

Original research article

## Comprehensive assessment of Somnolence Syndrome in patients undergoing radiation to the brain



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#### ABSTRACT

Aim: The aim of this prospective study was to assess Somnolence Syndrome (SS) in patients undergoing radiation to the brain.

*Background*: SS is one of the sequelae of radiation to the brain, which is observed within three months of radiation. This is a self-limiting condition and a failure to diagnose leads to unnecessary investigations. This study was undertaken to objectively and subjectively analyze the occurrence, clinical presentation and severity of SS.

Materials and methods: Thirty-three patients receiving radiation to the brain were included in the study. Visual Analog Scale (VAS) was used for subjective assessment and the Littman Somnolence Syndrome (LSS) scale was used for objective assessment of SS. Sleep Latency Test (SLT) was used to quantify SS.

Results: VAS scores showed an initial fall until week 3, followed by a plateau and a sudden increase after week 10. LSS scale at week 11 and 12 showed that 13 patients (43.3%) had grade 2, 5 (16.7%) had grade 3; and 2 (6.7%) had grade 4 SS. SLT revealed a shift of predominant sleep pattern from NREM 1 to NREM 2 at 6 weeks after radiation with a p value of 0.0412.

Conclusions: An insight into SS, its features, frequency of occurrence and self limiting nature can prevent anxiety and unwarranted investigations in the immediate post radiation period. © 2016 Greater Poland Cancer Centre. Published by Elsevier Sp. z o.o. All rights reserved.

#### 1. Background

Radiation is the main treatment option for the management of primary brain tumors as well as for palliation in metastatic brain tumors. The sequelae of cranial irradiation have been described as early, early delayed and delayed, which are observed during, within a few months and beyond six months of radiation therapy (RT), respectively.

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Early effects are due to peri-tumoral edema and are usually detected during radiation and immediately after radiation therapy. Delayed effects mandate immediate hospital care due to their grave nature. However, an early-delayed effect, Somnolence Syndrome (SS) occurs at a time when patients are recovering after irradiation. First reported by Druckmann in 1929,<sup>1</sup> SS comprises non-specific symptoms like excessive sleepiness, fatigue, drowsiness and decreased appetite. It occurs at five to six weeks post-irradiation and is self-limiting, lasting for about two weeks. A number of hypotheses have been postulated to explain SS, with the strongest one attributing it to transient demyelination occurring post-radiotherapy.<sup>2</sup>

Various subjective and objective methods of assessing somnolence have been described. Subjective methods include Visual Analog Scales (VAS)<sup>3</sup> and Epworth Sleepiness Scale.<sup>4</sup> Objectively, a physician rated scale, the Littman Somnolence Syndrome (LSS) scale has been used.<sup>5</sup> Electro-Encephalographic (EEG) changes have also been studied.<sup>6</sup>

The timeline of occurrence of SS and failure to recognize it as a distinct radiation sequel causes undue anxiety among patients as well as healthcare providers and triggers the performance of investigations to rule out recurrence of the tumor. Awareness among healthcare personnel coupled with patient counseling during initiation of RT would go a long way in allaying patient anxiety and reducing unnecessary investigations.

There is limited data available on SS, with this entity being mainly reported in children with leukemia receiving prophylactic cranial irradiation.<sup>5–14</sup> There are very few reports of its occurrence in adults.<sup>3,15,16</sup> This study was undertaken to objectively and subjectively analyze the incidence, clinical presentation and severity of SS in adults receiving cranial irradiation for primary and metastatic brain tumors.

#### 2. Materials and methods

This prospective study was conducted in 33 patients primary as well as metastatic brain lesions with histologically proven malignancies who were receiving RT in Radiation Oncology department of a tertiary care center from November 2012 to September 2014.

A clinical examination, including an exhaustive neurological examination was performed at initiation of RT as well as on follow-up visits. Exclusion criteria included age less than 18 years, those on benzodiazapines or any medications which could induce or modify sleep and those with pre-existing sleep disorders. Patients with Karnofsky performance status less than 30 were also excluded as their altered mental status could make the assessment difficult.

#### 2.1. Radiation protocol

Patients with brain metastases were treated with palliative whole brain radiation therapy to a dose of 30 Gy in 10 fractions using a conventional technique or 3 Dimensional Conformal Radiation Therapy (3DCRT) at the physician's discretion. Those with primary tumors underwent maximal safe resection or decompression. They were treated with Adjuvant RT using 3DCRT or IMRT to a dose of 54–59.4 Gy as indicated. For Glioblastoma multiforme, gross tumor volume

Table 1 – Assessment for Somnolence Syndrome.			
Pattern of assessment			
Week 1	Week 2–11	Week 12	
VAS scoring	VAS scoring	VAS scoring	
Littman	Littman	Littman	
Somnolence scale	Somnolence scale	Somnolence scale	
Sleep Latency Test		Sleep Latency Test	

was considered to be gross residual disease along with the tumor bed. A 2 cm isotropic margin along with adequate coverage of peri tumoral edema was considered as the clinical target volume. Planning target volume margin was 0.5 cm as per institutional protocol. Lesser margins were used for lower grade tumors. Concurrent Temozolamide was given when indicated.

#### 2.2. Assessment of Somnolence Syndrome

Assessment of SS was done as shown in (Table 1). Subjective assessment was made using VAS on a scale of 1–4 mm of opposing variables (alert–drowsy, strong–feeble, well-coordinated–clumsy, happy–sad, normal appetite–cannot face food, sleep all day–do not sleep during day, energetic–exhausted), at baseline, once a week during radiation and for six weeks after treatment was completed. The VAS score for each set of opposing variables was added to obtain a total VAS score for each week.

Objective assessment was done by the treating physician using LSS Scale (Table 2). This physician-rated scale is the most commonly used scale which grades tiredness, activity level, pyrexia appetite, hours of sleep per day on a scale of 0–4.<sup>8</sup> Subjects were graded at baseline, once a week during radiation and weekly thereafter for six weeks using the LSS scale.

Patients also underwent a Sleep Latency Test (SLT) for 20 min at baseline and at six weeks post RT. In the ideal context, it is known as multiple SLT, where after an overnight polysomnography (PSG) to map the patients sleep pattern, patient is given five nap opportunities, each for 20–40 min at two hour intervals.<sup>17</sup> An overnight PSG as well as provision of five nap opportunities was not feasible in our set-up owing to patient constraints and long waiting lists in the Sleep Laboratory. Besides, there is no data suggesting its use earlier, we gave the patient a single nap opportunity four to five hours after awakening from a self-reported good night's sleep. The conventional montage for the MSLT included central EEG

Table 2 – Littman's Somnolence Syndrome scale.			
Grade	Severity	Description	
0	None	No evidence of change in behavior	
1	Minimal	Disturbance with some tiredness, but activity not curtailed	
2	Mild	Decreased activity and increased tiredness, may have a low grade pyrexia	
3	Moderate	Sleeping much of the day, decreased appetite, low grade fever, most activities curtailed.	
4	Severe	Inactive, sleeping 18–20 h per day, low grade fever, markedly decreased appetite and only taking oral fluids	

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