Reim et al. Clin Med Rev Case Rep 2016, 3:112
Volume 3 | Issue 6
ISSN: 2378-3656

Clinical Medical Reviews and Case Reports

Case Report: Open Access

Successful Treatment of Insomnia with Melatonin in a Patient with Malignant Glioma after Radiotherapy-Involving the Pineal Gland

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Abstract

A 29-years-old female patient suffering from a biopsy proven anaplastic astrocytoma in the right basal ganglia was treated by conformal radiation therapy with 2 Gy/fraction up to 60 Gy. Near the end of radiotherapy she complained about insomnia. Her previous sleep pattern had been inconspicuous, but now - despite high dose benzodiazepines provided by her family physician - she was unable falling asleep until 2 a.m. and to stay asleep for longer than two hours. Following the hypothesis that melatonin secretion had been impaired by radiotherapy, the patient was given oral 3 mg of melatonin at bedtime with immediate and ongoing restauration of sleep pattern.

Introduction

A recent survey reported on conspicuous prevalence and severity of sleep disorders in patients with cancer. Insomnia is defined as difficulty falling asleep, difficulty staying asleep - with wake episodes of more than half an hour, unintended early awakening and/or non restorative sleep. This symptom complex qualifies as insomnia when it occurs at least three times a week, results in distress and impairs day time functioning. In cancer patients, especially in patients complaining about fatigue, insomnia is under diagnosed and undertreated [1-7]. Insomnia is also very common in patients with malignant gliomas, although not frequently as striking as in the patient reported here [8].

Case Report

A female patient aged 29 years was diagnosed with anaplastic glioma of 3 cm diameter in the basal ganglia of the right hemisphere (Figure 1). The tumor was biopsied. Subsequently the patient underwent conformal radiotherapy with 2 Gy single doses up to 60 Gy. Because of headache three weeks after the start of radiation, she was treated with dexamethasone up to 12 mg daily.

Two weeks later, she reported that her headache was gone, but that she was continuously active day and night, felt restlessly "driven from outside". She was unable to fall asleep before 2 o'clock a.m. and woke up 1.5 to 2 hours later. Because of sleep deprivation, her family physician prescribed nitrazepam 5 mg taken at bedtime. Despite an increase of the nitrazepam dose of up to 4 tablets her sleep lasted not longer than two hours. Her sleep pattern before the start of radiotherapy had been inconspicuous.

A capsule with 3 mg of melatonin taken at 10 p.m. allowed her again to fall asleep and to stay asleep for five to six hours without benzodiazepine medication. She had again regenerative sleep and felt active at day time. Unfortunately, no quantification of salivary or plasmatic melatonin at bedtime was done prior to starting melatonin substitution.

Discussion

The hormone melatonin (*N*-acetyl-5-methoxytryptamine) is secreted in the pineal gland during darkness or when the absorption of blue light (484 nm) is blocked. Melatonin is an important factor of the sleep-wake cycle, mainly regulated by the suprachiasmatic nuclei of the hypothalamus [9,10]. In the US, melatonin is widely used as over the counter medicine against sleep disorders, jet lag and various other conditions as it is a powerful antioxidant, whereas in Europe, its medical use focuses on insomnia in persons above the age of 55 years. However, with rare exceptions, melatonin is well tolerated in doses below 5 mg

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Citation: Reim A, Strobl D, Saletu-Zyhlarz G, Preusser M, Schmook MT, et al. (2016) Successful Treatment of Insomnia with Melatonin in a Patient with Malignant Glioma after Radiotherapy-Involving the Pineal Gland. Clin Med Rev Case Rep 3:112

Received: April 21, 2016: **Accepted:** June 23, 2016: **Published:** June 25, 2016

