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Original Article

Incidence of Steroid-Induced Cushing Syndrome, its Treatment Outcome and Influence on Quality of Life in Primary Brain Tumor Patients Receiving Radical/Adjuvant Radiation Therapy

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ABSTRACT

Background: Steroids are more commonly used in the treatment of tumor-induced edema in primary brain tumor patients receiving radiation therapy. Steroid-induced Cushing syndrome is one of the adverse effects of steroid therapy. The present study aimed to find out the incidence of steroid-induced Cushing syndrome, their treatment outcome and the influence of steroid induced Cushing syndrome on health-related quality of life in primary brain tumor patients. **Materials and Methods:** A prospective observational study was conducted for the period of 4 months in the department of radiation oncology, Sri Ramachandra Institute of Higher Education and Research (DU) from April 2024 to July 2024. A total of 10 patients treated with radical/adjuvant radiation therapy were included as per inclusion and exclusion criteria. The health-related quality of life was assessed using validated Cushing-QOL questionnaire. **Results:** Out of 10 patients, females were predominant (60%) over males (40%). Among 10 patients, 2 developed Cushing syndrome. Patients with steroid-induced Cushing syndrome have an impaired quality of life compared to other patients. Patients with Cushing syndrome have trouble brushing easily, irritability, mood swings and a poor quality of life. **Conclusion:** In this study, the incidence of steroid-induced crushing syndrome was found to be 20%. The treatment outcome of steroid-induced Cushing syndrome was found to be improved after tapering the dose of steroids. Patients with steroid-induced Cushing syndrome experienced significant impairments in various aspects of their quality of life, including physical health, psychological well-being and social functioning.

Keywords: Brain Tumor, HRQOL, Radiation Therapy, Steroid-Induced Cushing Syndrome.

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INTRODUCTION

A brain tumor is a collection or mass of abnormal cells in the brain and it is one of the most lethal variabilities of cancer. Brain tumors are classified into two types: Primary tumor and secondary tumor. Primary tumors are often benign or malignant (Doshi *et al*., 2021) (Tiwari *et al*., 2020). Radiation therapy plays a critical role in the management of brain tumors (both primary and secondary). Technological developments in Radiotherapy (RT) have improved patient immobilization, imaging, treatment planning and delivery during the last few decades. The amount of normal brain tissue exposed to high radiation doses has decreased as a result of improvements in imaging and radiation therapy technologies that allow for more accurate tumor location and dose distribution (Scaringi *et al*., 2018). But long-term treatment with radiation therapy can impair the integrity of the BBB, leading to increased permeability and fluid leakage into the brain tissue. This process is often accompanied by an inflammatory response (Makale *et al*., 2017) (Surma-aho *et al*., 2001). Radiation triggers an inflammatory response that results in the release of cytokines and other inflammatory mediators, contributing to edema (Yamaguchi *et al*., 2014).

Cerebral edema associated with brain tumor is very common and occurs in both primary and metastatic tumor. Cerebral edema, or peritumoral edema, is one of the most common and serious complications caused by radiation therapy for brain tumor and

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can complicate therapy related to mechanisms, types, clinical manifestations and diagnostic approaches (Perry *et al.*, 2006).

Corticosteroids have been widely used and found to be particularly beneficial in brain cancer patients with significant peritumoral edema and associated neurological deficits. Glucocorticoids have been used for decades in the treatment of brain tumor patients for reducing tumor-associated edema and the risk of encephalopathy in patients undergoing radiation therapy. Corticosteroids are associated with numerous and well-characterized adverse effects, constituting a major challenge for patients requiring long-term application of corticosteroids (Dietrich *et al.*, 2011) (Ryken *et al.*, 2010).

Chronic exposure to high levels of circulating glucocorticoids increases cortisol levels in the blood and causes Cushing syndrome. Most patients with brain tumor often receive high doses of glucocorticoids over a prolonged period of time to decrease the resulting cerebral edema and relieve symptoms of raised Intracranial Tension (ICT) (Shaw *et al.*, 2002) (Nieman *et al.*, 2018). Iatrogenic Cushing syndrome is the end result of chronic exposure to exogenous steroids and is associated with significant morbidity and poor health related quality of life (Burleson *et al.*, 2002).

The study aims to find out the incidence of steroid-induced Cushing syndrome in primary brain tumor patients receiving radical/adjuvant radiation therapy and to assess their treatment outcome and health related quality of life among the steroid-induced Cushing syndrome patients.

MATERIALS AND METHODS

The study was conducted from April 2024 to July 2024. After obtaining IEC approval IEC REF. CSP/24/MAR/145/119, the patients were enrolled during regular hospital visits. Then, informed consent was obtained from the recruited patients. The demographic details were collected from the patient, i.e., name, age, sex, chief complaints, past medical and medication history, physical examination and treatment details from primary brain tumor patients undergoing radiation therapy. The level of cortisol was assessed for all the patients. Treatment details for Cushing syndrome were obtained from the patients. The health related quality of life was assessed in patients with Cushing syndrome by the Cushing-QOL questionnaire.

