotid artery involving it from just above the carotid bifurcation to the supraclinoid segment. There was almost complete occlusion of the terminal segment of the right internal carotid artery with evidence of basal and cortical collateral circulation (moyamoya vessels) from the right superficial temporal artery and right middle meningeal artery to the right middle cerebral artery (Fig. 2). Collateral circulation *via* the meningeal branch of the right occipital artery and posterior branch of the right middle meningeal artery to right middle cerebral artery as well as posterior ethmoidal branch and branch of the right ophthal-

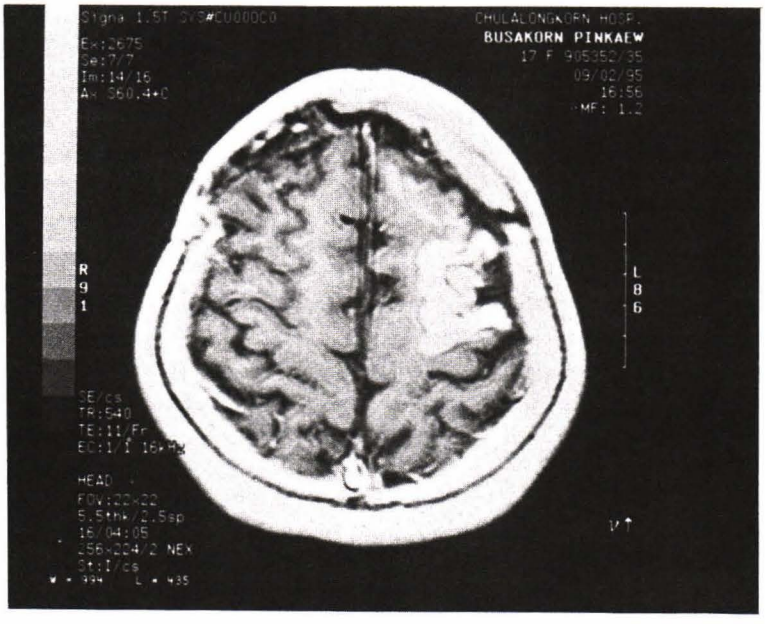

Fig. 1. Follow-up MRI revealed ischemic lesion with luxuary perfusion in the territory of left middle cerebral artery.

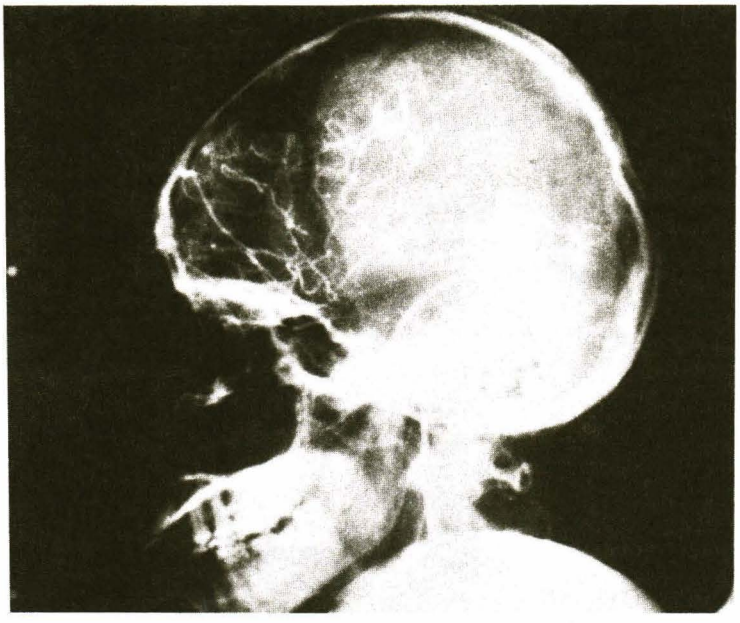

Fig. 2. Angiogram demonstrated occlusion of internal carotid artery above the carotid bifurcation to supraclinoid segment with vault moyamoya and ethmoid moyamoya vessels.

mic artery to right anterior cerebral artery were also detected. There was long segmental narrowing of the left internal carotid artery involving just above the carotid bifurcation to supraclinoid portion. Marked narrowing of the left anterior cerebral artery and occlusion of left proximal middle cerebral artery with basal and cortical collateral circulation and narrowing of left posterior cerebral artery were also detected. Vertebrobasilar system was unremarkable.

The clinical status of the girl did not improve and she expired one month after multiple infarctions. The cause of death was a urinary tract infection complicated by septicemia, septic shock and disseminated intravascular coagulopathy. Autopsy was not done.

