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ORIGINAL ARTICLE

Melatonin secretion in patients with pineal region tumors—preliminary report

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Abstract

Tumors of the pineal region, though not very common, are recently more often diagnosed due to the introduction of computer tomography and magnetic resonance examinations into neurosurgical practice. However many controversies about the treatment of them still exist. Some of them need aggressive treatment. The others are benign and asymptomatic. Thus it seems to be important to improve our diagnosis of mass lesion of the pineal region, especially before taking a decision for surgery. The purpose of this study was to find any significant changes in the circadian pattern of melatonin secretion in patients with pineal region tumors. Blood samples were collected preoperatively from 21 patients with diagnosed pineal region tumors. In 13 patients sampling was performed at 08:00, 14:00, 20:00 and 02:00 h during a 24-hour period but in 8 former ones only at 02:00 h at night. The samples were immediately centrifuged and the serum stored at -20°C until analysis. The patients stayed in the darkened room from 23:00 to 05:00 h. Plasma melatonin was measured by direct and specific radioimmunoassay. The following three groups of results were found: (1) eight patients showed normal melatonin secretion profiles, (2) six cases with lack of the night maximum plasma value, and (3) seven cases with nocturnal melatonin concentration higher than in the healthy population (>100 pg/ml). We observed no correlation between melatonin secretion and histological type of tumor. In conclusion, we suggest that changes of melatonin secretion could indicate the pineal region pathology. However further studies with a larger group of patients, especially with tumors originating from the pineal gland (pinealocytoma, pinealoblastoma), are necessary.

Introduction

Tumors of the pineal region, though not very common, are recently more often diagnosed due to the introduction of computer tomography and magnetic resonance examinations into neurosurgical practice. Some of them need aggressive treatment; the others are benign and asymptomatic. It seems to be important to improve our differential diagnosis of mass lesion of the pineal gland, especially before taking a decision for surgery.

Until now we know several markers of pineal region pathology like alpha-fetoprotein, human chorionic gonadothropin, carcinoembryonic antigen and placental alkaline phosphatase [1, 2]. All of them play an important role in modern diagnostics and therapy of the posterior third ventricle tumors, helping to determine the histological type of tumor and the degree of its malignancy. We ask if melatonin could be a marker of pineal tumors?

Melatonin (MLT) or N-acetyl-5-methox-ytryptamine is synthesized nearly exclusively by the pineal gland and exhibits a circadian rhythm with maximum production occurring during the night and low values during the daytime. MLT production is inhibited by light and stimulated by darkness via a multi-

