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Clinical Study

Delayed complications after Gamma Knife surgery for intractable epilepsy

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ABSTRACT

Despite the controversy concerning the clinical usefulness of Gamma Knife surgery (GKS; Elekta AB, Stockholm, Sweden) for intractable epilepsy, this treatment modality has attracted attention due to its low invasiveness. We report the long-term outcomes of four patients, focusing particularly on the efficacy and complications of GKS. We reviewed the data of four patients with medically intractable epilepsy who underwent GKS between 1998 and 2000 at our hospital. The marginal dose to the 50% isodose line was 24 Gy in one patient and 20 Gy in the remaining three patients. Two of the four patients were treated in the right temporal lobe, one was treated in the left parietal lobe, and one was treated in the right frontal lobe. The mean follow-up was 12.5 years (range 12–14 years). One patient was seizure free (Engel class IA) 24 months after GKS, and two patients failed to show any seizure reduction (Engel class IVA). However, a clear aggravation was evident in one patient (Engel class IVC). All four patients underwent resective surgery due to radiation necrosis (RN) 7, 10, 10 and 12 years after GKS. Three patients were seizure free (Engel class IA), and one was considered to have Engel class IB status following the resective surgery. GKS treatment resulted in insufficient seizure control and carried a significant risk of RN after several years. Drawbacks such as a delay in seizure control and the risk of RN should be considered when the clinical application of this treatment is evaluated.

1. Introduction

Epilepsy surgery, an effective treatment for properly selected patients with intractable seizures, has achieved encouraging outcomes in the treatment of medically intractable epilepsy [1]. However, there are associated risks, including intracranial hemorrhage, infection, neurological deficits, and anesthesia complications [2]. Accordingly, the use of Gamma Knife surgery (GKS; Elekta AB, Stockholm, Sweden) for epilepsy has attracted attention as an alternative treatment option. In a recent prospective multicenter pilot trial in which two different radiosurgery doses were compared, an overall seizure remission rate of 69% was observed at the 3 year follow-up, a finding that is comparable to that reported for respective temporal lobectomy [3]. However, another report with 8 years of follow-up failed to demonstrate that GKS successfully controlled seizures in the long term [4]. Accordingly, the clinical efficacy of GKS for medically intractable epilepsy remains controversial, and its role in the treatment of medically intractable epilepsy needs to be further evaluated for efficacy and safety.

In this article, we report the long-term outcomes of four patients with intractable epilepsy who underwent GKS and required resective surgery due to radiation necrosis (RN).

2. Methods

Between 1998 and 2000, four patients underwent GKS. All four patients had medically intractable generalized tonic-clonic seizure or complex partial seizure epilepsy associated with sudden falls or other seizure types, documented by video-electroencephalography analysis and cranial MRI (Fig. 1a), and based on descriptions from family members. Histological specimens obtained during the resective surgery were reviewed to confirm the diagnosis of RN.

Seizure outcome was classified according to a modified version of the Engel classification [5]. For this evaluation stable status had to be achieved for a minimum of 2 years before final outcome classification. Antiepileptic drugs were initially continued, and an

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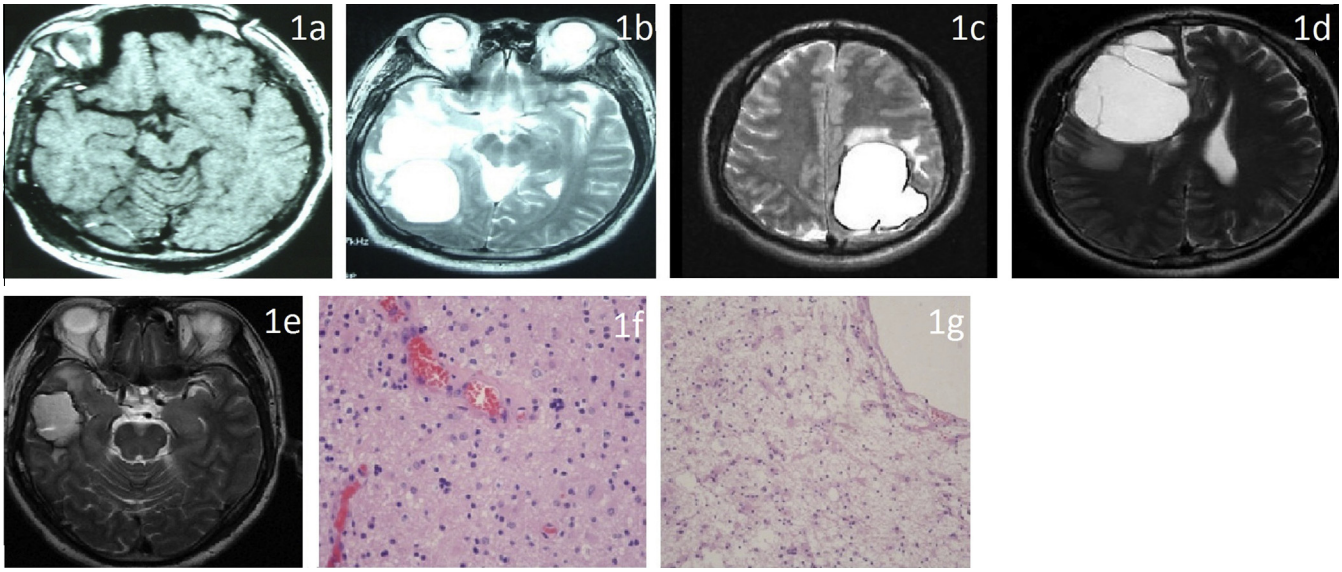

