

Parkinsonism Related to Brain Tumors: A Case Report and Review of the Literature

Takao Yasuhara*, Takashi Agari, Hirokazu Kambara, Tomotsugu Ichikawa, Kazuhiko Kurozumi, Shigeki Ono, Yasuyuki Miyoshi, Koji Tokunaga and Isao Date

Department of Neurological Surgery, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama, 700-8558, Japan

Abstract: Parkinsonism related to brain tumor is reviewed with the presentation of our case. Neurosurgeons or neurologists know that some patients with brain tumor present parkinsonism, although further enlightenment is required. The mechanisms are divided into 6 subgroups, 1. direct oppression to the basal ganglia; 2. distortion and stress to the mid-brain; 3. neuronal loss in the substantia nigra; 4. involvement of the basal ganglia; 5. damage of the fiber connection between the basal ganglia and supplementary motor area; 6. old age. In the recent 11 years, 16 cases were reported. Pediatric cases, localized cases with relatively small lesion and post-irradiation cases were increasingly reported. The prognoses of brain tumor-related parkinsonism varied and independent of the pathology, location, and therapies of the tumor. All we can do is to select the appropriate therapy including surgical removal of the tumor by the correct estimation of the damaged region.

Keywords: Basal ganglia, brain stem, pediatric brain tumor, parkinsonism.

INTRODUCTION

The cardinal symptoms of Parkinson's disease are akinesia, rigidity, resting tremor and impairment of the postural reflex. As widely understood, parkinsonism is divided into idiopathic parkinsonism including Parkinson's disease and symptomatic parkinsonism with causative diseases. In this article, our case of parkinsonism related to brain tumor is presented with review of the literature.

CASE PRESENTATION

1. Our Case with Dystonia after Multimodal Therapy for Germ Cell Tumor at the Pineal Region

A 29-year-old man admitted to our institute for the movement disorder of eyes and gait disturbance. CT and MRI demonstrated heterogeneously enhanced mass at the pineal region with involvement in the right substantia nigra (Fig. 1A). The patient received endoscopic biopsy and subsequently diagnosed as germ cell tumor (germinoma). Three courses of chemotherapy using Ifosfamide, carboplatin and etoposide were performed. Then irradiation to the whole brain at 30Gy and local irradiation at 24 Gy were added. The tumor was completely controlled with no enhanced lesion in Gd-T1 weighted image of MRI after another course of chemotherapy, although the scar remained at the right midbrain (Fig. 1B). On the course of chemotherapy, the patient received endoscopic third ventriculostomy for hydrocephalus. At 2 months after discharge, dystonia with rigidity of the left elbow and hand appeared. Medication using dopamine,

efficient effects on the symptoms. Thalamotomy was performed after our diagnosis that the tumor damaged the dopaminergic neuronal systems at the substantia nigra and the surrounding structures, even though the tumor was controlled. The rigidity of his elbow was moderately ameliorated by the surgery, although the symptoms of his hand were not improved at all. Additionally, we tried the electrical stimulation for the left forearm at low frequency. However, the symptoms of his hand were minimally improved. For 2 years, the ADL of the patient was stable with the impaired hand (KPS: 70), although the tumor was completely controlled.

DISCUSSION

1. Historic Background of Brain Tumor and Parkinsonism

After the case report of brain tumor with parkinsonism was initially reported in 1953 [1], several reports and reviews were followed. In 1997, Kondo and colleagues reported an excellent review paper entitled as 'brain tumor and parkinsonism' [2]. They demonstrated that the number of reports on brain tumor and parkinsonism might decrease, although there were many reports before publication of their initial review. The reason might be the publicity of parkinsonism induced by brain tumor among clinicians and the early diagnosis of brain tumor before manifestation of parkinsonism by development of the diagnostic imaging technique. Between 1997 and 2008, only 16 cases were reported for 11 years (Table 1). Pediatric cases, localized cases and post-irradiation cases were increasingly reported for recent 11 years. At the same time, as recognized in previous reports, large brain tumors such as frontal astrocytoma and meningioma of adult might constitute a majority including unreported cases.

