

Locked-in Syndrome Due to Metastatic Pontomedullary Tumor

—Case Report—

Servet INCI and Tuncalp ÖZGEN

Department of Neurosurgery, School of Medicine, University of Hacettepe, Ankara, Turkey

Abstract

A 21-year-old man presented with an extremely rare case of locked-in syndrome caused by a metastatic brainstem tumor manifesting as quadriplegia, lower cranial nerve pareses, and irregular respiration. Cranial magnetic resonance imaging revealed a large pontomedullary tumor. An emergency operation was performed via a posterior fossa approach and the tumor was grossly totally removed. The histological diagnosis was malignant melanoma. The clinical status of the patient remained unchanged and he died on postoperative day 34 of diffuse bronchopneumonia. Locked-in syndrome is characterized by quadriplegia, lower cranial nerve paralysis, and mutism but with maintenance of consciousness, as well as vertical eye movements and eyelid blinking. This case suggests that locked-in syndrome should be considered in any patient seemingly comatose or stuporous, this syndrome may be due to a pontomedullary tumor, and malignant melanoma metastasis should be considered in the differential diagnosis of patients who present with brainstem tumor.

Key words: locked-in syndrome, pontomedullary tumor, malignant melanoma

Introduction

Locked-in syndrome is characterized by quadriplegia and lower cranial nerve paralysis with preservation of vertical gaze and upper eyelid movement only.¹⁹⁾ The patients remain fully conscious and alert. Most cases of locked-in syndrome are caused by ventral pontine infarction due to basilar artery occlusion,¹⁸⁾ but cases also result from other pathological processes such as trauma and infection. We treated a patient with locked-in syndrome caused by metastatic malignant melanoma.

Case Report

A previously healthy, 21-year-old man was admitted to a local hospital at the end of January 2001 because of progressive quadriparesis as well as difficulty in swallowing. Routine laboratory tests were unremarkable. Cranial cervical computed tomography did not disclose any gross abnormality. Routine cerebrospinal fluid analysis results were also within normal limits. His past medical history was

unremarkable except for suspected tuberculosis. During the following several weeks, he became almost quadriplegic. The patient was transferred to Hacettepe University Hospital, in Ankara.

On admission to our department on February 28, 2001, the patient was found to be stuporous and quadriplegic. No response to painful stimulation of the trunk and limbs was obtained. His pupils were miotic but reactive to light. The corneal reflexes were absent bilaterally. The palate was immobile and the pharyngeal reflex was absent. All deep tendon reflexes were hyperactive and the plantar responses were extensor. The only volitional movements were ocular. The patient was able to blink and move his eyes vertically, but horizontal eye movements were not possible. He was intubated and artificially ventilated because of irregular and shallow respiration. He became more alert after bronchial aspiration and mechanical ventilation.

Cranial magnetic resonance (MR) imaging revealed two intraparenchymal masses. The first lesion, extending from the medulla oblongata to the mid-pontine area, appeared as isointense on T₁-weighted images and slightly hyperintense on T₂-weighted images. The 4 × 3 × 3 cm mass showed intense, uniform enhancement after the administra-

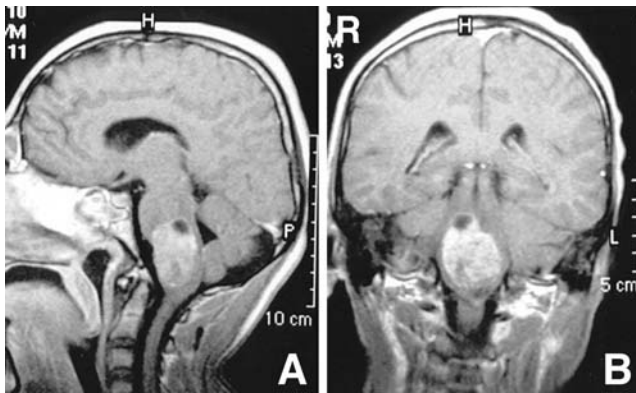


Fig. 1 Sagittal (A) and coronal (B) T₁-weighted magnetic resonance images with gadolinium revealing a large pontomedullary tumor.

tion of gadolinium-diethylenetriaminepenta-acetic acid (Fig. 1). The second lesion was located in the left frontal lobe adjacent to the frontal horn. This small 1 × 1 × 1 cm lesion had similar radiological features. On the basis of these imaging studies, the diagnosis was metastatic tumor or tuberculoma. We thought removal of the pontomedullary tumor was justified because of the neurological signs.

