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Research Article / Araştırma Makalesi

Magnetic Resonance Imaging Findings of Pineal Gland Metastasis

Pineal Metastazların Manyetik Rezonans Görüntüleme Bulguları

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Abstract

The pineal gland metastatic disease is relatively uncommon. Our research's objective was to assess pineal gland metastasis findings from magnetic resonance imaging (MRI). We queried the radiology reports of brain MRI examinations performed between September 2010 and December 2019. After identifying cases, patient characteristics including sex, age, diagnosis, survival time, and MRI features including size (largest cross-sectional diameter), T1- Weighted Image (WI) signal, T2-WI signal, contrast enhancement, and additional brain metastatic involvement area were evaluated. Our investigation identified 7 patients with pineal gland metastasis. Underlying malignancies were lung (N 2), breast (N 2), prostate cancer (N 1), neuroblastoma (N 1), and non-Hodgkin lymphoma (N 1). The average survival period after the detection of the pineal gland metastasis is 3.14 ± 3.93 months. The lesions ranged in size from 0.8 to 1.8 cm (mean 1.18±0.38 cm). Six tumors were isointense to gray matter both on T1-WI and T2-WI. One showed heterogeneous signal intensities on T1-WI and T2-WI. 6 out of 7 tumors showed homogenous solid enhancement while one tumor showed heterogeneous enhancement due to necrosis. Two patients had leptomeningeal, one patient had pituitary stalk, one patient had parenchyma, and one patient had calvarium-dural metastases. In the remaining 3 patients, no accompanying metastases were observed in brain. The presence of pineal gland lesions in patients with known malignancy should increase suspicion of metastatic involvement.
Keywords: pineal gland, metastasis, magnetic resonance imaging, pineal, magnetic resonance

Özet

Pineal bez metastazları oldukça nadirdir. Çalışmamızın amacı, pineal bez metastazlarının manyetik rezonans görüntüleme bulgularını değerlendirmektir. Bu çalışmada Eylül 2010 ile Aralık 2019 tarihleri arasında hastane/ radyoloji arşivindeki beyin manyetik rezonans görüntülemelerinin raporları retrospektif olarak tarandı. Olgular belirlendikten sonra, hastaların cinsiyet, yaş, tanı, sağkalım süresi gibi özellikleri ve boyut (en büyük kesit çap), T1 ağırlıklı, T2 ağırlıklı sinyaller, kontrast tutulumu, ek beyin metastatik tutulum alanları gibi özellikler değerlendirildi. Araştırmamızda pineal metastazlı 7 hasta tespit edildi. Altta yatan maligniteler akciğer (N 2), meme (N 2), prostat kanseri (N 1), nöroblastom (N 1), non-Hodgkin lenfoma (N 1) idi. Pineal metastaz saptandıktan sonra ortalama yaşam süresi 3.14 aydı. Lezyonların boyutları 0.8 ile 1.8 cm arasında değişiyordu. Altı tümör, hem T1 ağırlıklı hem de T2 ağırlıklı olarak gri cevhere göre izointens idi. Biri T1 ağırlıklı ve T2 ağırlıklı görüntülerde heterojen sinyal intensitesi gösterdi. 7 tümörden 6'sı homojen solid kontrastlanma gösterirken, bir tümör nekroza bağlı heterojen kontrastlanma gösterdi. İki hastada leptomeningeal, bir hastada hipofiz sapı, bir hastada parankim, bir hastada kalvaryum-dural metastaz vardı. Kalan 3 hastada ise beyinde eşlik eden metastaz izlenmedi. Bilinen malignitesi olan hastalarda pineal lezyonların varlığı metastatik tutulum şüphesini artırmalıdır.
Anahtar Kelimeler: pineal bez, metastaz, manyetik rezonans görüntüleme, pineal, manyetik rezonans

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1. Introduction

The pineal gland is an uncommon location for metastatic disease, although neoplasms from almost every tissue have been reported to metastasize to the pineal gland (1). When we reviewed the literature according to "pineal gland metastasis", we found 43 cases (1-3). In one autopsy study of 130 patients with lung and breast cancers, pineal metastases were discovered in 5 cases (2). In a surgical study by Lassman et al, 10 pineal gland metastasis were found among 191 patients with surgically managed pineal gland tumors of unknown etiology (3). The remaining 28 cases were reported as clinical cases only (1). Melatonin (N-acetyl-5-methoxy-tryptamine) is a molecule produced and released from the pineal gland. Apart from sleep and circadian regulations, melatonin displays inhibitory properties during tumor progression (4-6). The prognosis of pineal gland metastasis is poor because it generally occurs in the late course of widely metastatic systemic cancer (7). Impaired synthesis and secretion of melatonin from suffered pineal tissue may contribute to worsening of prognosis. Thus, pineal metastasis may be more important than just a metastasis site.