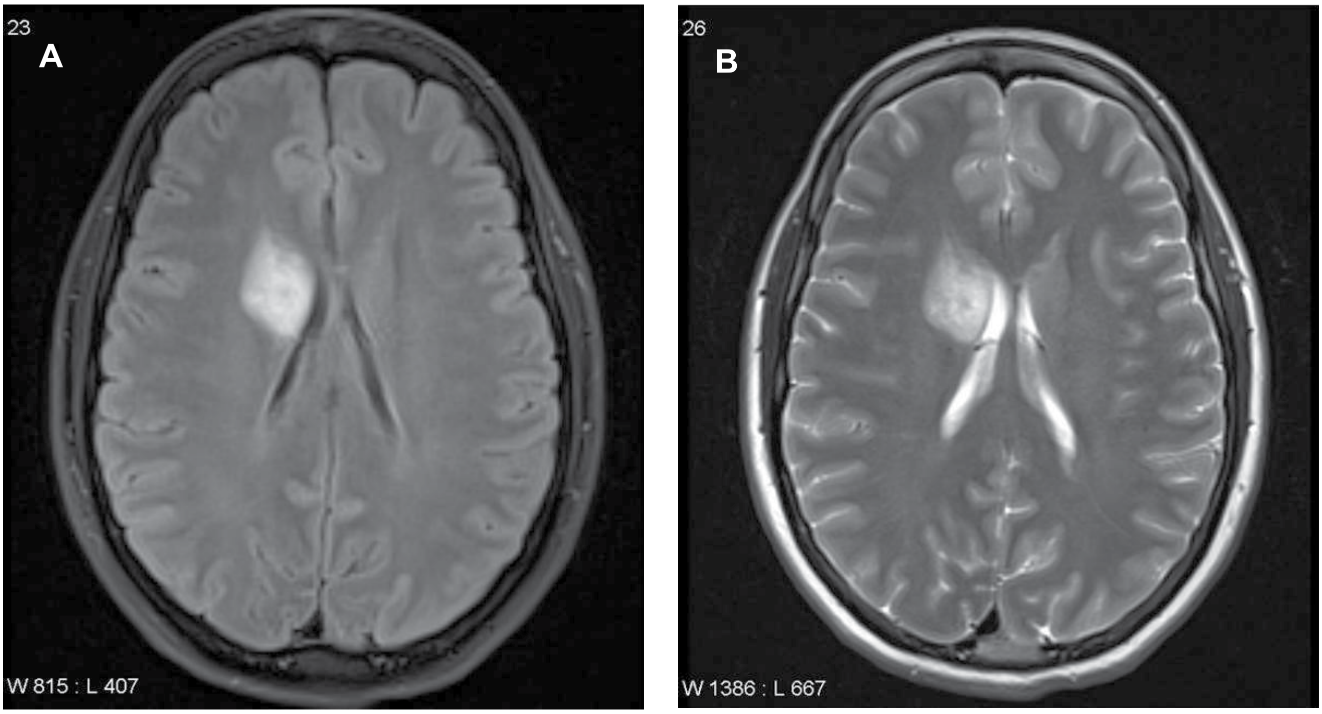

Figure 1: Initial radiologic findings. Brain MRI demonstrates 3.2 × 2.8 cm lesion without contrast enhancement in the T1 weighted image. (A) and with edema on flair image; (B) before biopsy and radiation therapy. MRI: magnetic resonance imaging.