RESULTS

A total of 10 patients were included in this study. The results showed that the maximum number of patients were female (60%). Table 1 shows the Baseline characteristics of the patient, the maximum number of participants were in the group of 40-59 years (32%), 40% of participants had no comorbid condition, the remaining 30% of patients had hypertension and 20% of patients had diabetes mellitus and remaining 10% had Asthma. The results showed that the maximum number of participants had Meningioma type of primary brain tumor. Table 2 shows about cortisol levels of patients, among 10 patients, 2 have elevated cortisol levels. Table 3 shows the status of steroid-induced Cushing's syndrome and the results showed that 2 patients (20%) among 10 have steroid-induced Cushing syndrome. Table 4 shows the health-related quality of life of patients and the results showed that quality of life issues faced by 2 patients with steroid-induced Cushing syndrome. Among 2 patients who had steroid Cushing syndrome the dose of steroids was gradually tapered. After tapering the dose of steroids therapy, cortisol level was found to be decreased.

DISCUSSION

Patients receiving steroid therapy for primary brain tumors during radiation therapy were enrolled in the study. In this study, Steroid-induced Cushing syndrome treatment outcome and quality of life were analyzed. The study involved ten patients who visited both the neurosurgery and the radiology

Table 1: Baseline characteristics of patients.

Characteristics of patients	No of patients (*n*=10)	Percentage (%) of patients
Gender		
Male	4	40
Female	6	60
Age in years		
30-39	2	20
40-49	3	30
50 -59	3	30
60-69	2	20
Comorbid Condition		
Hypertension	3	30
Diabetes Mellitus	2	20
Asthma	1	10
No Co-Morbid conditions	4	40
Tumor Type		
Meningioma	3	30
Astrocytoma	2	20
Pituitary adenoma	1	10
Medulloblastoma	2	20
Oligodendroglioma	2	20
Drug Name		
Hydrocortisone	3	30
Dexamethasone	4	40
Prednisone	3	30

Table 2: Cortisol level.

Sl. No.	Cortisol level	No of patients *n*=10	Percentage (%)
1.	More than 20 µg/dL.	2	20
2	Less than 20 µg/dL.	8	80

Table 3: Steroid-induced Cushing syndrome.

Sl. No.	Status of Cushing syndrome	No of patients *n*=10	Percentage (%)
1	Yes	2	20
2	No.	8	80

Table 4: Health-related quality of life by Cushing syndrome QOL questionnaire.

Sl. No.	Quality of life issues	Response of patient 1	Response of patient 2
1	Problems Sleeping	Often	Sometimes
2	Pain	Often	Sometimes
3	Wounds healing	Sometimes	Rarely
4	Bruising easily	Always	Often
5	Irritability and Mood Swings.	Always	Sometimes
6	Less Confidence and Insecurity.	Often	Sometimes
7	Worry About Physical Appearance.	Quite a bit	Somewhat
8	Less Social Engagement.	Often	Sometimes
10	Giving Up Social Activities.	Sometimes	Rarely
11	Impact on Everyday Activities.	Often	Sometimes
12	Memory Issues	Often	Rarely

oncology departments of the hospital. Among the participants in this study, the majority were female (60%) as compared to males. The findings were consistent with the research carried out by Lindholm *et al.*, (2001) which revealed that 70% of the participants were female. In this study, the majority of participants were in the age group of 40-59 (32%). The study by Ostrom *et al.*, (2019) found that the median age at diagnosis for primary brain tumors is around 59 years. In this study, the most common type of tumor is meningioma (30%). According to a study by Ostrom *et al.*, (2019) meningiomas represent about 37.6% of all primary brain and central nervous system tumors. According to this study, dexamethasone is a commonly used drug to treat cerebral edema in primary brain tumor patients. Studies by Vecht *et al.*, (2010) support the preference for dexamethasone in managing symptoms associated with brain tumors and their treatments. Among 10 patients, 2 of them developed Cushing syndrome due to steroid therapy and both patients had elevated cortisol levels. This incidence of SICS was found to be 20%. By comparing with a study by Hatipoglu *et al.*, (2012) they reported that the incidence rate of SICS was found to be 18% in patients with brain tumors treated with steroids. In this study, among 2 patients who developed Cushing syndrome, the dose of steroids was tapered gradually and the cortisol level was decreased. Similarly, a study by Bornstein *et al.*, (2016) concluded that tapering the dose would reduce the symptoms of Cushing syndrome. In this study, patients with Cushing syndrome have an impaired quality of life compared to other patients. Patients with Cushing syndrome have trouble brushing easily, irritability, mood swings and quality of life issues. In accordance with the study conducted by Papoian *et al.*, (2016) which emphasized that Cushing syndrome significantly affects both physical and mental health, it was concluded that patients with Cushing syndrome have an impact on their health-related quality of life. The study's main limitations are a small sample size and limited study period.

CONCLUSION

This study evaluated the incidence of steroid-induced Cushing syndrome, treatment outcome and influence of steroid-induced Cushing syndrome on quality of life in primary brain tumor patients receiving radical/adjuvant radiation therapy. The incidence rate of steroid-induced Cushing syndrome was found to be 20%. There was an increase in cortisol level in steroid induced Cushing syndrome patients. The treatment outcome of steroid-induced Cushing syndrome was found to be improved after tapering the dose of steroids. Patients with steroid-induced Cushing syndrome experienced significant impairments in various aspects of their quality of life, including physical health, psychological well-being and social functioning. These findings emphasize the importance of early detection and management

of steroid-induced Cushing syndrome to improve the overall well-being and quality of life of primary brain tumor patients undergoing steroid therapy.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

SICS: Steroid-induced Cushing syndrome; **RT:** Radiation Therapy; **HRQOL:** Health-related quality of life; **ICT:** Intra cranial tension; **BBB:** Blood-brain barrier.

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