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Familial occurrence of cerebral cavernous malformation in a Chinese family and treated by Gamma Knife radiosurgery

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ABSTRACT

Familial cerebral cavernous malformation (FCCM) is a rare autosomal dominant inherit vascular disorder of the central nerves system. The authors reviewed the literature and presented four members who harbored FCCM within a Chinese family: A 14-year-old male (proband, III-1) was admitted to our hospital for a sudden onset of headache and dizziness; his elder parental cousin(III-3) without any symptoms nor other medical history but multiple brain lesions were detected by magnetic resonance imaging (MRI); his mother(II-2), a 38-year-old female, presented with recurrent headaches for more than 2 years. All of the three patients above were treated upfront with Gamma Knife radiosurgery (GKS). Besides, the proband's paternal uncle (II-3) had previously undergone surgery and cerebral cavernous malformation (CCM) was confirmed by the pathological examination. All the patients above are now leading a normal life with the condition and follow-up periodically.

1. Introduction

Cerebral cavernous malformation(CCM) is common vascular abnormality of the brain and spinal cord that histologically characterized by abnormally enlarged capillary without intervening brain parenchyma (Winn et al., 2011; Labauge, Denier, & Bergametti, 2007). Both sporadic and familial forms of the disease have been described. The prevalence of CCM in the general population has been estimated at 0.1%–0.5% (Robinson, Awad, & John, 1991; Otten, Pizzolato, Rilliet, & Berney, 1989; Rigamonti, Drayer, & Johnson, 1987), while FCCM account for 10–50% in CCM (Labauge et al., 2007; Rigamonti, Hadley, & Drayer, 1988). The pattern of the FCCM, characterized by multiple lesions and autosomal dominant transmission, has mainly been described in the Hispanic-America population (Rigamonti et al., 1988), while been sporadic described in a Chinese family (Chen, Lipe, Qin, & Bird, 2002a; Ji, Qin, & Sun, 2006; Mao, Zhao, & Zhou, 2005; Xu, Zhao, & Wu, 2003; Zhao, Xie, & Li, 2011; Xue, Xue-wu, & Lee, 2013; Chen, Lipe, & Qin, 2002b; Zhu, Guo, & Feng, 2014). Herein the authors report a typical Chinese family with CCM to gain an understanding of the FCCM and take good care of patients in the clinical practice.

2. Cases description

Two years ago, a boy was admitted to our hospital for presented with a sudden onset of headache and dizziness and the MRI revealed multiple lesions within his brain. Two months later, his cousin (III-3) also was found the similar lesions through the MRI examination. Then a detail inquiry about family history was performed and obtained. According to these clinical findings and with the help of the proband's aunt, a pedigree of the studied family was established (Fig. 1).

Case 1. The proband, a 14-year-old male (III-1) was admitted to our hospital for a sudden onset of headache and dizziness. Before that, he had been sent to the other hospital, where a computed tomography (CT) scan had been performed and showed a high-density lesions in the cerebral hemisphere. The young male was then transferred to our hospital for further diagnosis and treatment. The physical and neurologic examination was unremarkable, while the brain MRI indicated multiple intracranial cavernous malformations. He was treated by the GKS twice with a prescription dose of 12 Gy and isodose line of 50% for the first time and a prescription dose of 12 Gy to the 35% isodose for the second time two days later. (Fig. 2).

Case 2. The proband's elder cousin (III-3) without any symptoms or medical history but the multiple brain lesions were detected by MRI in his 15-year-old. With the patient and his family arguing strongly for treatment, a defined schedule of GKS

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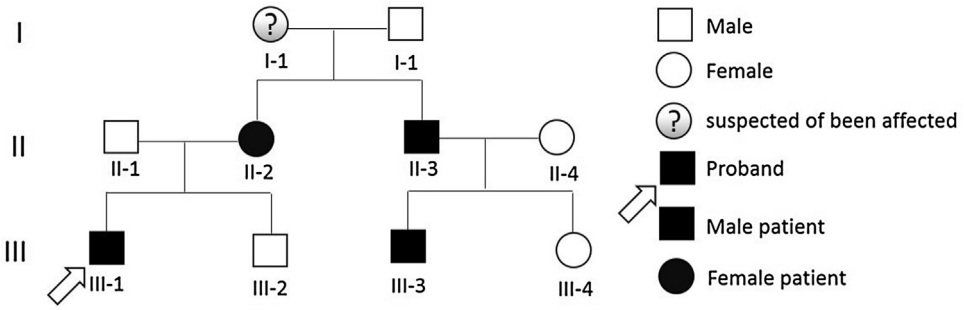

Fig 1. The pedigree of the studied Chinese family with CCM.

performed and the prescribed dose of 13 Gy was directed to the 50% isodose line (Fig. 3).