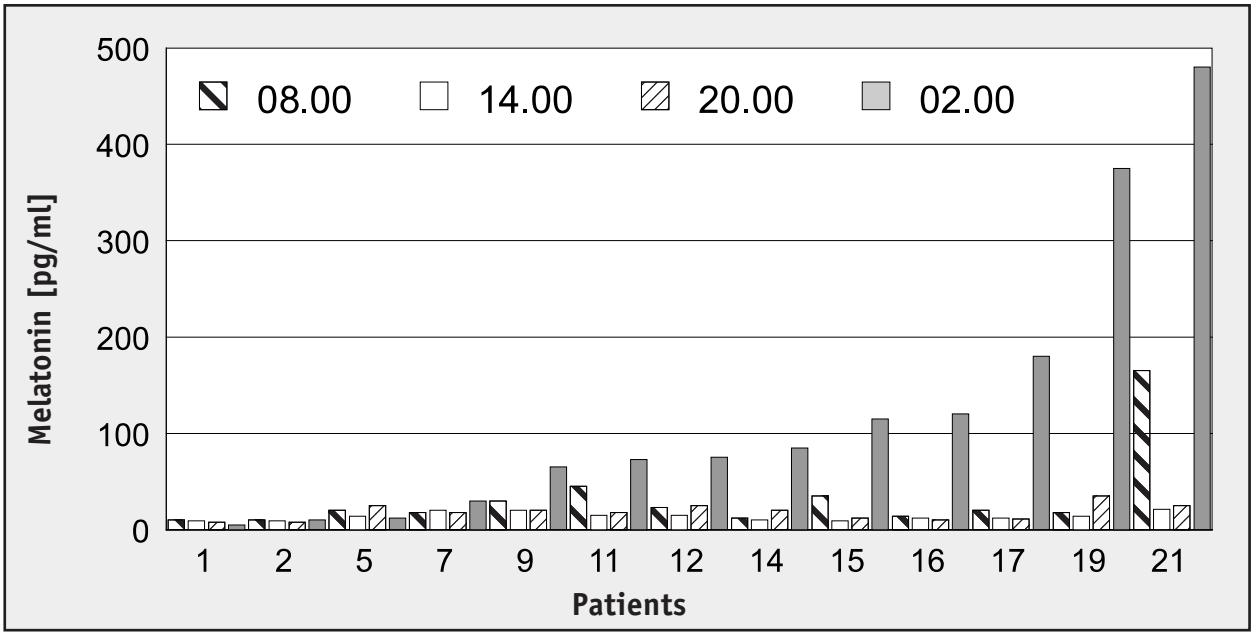

Fig. 1. Serum melatonin levels.

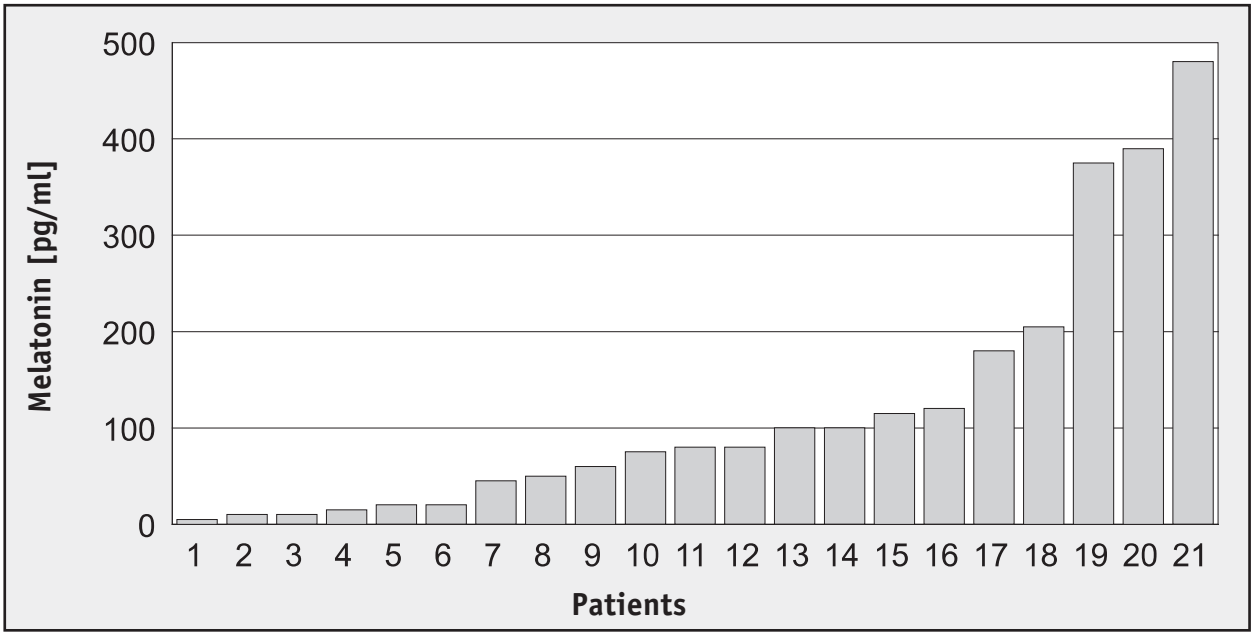

Fig. 2. Serum melatonin levels at 02:00 h at night.

synaptic neural pathway connecting the retina with suprachiasmatic nucleus by the retinohypothalamic tract and further the superior cervical ganglia to the pineal gland [3]. Half-life of melatonin in human circulation is relatively short (approximately 47 minutes). Most of the circulating melatonin is metabolized in the liver to 6-hydroxy-melatonin and subsequently conjugated to 6-sulfatoxymelatonin, which is excreted into the urine [3, 4].