Primary tumors of the pineal gland can originate from a wide variety of cell sources, such as pineal parenchymal tumors, germ cell tumors, glial tumors, ependymomas, papillary pineal tumors, meningiomas, and lipomas (1-3). Histological diagnosis maybe not practical because of the highly invasive nature of biopsy and the deep location of the pineal gland. Magnetic resonance imaging (MRI) has an important place in the diagnosis of pineal metastasis as in the diagnosis of many diseases (8).

There is no prior report specifically focused on the radiological findings of pineal gland metastasis. In this article, we aimed to evaluate MRI findings of metastases to the pineal gland.

2. Materials and Methods

Subjects

MRI examinations were performed either on a 1.5 Tesla (T) MRI device (Magnetom vision plus, Siemens, Germany) or a 3T MRI device (GE Healthcare, Waukesha, WI). Conventional brain MRI protocol was as follows: T2-weighted image (WI) (Echo time (TE): 85, Repetition Time (TR):7711, Window Contrast/Window Width (WC/WW): 4434/8868 for 3T, TE: 91, TR:3940,WC/WW: 798/1698 for 1.5T) fluid-attenuated inversion recovery imaging (TE: 37, TR:2095,WC/WW: 3256/6513 for 3T, TE: 88, TR:8001,WC/WW: 474/973 for 1.5T) non-enhanced T1-WI (TE: 11, TR:829,WC/WW: 2082/4165 for 3T, TE: 17, TR:750,WC/WW: 660/1395 for 1.5T), and contrast-enhanced T1-WI (TE:9, TR:820, WC/WW: 5508/11017 for 3T, TE: 17, TR:750,WC/WW: 486/1021 for 1.5T) with a slice thickness: 5 mm. MRI images were transferred to the MR protocol workstation. From conventional MR images, a neuroradiologist with 12 years of experience (SS) and a radiologist with 6 years of experience (NA) evaluated the pineal gland metastasis with consensus. Due to the invasive nature of the biopsy and the deep location of the pineal gland, if the lesion became large on follow-up MRI examination, the pineal gland lesion was accepted as metastasis (Figure 1). MRI features including size (largest cross-sectional diameter), T1- WI signal, T2-WI signal, contrast enhancement, and additional brain metastasis were recorded.

Statistical analysis

Statistical analysis was evaluated with the SPSS v.22 package program (IBM Corp, Chicago, USA). Descriptive statistics were given as a mean ± standard deviation.

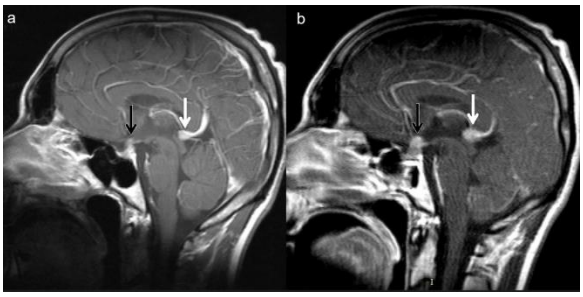

Figure 1. *A pineal lesion that increased in size in 2 months in a 23-year-old man with non-Hodgkin lymphoma. Figure 1a. A nodular lesion is seen on sagittal post-contrast T1-WI image (white arrow). Figure 1b. Sagittal post-contrast T1-WI image 2 months later shows marked progression of the lesion size, suggesting metastasis (white arrow). Also pituitary stalk involvement is progressed (black arrows).*

3. Results

Patient characteristics of these patients as well as their primary neoplasm are described in Table 1. We analyzed 7 patients (age range 23-71 years; mean age 46.28± 16.89 years, 3 male, 4 female) who were diagnosed with pineal gland metastasis from September 2010 to December 2019. Underlying malignancies were lung cancer (N 2), breast cancer (N 2), neuroblastoma (N 1), prostate cancer (N 1), and non-Hodgkin lymphoma (N 1). The survival period after the detection of the pineal gland metastasis ranged from 1 to 12 months (mean 3.14 ± 3.93 months).

The imaging characteristics including size, T1-WI signal, T2-WI signal, contrast enhancement, and additional brain metastasis were described in Table 2.

