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Stereotactic Radiosurgery (SRS) in the Management of Drug Resistant Non Neoplastic Epileptic Seizure; A Case Report and Review of Literature

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Abstract: ***Apart from neoplastic lesions there are many non-neoplastic pathological lesions which causes epileptic seizures. Surgical resection is primary treatment for such seizures. Stereotactic Radiosurgery (SRS) is an alternative choice for lesion located deep in brain and eloquent area. We present a case of 18 year old boy who presented with drug resistant epileptic seizure patient. He had received various antiepileptic drugs (AEDs) over the years, all of which were only partially effective in maintaining freedom from GTCS. His symptoms subsequently became totally refractory to AED. MRI brain revealed a gliotic lesion in the right occipital area near optic radiation. Subsequently, in view of ineffectiveness of AEDs in preventing seizures, he was offered definitive treatment, given the risk of progression to epileptic encephalopathy. Since the patient desired to undergo a non-surgical approach for treatment, he was offered SRS. He received SRS with 27 Gy in 3 fractions over 6 days. After one year of follow up, he is now having only occasional seizures associated with anger and fever.***

Keywords: Stereotactic Radiosurgery, Exac Trac, drug resistant epileptic seizures

1. Introduction

Epilepsy is one of the most common, severe neurological disorder. The World Health Organization has estimated that more than 50 million patients suffer from epilepsy worldwide [1–3].

Apart from the neoplastic lesions as one of the main cause of the epilepsy, The European Epilepsy Brain Bank consortium has identified the following types of non-neoplastic lesions as the pathological cause of seizures. These includes, Mesial Temporal Lobe Epilepsy (MTLE) associated with Hippocampal Sclerosis-36.4%, Gelastic seizures associated with Hypothalamic Hamartoma-23.6%, Malformations of cortical development (Cavernous Malformation-19.8%), Vascular Malformations (AVM-6.1%) and Glial Scars (Gliosis-4.8%) as well as no lesion (7.7%) [4].

The type and origin of epilepsy determines the prognosis and the efficacy of the treatment. Currently, the two most frequently used therapeutic options include antiepileptic drug (AED) therapy and surgical resection of the epileptic focus. The third and yet less frequently used therapeutic option is Radiation Therapy (RT)-Stereotactic Radio-Surgery (SRS). This non-invasive approach may be superior to surgery when the epileptogenic region is located near the eloquent cortex or deeply sited brain areas. In theory, RT may achieve better neurotransmitter equilibrium than resective epilepsy surgery, and thus results in better neuropsychological outcome despite the late response effects [5, 6].

Stereotactic Radiotherapy (SRT) is a high-precision three-dimensional external beam radiation therapy technique directing beams to a well-defined target, relying on detailed imaging and precise treatment set-up to deliver the radiation dose while sparing the surrounding normal tissue. Fractionated SRT has been proven to be superior to SRS when considering tolerance dose of normal brain tissue and cranial nerves and thus higher radio-biologically equivalent doses can safely be delivered [7].

2. Case

We discuss a case of 18 year old boy who presented with recurrent, drug resistant generalised tonic clonic seizure (GTCS). He had first episode of seizure at age of 5. Initially he had one or two episodes of seizures per day which has been increased up to 8-10 episodes per day. He had received various antiepileptic drugs (AEDs) across the years, all of which were only partially effective in maintaining freedom from GTCS. His symptoms subsequently became totally refractory to AED.

He was of normal intelligence with an average performance at school, with no cognitive impairments. There were no histories of precocious puberty, eating disorders, behavioral disorders, trauma or metabolic disorders.

MRI brain with contrast (Fig 1) have done on multiple occasions which revealed focal gliotic lesion in right parietal-occipital region medial to occipital horn of right lateral ventricle, No mesial sclerosis with normal hippocampal volumetric study.

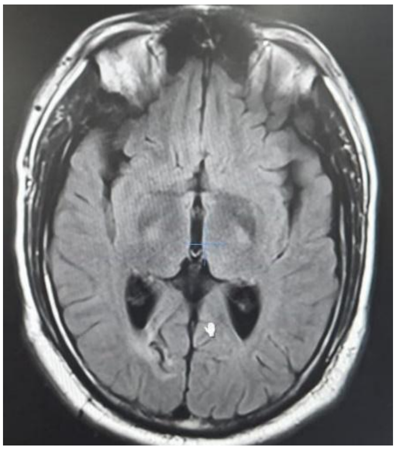

Figure 1: T2W MRI showing gliotic lesion in the right occipital area near optic radiation

EEG (12/03/18): The inter-ictal EEG is abnormal S/O epileptiform discharges arising from b/l fronto-temporal and occipital regions with possibility of underlying structural pathology and generalized epileptiform discharges. The clinical events recorded had no localization.