Case 3. The proband's mother (II-2), a 38-year-old female, obsessed with recurrent headaches for more than 2 years, and came to our department because of the aggravation of headache. No abnormality was found through physical and neurologic examination. However, MRI showed a multiple popcorn-like lesions in both cerebellar and cerebral hemisphere (Fig. 4a). It was the largest lesion, with size of 0.8cm × 0.8cm × 0.7 cm and volume of 0.16 cm^3, irradiated by the GKS with a prescription dose of 13 Gy and isodose line of 50% (Fig. 4b).

Case 4. The proband's paternal uncle (II-3) presented seizure and was treated with a surgery of excision of the bleeding lesions at the age of 22 in another medical department and CCM was diagnosed pathologically. Unfortunately, the more detail information did not obtained for some reasons.

The other family members. The grandmother (I-1) presented repeatedly headache for several years which was similar to the proband's mother, but she has not to the hospital for any physical examination. Besides, the younger female cousin (III-4) had performed MRI 3 year ago without any lesions reported.

3. Outcome and follow-up

Not all the patients performed MRI examinations periodically for their family economics, while their clinical examinations were evaluated as possible as we can after GKS. The mean follow-up period was 27.3 months. Compared with pre-GKS, the symptoms of case 1 and case 3 were improved at the latest follow-up, along with

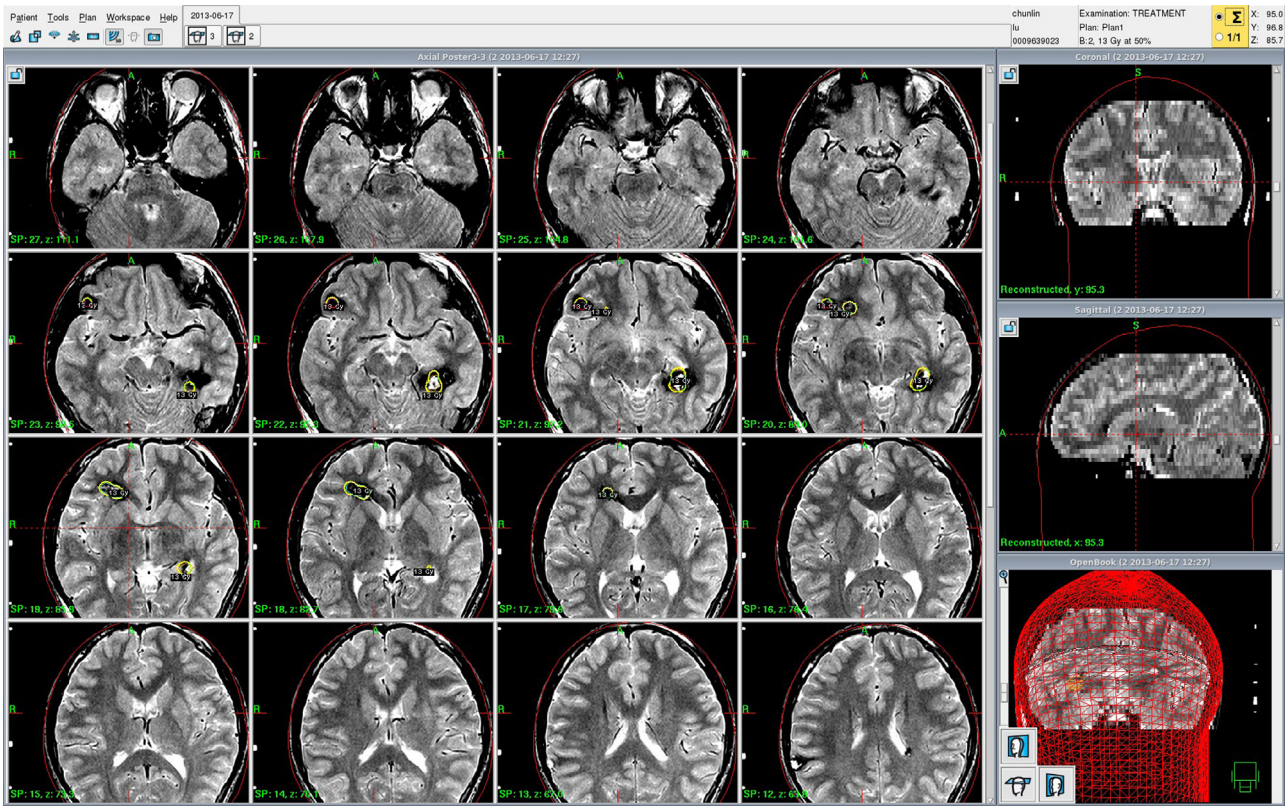

Fig. 2. a and b Case 1. GKS planning for FCCM. This 14-year-old male harboring multiple lesions within his brain underwent GKS twice. Isodose lines for planning are clearly seen on MR images.