*Address correspondence to this author at the Department of Neurological surgery, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, 2-5-1, Shikata-cho, Okayama, 700-8558, Japan; Tel: 81-86-235-7336; Fax: 81-86-227-0191; E-mail: tyasu37@cc.okayama-u.ac.jp

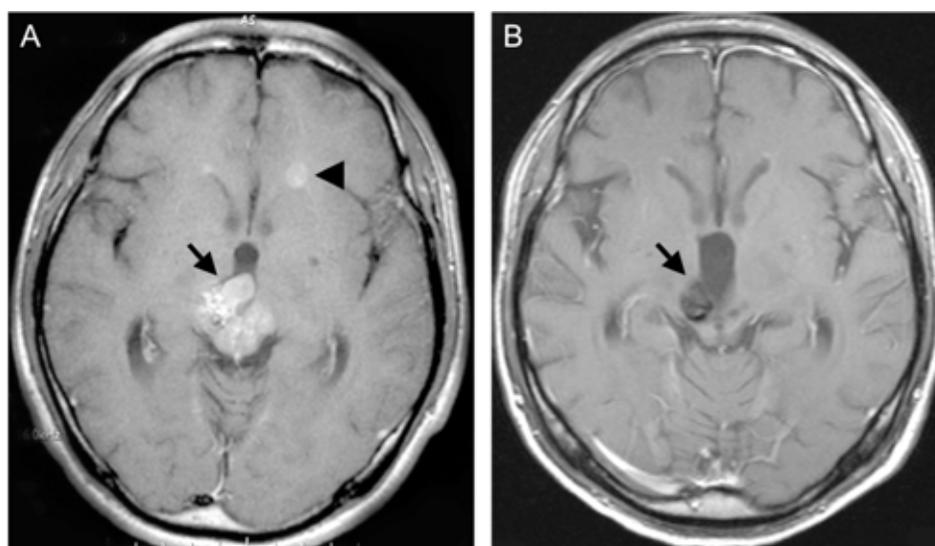


Fig. (1). Germ cell tumor at the pineal region.

A: Gd-enhanced T1-weighted image of MRI demonstrates the heterogeneously enhanced lesion (arrow) with the longitudinal extension from the pineal region and involvement in the right substantia nigra. A small round lesion with slight enhancement (arrowhead) was also found at the anterior horn of the left lateral ventricle.

B: Gd-enhanced T1-weighted image of MRI demonstrates the non-enhanced small lesion (arrow) with the involvement in the right substantia nigra.

Table 1. A Summary of Case Reports about Parkinsonism Related to Brain Tumor in the Recent 11 Years

Year	Author	Age, Sex	Pathology	Legion Site	Clinical Symptoms	Therapy	Prognosis
1999	Pohle T	10y. M	low grade glioma	iencephalons-cerebral peduncle	resting tremor, bradykinesia, rigidity	surgery+radiation	improved
		3.5y. M	low grade glioma	pontomesencephalon	reduced appetite, gait disturbance	N/A	N/A
1999	Cicarelli G	39y. F	cystic glioma	pontomesencephalon	vertigo, rigidity	surgery	improved
1999	Pramstaller PP	75y. M	PCNSL	bilateral basal ganglia	micrographia, nuchal ridigity	steroid+radiation	worsen/died
2000	Wenning GK	59y. F	meningioma (1y. post surgery)	frontal lobe	resting tremor	no treatment	improved
2000	Salvati M	61y. M	meningioma	fronto-temporal lobe	tremor, rigidity, bradykinesia	surgery	improved
2001	Vhora S	55y. F	cavernoma	pineal region	tremor, rigidity, akinesia	DOPA, amantadine	no change
						surgery	improved
2001	Guerra MS	64y. F	PCNSL	basal ganglia, cerebellum	bradykinesia, rigidity, tremor	N/A	died
2003	Skiming JA	1.5y. F	pNET	posterior fossa		surgery+CT+radiation	
			(radiation)	(T2 high lesion in bil. GP)	akinesia, tremor	benztropine	improved
2003	Yoshikawa H	12y. F	glioma	frontal lobe (tumor)		surgery	no change
			calcification	striopallidodentate region	rigidity	no treatment	improved

(Table 1). Contd.....