One day after admission, a midline suboccipital craniotomy was performed. Apparent swelling of the medulla oblongata was observed. A dark brown tumor was seen between the cerebellar tonsils. The tumor was very vascular and bleeding was controlled with difficulty. The tumor borders were clearly defined. The cleavage plane between the tumor and neural tissue allowed gross total removal of the tumor. The left frontal tumor, which was small and silent, was not removed.

On the following day, the patient regained consciousness but remained completely quadriplegic. The right corneal reflex returned to normal, but the left reflex was still absent. Opening and closing of the eyes and vertical eye movements remained the only means of communication, typical of locked-in syndrome. Tracheotomy was performed on the 4th postoperative day. Control MR imaging demonstrated gross total removal of the tumor (Fig. 2).

Histological examination revealed a highly vascular and necrotic neoplasm with distinct borders. The tumor consisted of neoplastic cells containing eosinophilic cytoplasm with large vesicular nuclei and prominent nucleoli (Fig. 3). Routine immunostaining of paraffin-embedded tissue was positive for S-100 protein and HMB-45 (melanoma-specific antigen) (Fig. 4). The tumor cells did not react with antibodies to glial fibrillary acidic protein, epithelial membrane antigen, and cytokeratin. The histologi-

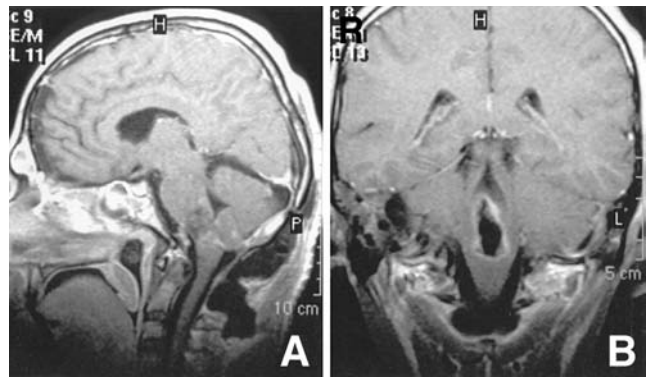


Fig. 2 Postoperative sagittal (A) and coronal (B) T₁-weighted magnetic resonance images with gadolinium demonstrating gross total removal of the tumor.

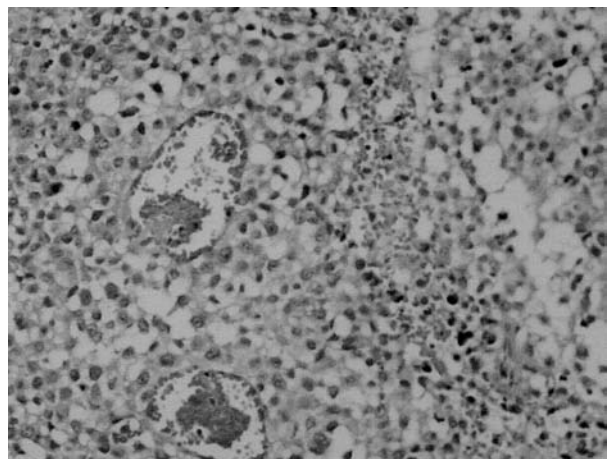


Fig. 3 Photomicrograph of the vascular and necrotic tumor showing large neoplastic cells containing nuclei with prominent nucleoli. Hematoxylin and eosin stain, ×40.

cal diagnosis was malignant melanoma.

Further examination found no pigmented skin lesion or lymphadenopathy, but his father indicated a superficial black lesion, 1 × 1 cm in diameter, had been excised from the patient's scalp one year previously. The clinical status of the patient remained unchanged until he died 34 days later of diffuse bronchopneumonia and sepsis. Unfortunately, necropsy examination was not possible.

Discussion

Locked-in syndrome is a state of quadriplegia and lower cranial nerve pareses in which vertical eye

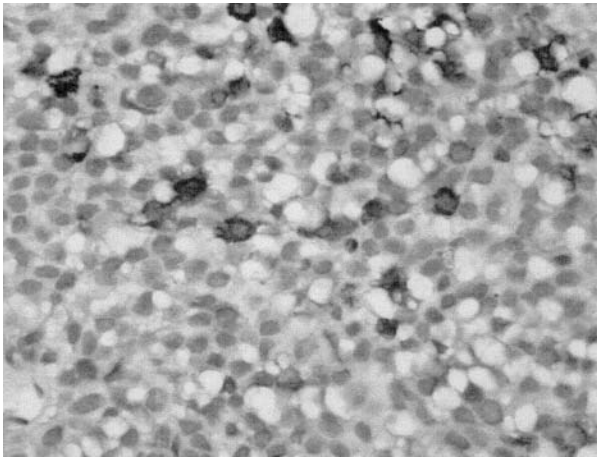


Fig. 4 Immunohistochemical staining showing focal but strong positivity for HMB-45 in the neoplastic cells. $\times 200$.