The patient had tried suicide many a times and has h/o phenol ingestion at 14 year of age. On psychiatric evaluation he was diagnosed with severe depressive disorder with suicidal tendencies at age of 15 year.

However, given the ineffectiveness of AEDs in preventing seizures, he was offered definitive treatment, given the risk of progression to epileptic encephalopathy. Since the patient desired to undergo a non-surgical approach for treatment, he was offered SRS with Exac Trac equipped Novalis Tx Linac

Treatment

For treatment planning, the patient was initially imaged with both MRI and CT scans, and the tumour volume was delineated upon the fused CT–MRI images, using Brain Lab I-plan. The target volume was 21.3 cc and the dose prescribed was 27 Gy in 3 fractions in six consecutive days. The prescription was made to the 95% isodose-line, with the maximum point dose within the volume being 1.59 times, and the minimum point dose within the prescription volume being 0.88 times that of the prescribed dose. The doses to the critical organs at risk were well within the tolerable limits. During imaging and treatment, the patient was immobilized with a thermoplastic immobilization cast (non-invasive) and the treatment was performed without sedation or anaesthesia of any sort. During treatment, the imaging and tracking method used was 6D Brain Lab Exac Trac positioning and verification system.

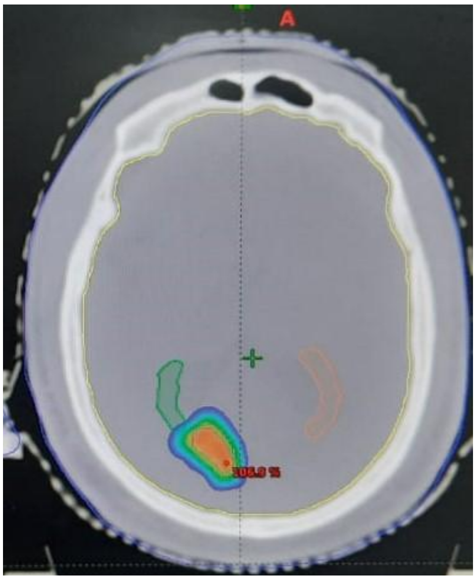

Figure 2a: Radiotherapy planning CT scan shows dose colour wash with differential dose distribution (red colour with high dose coverage area and blue colour with low dose coverage area

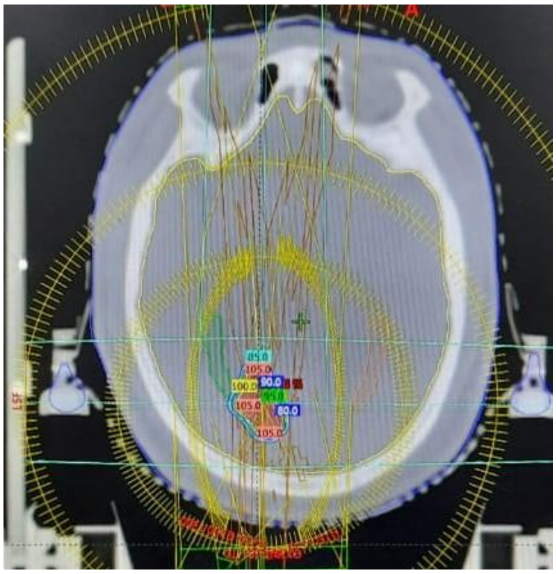

Figure 2b shows multiple non-coplanar beam arches and isodose curves showing dose coverage of more than 95% of prescribed dose

Outcome and Follow Up

The patient reported a decrease in seizure activity as early as in the first week after treatment. A complete cessation of seizures at the third month after treatment has been reported. Imaging carried out at 3 months of treatment revealed significant changes. Currently, at 12 months post-treatment, the patient remains totally free of seizures, and with no hormonal or neurological side effects, has returned to normal activities of daily living.

3. Discussion

Radiosurgery involves the application of focused radiation to a brain target using 3 dimensional stereotactic systems. Initially, SRS was invented by Lars Leksell for use in functional neurosurgery, it is now considered for a greatly expanding number of neoplastic and non-neoplastic abnormalities [8, 9]. Destruction of the epileptic focus and its pathway of spread by necrotizing radiosurgical doses or, alternatively, suppression of the epileptic activity by a neuro-modulatory effect at non-necrotizing doses have been postulated as the basis of the anti-epileptic effect of focal irradiation [10-11].