Year	Author	Age, Sex	Pathology	Legion Site	Clinical Symptoms	Therapy	Prognosis
2004	Molho ES	85y. M	gliomatosis cerebri	cerebral white mater-brain stem	gait disturbance	L-DOPA	worsened/died
2005	Ertan S	56y. M	cavernoma	basal ganglia	tremor, bradykinesia	L-DOPA	no change
2006	Voermans NC	14y. F	craniopharyngioma	seller region	hypokinesia, rigidity	surgery+radiation	
			(radiation)	(T2 high lesion in bil. GP)		L-DOPA	a little improved
							then, spontaneously improved
2007	Burkhardt K	85y. M	pilocytic astrocytoma	brain stem	N/A	N/A	N/A
2007	Asada T	70y. M	gliomatosis cerebri	bilateral fronto-parietal lobe	frozen gait, tremor, rigidity	anti-convulsant	worsened
2008	Ho BL	60y. M	glioma	temporal lobe-basal ganglia	tremor, bradykinesia	surgery	improved

The age of cases varied from 1.5 to 85 years old. The most common histology was glioma. Tumors usually localized at the basal ganglia or brain stem. Almost all cases presented several symptoms of the cardinal symptoms of parkinsonism. The selected therapies and responses also varied, which indicated that appropriate therapies can not be selected by the histology or the location of the tumor. PCNSL: primary central nervous system lymphoma, GP: globus pallidus, N/A: not applicable.

2. Symptoms of Parkinsonism Induced by Brain Tumor

As shown in the table, most of the cases presented more than one symptoms of Parkinson's disease. In the review paper by Kondo [2], 44% (32/73 cases) of the patients with brain tumor presenting parkinsonism began at only parkinsonism and the half began at parkinsonism with or without other symptoms. Taking into account 16 cases found for recent 11 years, 63% (56/89 cases) of the patients initially manifested parkinsonism, which indicated that cases presenting parkinsonism as an initial symptom might be increasingly reported. In association with this, half of the cases, reported recently (8/16 cases) had a relatively small lesion, which directly affected nigrostriatal systems or nucleus in the circuit of the basal ganglia. In consideration of these facts, the cases of a large brain tumor with brain edema, presenting initially other neurological deficits followed by parkinsonism might decrease in number.

3. Pathology of Brain Tumors which Cause Parkinsonism

As described in the previous section, large meningiomas or astrocytomas were frequently reported. The pathology of the recent 16 cases were 8 gliomas (including 2 gliomatosis cerebri) [3-10], 2 meningiomas [11, 12], 2 malignant lymphomas [13, 14], 2 angiomas [15, 16], 1 craniopharyngioma [17], 1 primitive neuroectodermal tumor (PNET) [18]. A case of gliomatosis cerebri was misdiagnosed and treated as multiple system atrophy, because of the unusual clinical manifestation including extreme old age, parkinsonism as an initial symptom, and the lack of high intensity area extending into the white matter in FLAIR and T2-weighted images of MRI. The necropsy revealed the diffuse cell infiltration into the whole brain including the substantia nigra. This case might be a good lesson, although it might be very rare [4].