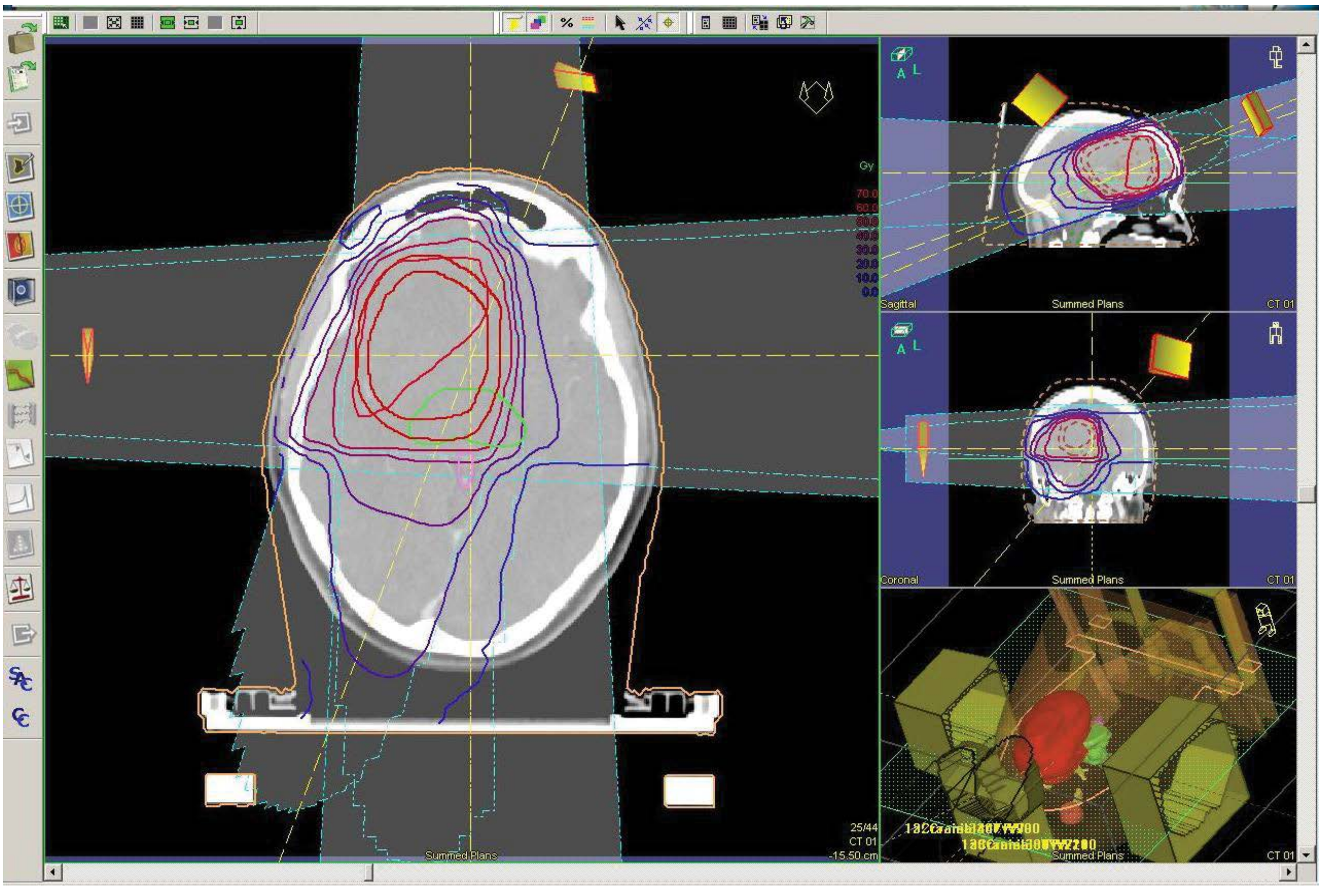

Figure 2: Irradiation plan showing the isodoses (red-violet-blue), brainstem (green), pineal gland (pink).

[11-15] and potential anti-tumoral effectiveness of melatonin has been discussed [16].

In the patient of this report, the radiation field covered the epiphysis as well as both hypothalamic suprachiasmatic nuclei, where the circadian rhythms of waking and sleep are regulated (Figure 2 and Table 1). Radiation therapy is known to cause irreversible depletion of the pituitary hormones [17-19], so in analogia, trying melatonin therapy was obvious - and successful. Thus, in patients with radiation fields covering the hypothalamus or the epiphysis with insomnia, the administration of melatonin may offer restoration of satisfactory sleep patterns.

Table 1: Minimal, maximal, median and average doses of the risk organs and CTV (clinical target volume), PTV (planning target volume).

Summed Plans

Name	Min [Gy]	Max [Gy]	Median [Gy]	Average [Gy]	Std. Dev. [Gy]
Brainstem	1.86	59.06	39.00	38.17	18.79
Chiasm	43.75	49.65	48.69	47.36	14.96
CTV	54.16	62.82	59.78	59.61	1.86
Eye, Left	2.11	3.63	2.67	2.69	0.37
Eye, Right	2.67	4.71	3.39	3.42	0.54
Lens, Left	-	-	-	-	-
Lens, Ri...	-	-	-	-	-
Optic N...	3.50	5.51	4.21	4.45	1.77
Optic N...	4.44	10.16	6.11	6.41	5.12
PTV 5mm	48.23	62.82	59.51	59.26	2.42
Tumor	56.93	61.97	59.71	59.65	1.02
Body	0.00	62.82	4.71	13.32	16.56
Epiphyse	33.99	54.03	42.78	42.89	7.85

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