Table 1. Patients and Disease Characteristics

Patient Number	Sex	Age (years)	Diagnosis	Survival days
1	M	23	Non-Hodgkin lymphoma	1 month
2	F	71	Breast	12 months
3	M	49	Lung	2 months
4	F	25	Neuroblastoma	2 months
5	M	52	Prostate	2 months
6	F	53	Breast	1 month
7	F	51	Lung	2 months

Table 2. Radiologic Manifestations of the Patients

Patient Number	Magnetic Resonance Imaging				
	Size (cm)	T1 signal	T2 signal	Enhancement	Additional brain metastasis
1	1.4	isointense	isointense	homogeneous	infundibular stalk, leptomeninges
2	1.8	heterogenous-hipointense	heterogenous-hyperintense	peripheral (necrotic)	-
3	1.1	isointense	isointense	homogeneous	-
4	1.5	isointense	isointense	homogeneous	-
5	0.8	isointense	isointense	homogeneous	calvarium-dural
6	0.8	isointense	isointense	homogeneous	leptomeninges
7	0.9	isointense	isointense	homogeneous	parenchymal

The lesions ranged in size from 0.8 to 1.8 cm (mean: 1.18±0.38 cm). Six tumors were isointense to gray matter both on T1-WI and T2-WI (Figure 2). One showed heterogeneous signal intensities on T1-WI and T2-WI. 6 out of 7 tumors showed homogenous solid enhancement while one tumor showed heterogeneous enhancement due to necrosis (Figure 3). In contrast-enhanced images, two patients had leptomeningeal metastases, and one of them also had pituitary stalk metastases. One patient had parenchymal metastasis (Figure 4), and one patient had calvarium-dural metastasis. The remaining 3 patients had no other metastases within the brain. Pineal gland lesions and accompanying metastatic lesions were not observed in the previous examinations of our patients (not shown) in our study.

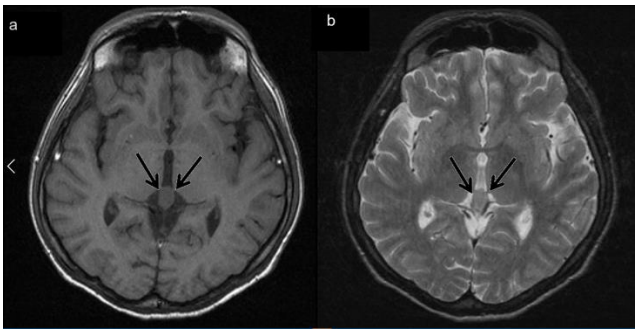

Figure 2. *Tumour is seen as isointense to gray matter both on axial T1-WI (Figure 2a) and on axial T2-WI (Figure 2b) (arrows).*

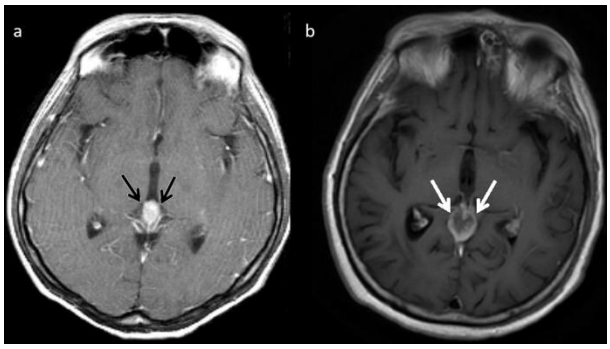

Figure 3. *On post-contrast T1-WI axial image, homogenous solid enhancement is seen within tumour (black arrows) (Figure 3a). Heterogenous enhancement is seen due to necrosis (white arrows) on post-contrast T1-WI axial image (Figure 3b).*

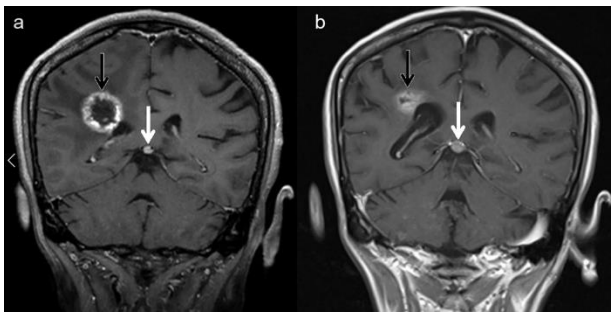

Figure 4*. Progression of pineal lesion size suggesting metastasis is seen (white arrows) in coronal post- contrast enhanced T1-WI images (Figure 4a). An additional parenchymal metastasis is regressed after radiotheraphy (black arrows) in coronal post-contrast T1-WI (Figure 4b)*

4. Discussion

Melatonin is a molecule synthesized and secreted by the pineal gland known as a regulator of sleep and circadian rhythms. The melatonin effect may be impaired in pineal metastases. In the last decade, many more reports have shown that melatonin leads to prolonged survival and improved quality of life in patients when included in chemotherapy or radiotherapy protocols designed to treat cancer (4-6). The diagnosis of pineal gland metastases is therefore important. Pineal gland metastases are most common in lung cancer (9). It has been reported that previously detected pineal gland metastases originate from other tumors such as the esophagus, breast, pancreas, kidney, stomach, liver, colon, melanoma, thyroid, and myeloma (1). Central nervous system lymphoma rarely involves the pineal gland. Kim et al. reviewed reported cases of primary and secondary pineal lymphoma in 2016 and found 10 cases, of whom 2 were secondary, with 1 retroperitoneal primary and 1 gastric primary (10). Since then, two additional cases of pineal lymphoma have been reported, one presenting with masses in the adrenal gland, the other one presenting as primary pineal lymphoma (11,12). When we look at the literature, pineal gland metastases are observed less frequently.