The purpose of this study is to find if there exist any changes of the pattern of melatonin secretion that could be significant for pineal region pathology.

Materials and Methods

The study population consisted of 21 patients aged 5 to 68 years (mean age 32 years), diagnosed by computer tomography or magnetic resonance examination with a pineal region tumor. There were 8 female and 13 male patients. Informed consent was obtained from all patients or if they were children, from their parents. Blood samples were collected preoperatively. In 13 patients sampling was performed at 08:00, 14:00, 20:00 and 02:00 h during a 24-hour period but in 8 former ones only at 02:00 h. The patients stayed in the darkened room from 23:00 to 05:00 h. The samples were immediately centrifuged and the serum stored at -20°C until analysis. Serum MLT concentrations were measured in duplicate by a direct and specific radioimmunoassay, using kits from DRG, Germany.

Results

The results are presented in Figures 1 and 2. Considering the night maximum plasma levels of MLT in serum, the following three groups of patients were found: (i) 8 patients showed normal melatonin secretion profiles, (ii) 6 cases lacked the night maximum plasma value and (iii) 7 cases had a nocturnal MLT concentration higher than in the healthy population (>100 pg/ml). We observed no correlation between melatonin secretion and histological type of tumor (Table 1).

Discussion

Until now only a few studies on the problem of MLT secretion in the posterior third ventricle pathology have been presented in the literature [5–7]. We found two papers reporting suppression of MLT secretion in patients with pineal region pathology or hypothalamic hamartoma [5, 6]. We speculated after Webb and Puig-Domingo [3] that excessive secretion of MLT could exist in the true pineal tumors like pinealocytoma while in lesions causing destruction or compression of the pineal gland, e.g. teratoma or hypothalamic hamartoma, low values of MLT are found. Vorkapic et al. [8] also suggested that low serum MLT levels might be diagnostic of pineal region tumors. However, the results obtained in our patients did not confirm this hypothesis, as we did not find any correlation of histological type of

Table 1. Melatonin secretion and histological type of tumor

Patient no.	Patient ID	MLT 08:00	MLT 14:00	MLT 20:00	MLT 02:00	HP
4.	2054/95				7.1	Germinoma
5.	6052/95; 2664/96	19.8	12.6	27.8	10.9	Ependymoma anaplasticum
6.	315/95				11.5	Ependymoma
8.	6423/94				38.1	Meningioma angiomatosum
9.	352/97	33.8	19.2	19.5	57.4	Ependymoma grade II
10.	1650/95; 2786/95; 1527/96				65.1	Astrocytoma anaplasticum
12.	5628/96	24.9	14.0	29.1	74.7	Haemangioblastoma
13.	4865/95				88.3	Astrocytoma anaplasticum
16.	213/96	11.2	9.9	9.0	108.0	Astrocytoma fibrillare
19.	998/96	16.5	12.4	39.2	366.0	Aneurysma permagnum AB
20.	1128/95				383.1	Ependymoma

tumor and melatonin secretion. On the other hand, the studied group was not sufficiently large and there were not cases of tumors originating from the pineal gland (pinealocytoma, pinealoblastoma) in our population. Thus the continuation of the research with more cases is necessary to prove our hypothesis.

In conclusion, our preliminary results suggest that changes in melatonin secretion could indicate pineal region pathology. However, its diagnostic significance does not seem to be very high as we did not find any correlation with particular types of tumors. Further studies with a larger group of patients, especially with tumors originating from the pineal gland (pinealocytoma, pinealoblastoma), are necessary.

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