movements and blinking are the only means of communication. The mind is literally locked inside the body with the patient remaining aware of the environment but unable to move. This syndrome was first described in 1966 in a patient who was quadriplegic and mute but fully alert.¹⁹⁾ The cause was bilateral interruption of the descending corticospinal and corticobulbar tracts by an infarction of the ventral pons. The preservation of consciousness in this syndrome is thought to reflect the sparing of the reticular structures located in the tegmentum of the pons and midbrain, essential for the maintenance of alertness.^{4,16)} The patients are not aphasic but are aphonic because of lower cranial nerve pareses. The preservation of vertical eye movements and blinking is due to the sparing of the tegmental corticobulbar tracts that innervate the third cranial nerve nuclei. Horizontal gaze palsy, a common feature of locked-in syndrome, is due to abducens nerve paralysis following destruction of the nerve nucleus or root crossing the ventral pons.²¹⁾ In incomplete cases, horizontal eye movement may be a favorable prognostic sign.²⁵⁾ The convergence movement systems are intact because the motor center is located in the mesencephalon. Ocular bobbing²³⁾ and oral automatism²⁾ have also been described in this syndrome but are not essential signs. Some involuntary motor phenomena such as yawning and mastication may rarely be seen.¹⁾

Locked-in syndrome has also been called a deafferented state, in reference to the interruptions in the motor pathways, pseudocoma, ventral pontine syndrome, and cerebromedullospinal disconnection, which describes the anatomical pathology.^{16,18,24)} This syndrome must be distinguished clin-

ically from coma and akinetic mutism. Coma is a state of complete unconsciousness in which the ascending reticular formation in the brainstem and diencephalon is damaged. The comatose patient cannot be aroused and the eyes remain closed. In akinetic mutism, first described in a patient with an epidermoid cyst of the third ventricle,⁶⁾ the patient is not quadriplegic and appears to be awake but is not aware of the environment, has no response to commands, and does not speak or react voluntarily. Communication cannot be established despite the superficial appearance of alert wakefulness. In contrast, the locked-in state preserves the consciousness and higher cortical functions. The patient can communicate by blinking and vertical eye movements, answer yes/no questions appropriately, and choose from a list. This differentiation is important for ethical and legal considerations.

The most common cause of locked-in syndrome is infarction of the basis pontis following basilar artery occlusion.^{18,21)} Other possible causes are head trauma,^{3,10)} pontine hemorrhage,¹²⁾ infection,^{13,15)} central pontine myelinosis,¹⁴⁾ and multiple sclerosis.⁸⁾ Some cases of locked-in syndrome were caused by primary pontomedullary tumor.^{5,9,11)} However, only one previous case of this syndrome caused by a metastatic pontomedullary tumor from adenocarcinoma of the lung has been reported.²⁰⁾

The prognosis for patients with locked-in syndrome is poor. Review of 139 cases of this syndrome found that the mortality is high, approximately 60%, and death most frequently occurs within the first 4 months.¹⁸⁾ Only two patients survived for more than one year. The most important cause of death is respiratory complications, as in our case.

Our case also presented with another rare condition, metastatic brainstem malignant melanoma. Malignant melanoma can spread throughout the body, including the central nervous system, and is the third most common tumor to metastasize to the brain, after lung and breast cancers.^{17,22)} However, metastasis to the brainstem is exceedingly rare. A series of 702 patients with metastatic central nervous system melanoma included only 0.9% of cases in the brainstem.²²⁾ The long-term prognosis for patients with metastatic melanoma of the brain is very poor. The mean duration of survival is less than 6 months following diagnosis.⁷⁾

This case raises three points: the possibility of locked-in syndrome should not be overlooked in any patient seemingly comatose or stuporous; this syndrome may be due to a pontomedullary tumor; and malignant melanoma metastasis, although rare, should be considered in the differential diagnosis of patients who present with brainstem tumor.

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Address reprint requests to: S. Inci, M.D., Department of Neurosurgery, School of Medicine, University of Hacettepe, Emek Mahallesi, 4. Cadde, No:70/8, 06510 Ankara, Turkey.
e-mail: servet@mailcity.com