DISCUSSION

This patient was a young girl and had only mild fair controlled diabetes mellitus as a risk factor for stroke other than the remote radiation therapy. The site of occlusive large vessel disease which began above the carotid bifurcation to the supraclinoid process is an uncommon site for atherosclerosis[5]. Moreover, the anatomical lesion in this case was confined to the field of previous radiation. Occlusive large vessel disease with or without moyamoya vessels develop subsequent to radiation therapy and this is a well-known complication[6]. Therefore, the progressive cerebral occlusive vascular disease in our patient strongly suggests that radiotherapy was the causative factor.

Progressive cerebral arterial occlusive disease or the moyamoya syndrome is characterized by stenosis or occlusion of large and intermediate cerebral arteries, abnormal net like vessels and transdural anastomoses[9,10]. Our case fulfilled these angiographic features. This progressive cerebral arterial occlusive disease may occur without any apparent associated disease (primary moyamoya syndrome) or may occur secondary to inflammatory cerebral arterial thromboembolic events, tuberculous meningitis, trauma or as a complication after radiation therapy[5-7,9,10].

Progressive irradiation-induced cerebral vasculopathy has been associated with radiation in various sites of the brain and in different types of tumor[5-7]. However, radiation therapy around the sella and parasellar region and especially radiation therapy for optic nerve glioma appears to be the

most common risk factor for this vasculopathy[6,7]. The majority of cases were in childhood (younger than 8 years) and the duration of radiation prior to the developement of occlusive vascular disease ranged from 2-20 years (most patients develop the disease within 8 years)[5-7]. The clinical syndrome consists of focal or multifocal neurovascular changes of large vessels or their medium branches. The clinical course may stabilize but usually progresses[6]. Death may occur as a direct or indirect sequalae of the vasculopathic changes[6]. The associated risk factors for progressive irradiation-induced cerebral vasculopathy are hyperlipoproteinemia, hypertension, diabetes mellitus and possibly other stroke risk factors[5]. Treatment of this vasculopathy resembles that of classical degenerative vasculopathy[5]. Control of associated risk factors and other interventions, which may be beneficial for degenerative vascular disease may be applied [5]. The pathogenesis of progressive irradiation-induced cerebral vasculopathy is accelerated atherosclerosis[5,11]. Irradiation during childhood appears to predispose patients to the development of abnormal net-like vessels and transdural anastomoses[6].

SUMMARY

Radiation therapy around the sellar and parasellar region is the most common risk factor for progressive irradiation-induced cerebral vasculopathy. The majority of cases receive the radiation therapy in childhood and the onset of vasculopathy may be delayed up to 20 years. The clinical course may be static or progressive and death may be related to the severity of neurological sequalae. An 18 year-old woman who received radiation therapy for hypothalamic astrocytoma at the age of 11 years, developed progressive cerebral occlusive vascular disease, 7 years after the radiation therapy. A brief review of this clinical entity is summarized.

(Received for publication on May 17, 1996)

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โรคหลอดเลือดสมองอุดตันที่เป็นมากขึ้นเรื่อย ๆ ภายหลังรังสีรักษาเนื้องอกแอสโตรไซโตมาบริเวณไฮโปธาลามัส

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หญิงอายุ 18 ปี ได้รับรังสีรักษาเนื้องอกชนิดแอสโตรไซโตมาบริเวณไฮโปธาลามัส เมื่ออายุ 11 ปี ผู้ป่วยรายนี้เกิดอาการโรคหลอดเลือดสมองอุดตันและมีหลอดเลือดโมยาโมยาเกิดขึ้นในระบบหลอดเลือดคาโรติดทั้ง 2 ข้าง ไม่พบปัจจัยเสี่ยงอื่น ๆ ของโรคหลอดเลือดสมองอุดตันนอกจากเบาหวาน การเกิดตำแหน่งของการอุดตันบริเวณที่ได้รับการฉายแสงและเกิดหลอดเลือดชนิดโมยาโมยา ทำให้สรุปได้ว่าการฉายแสงน่าจะเป็นสาเหตุของโรคดังกล่าว การฉายแสงบริเวณเซลลาและพาราเซลลา พบว่าเป็นปัจจัยเสี่ยงที่สำคัญที่สุดของการเกิดโรคหลอดเลือดชนิดนี้ สาเหตุของโรคหลอดเลือดสมองที่เป็นมากขึ้นเรื่อย ๆ ภายหลังฉายแสงเกิดจากภาวะหลอดเลือดแข็งที่เป็นอย่างรวดเร็ว

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