Fig. 1. (a) Axial T1-weighted MRI before Gamma Knife surgery (GKS; Elekta AB, Stockholm, Sweden) and (b) axial T2-weighted MRI showing a hyperintense region in the right temporal lobe 83 months after GKS in Patient 1. (c) Axial T2-weighted MRI showing a hyperintense region in the left parietal lobe 10 years after GKS in Patient 2. (d) Axial T2-weighted MRI showing a hyperintense region in the right frontal-temporal lobe 10 years after GKS in Patient 3. (e) Axial T2-weighted MRI showing a hyperintense region in the right temporal lobe 12 years after GKS in Patient 4. (f) Coagulation necrosis on a hematoxylin and eosin stained sample from Patient 1 (original magnification × 200). (g) Protoplasmic astrocyte degeneration around the lateral wall of the cyst from Patient 3 (hematoxylin and eosin stain, original magnification × 100). (This figure is available in colour at www.sciencedirect.com)

attempt to gradually decrease their dosage and number was made in patients with good results (Engel class I) after 2 years.

All information concerning the clinical histories, symptoms, surgical approaches, drug treatments, outcomes, and follow-up were retrospectively obtained by case note review and telephone interviews as appropriate. After GKS, all patients were observed for seizure frequency and complications, and postoperative changes were evaluated by periodic MRI examinations.

3. Results

3.1. Long-term efficacy

Four male patients with a mean age of 31.6 years (range 19–39 years) underwent GKS. Two were treated in the right temporal lobe, one was treated in the left parietal lobe, and one was treated in the right frontal lobe. The characteristics of the population are listed in Table 1. The mean follow-up duration was 12.5 years (range 12–14 years). One patient was seizure-free (Patient 4, Engel class IA) 24 months after GKS, and Patient 2 and Patient 3 failed to show any seizure reduction (Engel class IVB), while a clear aggravation was observed in Patient 1 (Engel class IVC). The four patients underwent resective surgery for RN at 7, 10, 10, and 12 years after GKS. Three patients were seizure-free (Patient 2, 3, 4, Engel class IA) and one patient (Patient 1) was considered to be Engel class IB following resection surgery (Table 1).

3.2. Long-term side-effects

RN was the main long-term adverse effect after GKS. MRI revealed a hyperintensity on T2-weighted images in the right temporal lobe 2.2 years after GKS treatment in Patient 1. Seven years after GKS, MRI demonstrated a space-occupying mass in the right temporal-occipital lobe (Fig. 1b). As the patient developed generalized convulsive seizures, he underwent a right anterior temporal lobectomy. The resected specimen showed hippocampus sclerosis and RN without malignant tumor cells (Fig. 1f).

Patient 2 presented with right limb weakness 10 years after GKS, and MRI revealed a cystic lesion in the left parietal lobe (Fig. 1c). A lesion resection was performed 5 months later. The resected specimen revealed RN without malignant tumor cells.

Patient 3 presented with headache 10 years after GKS, and MRI revealed a cystic lesion in the right frontal-temporal lobe (Fig. 1d). A lesion resection was performed 1 month later. The resected specimen revealed RN without malignant tumor cells (Fig. 1g).

Patient 4 showed a cystic lesion in the right temporal lobe on MRI studies 12 years after GKS (Fig. 1e). A right temporal

Table 1
Characteristics of patients with medically intractable epilepsy who underwent Gamma Knife surgery

Patient	Age, years/Sex	Seizure origin on video-EEG	Preoperative MRI finding	50% isodose line	Volume (mm^3)	Outcomes after GKS*	Interval between GKS and surgery, years	Outcomes after resective surgery*
1	25/M	RTL	HSD	20 Gy	7500	Class IVC	7	Class IB
2	19/M	LPL	NA	20 Gy	7500	Class IVB	10	Class IB
3	39/M	RFL	NA	20 Gy	6500	Class IVB	10	Class IA
4	37/M	RTL	NA	24 Gy	7500	Class IA	12	Class IA

EEG = electroencephalography, GKS = Gamma Knife surgery (Elekta AB, Stockholm, Sweden), HSD = hippocampal size decrease, LPL = left parietal lobe, M = male, NA = no abnormality, RFL = right frontal lobe, RTL = right temporal lobe.
* Engel's classification.

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