Brain MRI of isolated pineal gland metastasis secondary to acute lymphocytic leukemia revealed a well-defined solid lesion with intense enhancement after contrast. In this case, significant diffusion restriction of the lesion was detected on diffusion-weighted images (13). The diffusion restriction feature of the cases was not included in our study. Mostly homogeneous enhancement was observed in our patients, and heterogeneous enhancement was observed in pineal gland metastasis of breast cancer in one patient of our study.

In the literature, hydrocephalus is the prominent finding in the brain MRI image of a lung adenocarcinoma metastasizing to the pineal gland. And in this case, the diagnosis was made as a result of a biopsy several times (14). Hydrocephalus was not observed in our patients. Our patients did not have a pathological diagnosis, and most of them showed progression in the lesions during their follow-up. In addition, pineal gland lesions and accompanying metastatic lesions were not observed in the previous examinations in our study.

Heterogeneous contrast enhancement was observed in the pineal gland metastasis of esophageal neuroendocrine tumor on contrast-enhanced T1-weighted examination, and calcification was detected on computed tomography in the literature (15). In our study, there were no calcifications in pineal metastasis, and in our patients, heterogeneous contrast enhancement was present in one of the 7 patients. The primary of this patient was breast cancer. And in the literature ring-like enhancement and hypointensity in T2-weighted examinations were observed in a patient with pineal gland metastasis of gastric adenocarcinoma (16). In our 6 of 7 patients, the signal feature was observed as isointense in T2-weighted examinations.

Due to the absence of the blood-brain barrier in the pineal gland, the basis of extracranial malignant tumors reaching the pineal region is considered to be hematogenous metastasis (1). In one study, it was mentioned that metastasis of the pineal gland may arise mainly from tumor cells entering the pineal gland via the posterior choroidal artery (2). Due to the proximity of the pineal gland to the third ventricle and quadrigeminal cistern, tumor cells may also reach the pineal gland via cerebrospinal fluid pathways. Primary pineal gland tumors can arise from a wide variety of cells (17). Histological diagnosis maybe not be practical due to the invasive nature of the biopsy and the deep location of the pineal gland. The presence of pineal gland lesions in patients with known malignancy increases suspicion of metastatic involvement. In the literature, some patients could not be diagnosed pathologically with an invasive procedure at one time, and more than one intervention was needed (18). Diagnosis may be made alone based on imaging. MRI has an important place in the differential diagnosis. The metastatic pineal tumors are generally significantly enhanced because of the absence of the blood-brain barrier. However, the metastatic lesions showed different degrees of

enhancement, such as heterogeneous enhancement, peripheral enhancement, or less obvious enhancement. To distinguish metastases from other tumors located in the pineal gland through imaging maybe not always possible. In these circumstances, a follow-up MRI examination needs to be considered.

One limitation of our study is the absence of a pathological diagnosis of pineal gland metastases. Another limitation of our study is the small number of patients in our study due to the rarity of pineal gland metastases. Studies that can be performed with homogeneous patient groups with a larger number of patients and with the same primary may provide more specific MRI findings in the future.

The prognosis of pineal gland metastasis is poor because it generally occurs in the late course of widely metastatic systemic cancer (5). Impaired synthesis and secretion of melatonin from suffered pineal gland may contribute to worsening of prognosis. Most of the patients in the present study died within a few months. Due to the anti-cancer effect of melatonin, melatonin may be replaced if pineal gland metastasis is discovered.

5. Conclusion

In conclusion, although uncommon, the pineal gland should not be overlooked as a site of metastases. Histological diagnosis maybe not be practical due to the invasive nature of the biopsy and the deep location of the pineal gland. Diagnosis may be made alone based on imaging. The presence of pineal gland lesions in patients with known malignancy should increase suspicion of metastatic involvement. However, a confident diagnosis through imaging maybe not always possible. In these circumstances, a follow-up MRI examination should be made.

Ethical approval

Ethical approval for this study was obtained from the ethics committee (No. E-25403353-050.99-142914, decision no: 18, Date: 12.01.2021). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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