Historically, SRS has been delivered using the Gamma Knife, a device originally developed by Lars Leksell in Sweden but now it can also be delivered using Linac equipped with Brain Lab Exac Trac tracking system and cyber knife.

In 1994, Barcia, et al. published the first dedicated report showing the effect of radiosurgery on Seizure control. The study reported 11 patients who had epileptic foci treated with doses ranging from 10 to 20 Gy [12].

Jean Regis et al. prospectively analysed 60 patients of hypothalamic hamartoma presented with gelastic seizures between 1999 and 2005, treated with Gamma Knife. All patients had benefit, with 37% patients being completely seizure free at a follow-up for more than 3 years. No instance of permanent neurotoxicity was observed. However, three patients experienced poikilothermia which was transient [13].

Recently, De Salles, et al. studied the efficacy of radiosurgery for gelastic seizures. Three patients were treated with 15-18 Gy doses. Two patients became seizure-free and the third patient experienced a substantial reduction in seizure frequency [14]

Mesial temporal lobe epilepsy associated with hippocampal sclerosis is perhaps the most well-defined epileptic lesion that is responsive to surgical treatment, with expected cure rate in 65-99% of patients [15, 16, 17]. Recently, radiosurgery has been explored as an alternative to open resective surgery for MTLE. In 1995, Regis, et al. first reported selective amygdala-hippocampal radiosurgery for MTLE [18]. In a prospective multicentric trial, patients were selected for the Gamma Knife procedure according to the same criteria used for microsurgical amygdalohippocampectomy, including the presence of hippocampal sclerosis and the absence of space-occupying lesions. The results demonstrated the same seizure reduction efficacy rates (65%) for radiosurgery and for conventional surgery at two years of follow-up [19]. Using a marginal dose of 24 Gy, the study again demonstrated that radiosurgery may be used as an alternative to resective surgery to treat MTLE and to improve quality of life with favourable rates of morbidity and mortality.

In a series of 100 patients with AVMs treated with LINAC radiosurgery, Eisenshenk, et al. found that 59 patients were seizure-free and 19 had a substantial reduction in frequency [20]. Kida, et al studied 462 patients with cerebral AVMs treated with Gamma Knife radiosurgery with a marginal dose of 19.8 Gy. The overall results indicate that seizures improved in 85% of cases, remained unchanged in 12%, and worsened in 3% [21].

Schauble, et al. identified 70 patients with seizures associated with AVM who had been treated with Gamma Knife radiosurgery [22]. Average prescribed dose was 18 Gy. Sixty-five patients were followed up for one year and 51 patients for three years. At one year and at three years, seizure rates were 45% and 51%, respectively. One patient died due to radiation-induced edema. Overall seizure improvement is quite common in patients with AVM treated with radiosurgery and rivals the results yielded by microsurgical resection. The limited morbidity and good outcomes associated with the radiosurgical treatment of epileptogenic AVM located close to or within the eloquent cortex makes radiosurgical treatment a valid alternative option.

A cavernous malformation (CM) is a congenital vascular abnormality that can cause hemorrhage or neurological deficit but more commonly manifests as recurring seizures [23, 24]. Although open microsurgical treatment of CM remains the standard efficacious therapy, a recent study by Regis, et al. suggested a role for radiosurgery in the treatment of seizures associated with CM near the "highly functional cortex", a location that may preclude open resection [23]. Using a mean dose of 19 Gy, 53% of 49 patients with refractory seizures became seizure-free and 20% of treated ones improved at two years [23].

SRS is increasingly being used since the past decade. The major advantage of SRS includes the avoidance of mortality and morbidity risks associated with invasive craniotomy and tumor resection. Unlike SRS with invasive head frame which is used in Gamma Knife, the advantage of frameless SRS is use of multiple fraction treatments, which allows the delivery of equivalent or higher doses of radiation to the target, while reducing the chances of normal tissue complications.

The main disadvantage of SRS in comparison to surgery is that the response after SRS has a latent period, with maximal effect usually experienced after a lag period of about 6 months post-treatment. However, our case is unique in that the response has been almost immediate. Surgery may be preferred over radiosurgery among patients with very large lesions that could be causing symptoms due to mass effect, since surgery can accomplish immediate decompression [25].

4. Conclusion

Stereotactic radiotherapy has been used limited and only in special circumstances in the management of epilepsy. Based on new technologies of delivering radiation combined with a better understanding of the radiobiology, the role of radiotherapy could be expanded. Further research is required to establish the role of radiotherapy in the epilepsy therapy.

No conflict of interest

No sponsorship for the study

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