4. Treatment and Prognosis of Parkinsonism Induced by Brain Tumor

In order to assess the appropriate therapy and the reliable prognosis of parkinsonism induced by brain tumor, the oc-

currence mechanisms should be considered. Kondo and colleagues propounded 6 reasonable mechanisms of it: 1. direct oppression to the basal ganglia of the tumor itself; 2. distortion and stress to the midbrain; 3. neuronal loss in the substantia nigra by the tumor invasion; 4. involvement of the basal ganglia by the deep-seated tumor; 5. damage of the fiber connection between the basal ganglia and supplementary motor area; 6. old age. In case of direct oppression to the basal ganglia of the tumor itself or damage of fiber connection between the basal ganglia and supplementary motor area, tumor removal and subsequent relief of the disease state might ameliorate symptoms. Practically, a case of large meningioma [12] or transient encephalopathy with brain edema after irradiation [18] might hold true. On the other hand, cases by distortion and stress to the midbrain or neuronal loss in the substantia nigra by the tumor invasion might respond well to the replacement of dopamine theoretically. However in the recent reports, the medication using dopamine exerted almost no or weak therapeutic effects on many cases with parkinsonism. The reason might be the severe and irreversible impairment at the initiation of the medication. Furthermore, the therapeutic effects on cases with involvement of the basal ganglia by the deep-seated tumor might depend on whether the function of dopamine receptor was preserved or not. Anyway, the early diagnosis and the exploration for the appropriate therapy including surgical removal might critically determine the outcomes of the patients. Additionally, severe prognoses of PCNSL patients with parkinsonism should be noted.

5. Characteristics of Tumor-Related Parkinsonism in Pediatrics

Parkinsonism in pediatrics is rare. Brain tumors as well as cerebral ischemia and trauma might also cause parkinsonism. The prognosis is generally good if the primary disease is correctly treated with the relief of symptoms at the acute stage [19]. In recent reports, 3 cases demonstrated remarkable amelioration of symptoms in the 4 cases under 14 years old [3, 6, 17, 18]. At 6 months after irradiation, 2 cases

with PNET and craniopharyngioma presented parkinsonism temporarily with high intensity lesion in T2-weighted image of MRI at the globus pallidum. The former ameliorated the symptoms with the administration of anti-cholinergic agent at 7 months after irradiation and the latter spontaneously resolved symptoms at 9 months after irradiation.

CONCLUSIONS

We reviewed the previous reports about parkinsonism related to brain tumor with the presentation of our related case. Recently, brain tumor is recognized as a reason for movement disorders including Parkinson's disease for neurosurgeons and neurologists. Further enlightenment is required for clinicians to prevent delayed diagnosis and wrong therapy for cases of brain tumor with movement disorders, although the effective therapy and prognosis might differ in each case. Unfortunately some cases are difficult to be treated finely. At now, we need to select the appropriate therapy for the patients by estimating the damaged region immediately.

REFERENCES

- [1] Margulies ME. Parkinsonism and brain tumor. *J Nerv Ment Dis* 1953; 117: 550-2.
- [2] Kondo T. Brain tumor and parkinsonism. *Nippon Rinsho* 1997; 55: 118-22.
- [3] Pohle T, Krauss JK. Parkinsonism in children resulting from mesencephalic tumors. *Mov Disord* 1999; 14: 842-6.
- [4] Molho ES. Gliomatosis cerebri may present as an atypical Parkinsonian syndrome. *Mov Disord* 2004; 19: 341-4.
- [5] Cicarelli G, Pellicchia MT, Maiuri F, *et al.* Brain stem cystic astrocytoma presenting with "pure" parkinsonism. *Mov Disord* 1999; 14: 364-6.
- [6] Yoshikawa H, Abe T. Transient parkinsonism in bilateral striopallidodentate calcinosis. *Pediatr Neurol* 2003; 29: 75-7.
- [7] Yoshimura M, Yamamoto T, Iso-o N, *et al.* Hemiparkinsonism associated with a mesencephalic tumor. *J Neurol Sci* 2002; 197: 89-92.
- [8] Asada T, Takayama Y, Tokuriki Y, *et al.* Gliomatosis cerebri presenting as a parkinsonian syndrome. *J Neuroimaging* 2007; 17: 269-71.
- [9] Burkhardt K, Heuberger F, Delavelle J. Pilocytic astrocytoma in the elderly. *Clin Neuropathol* 2007; 26: 306-10.
- [10] Ho BI, Lieu AS, Hsu CY. Hemiparkinsonism secondary to an infiltrative astrocytoma. *Neurologist* 2008; 14: 258-61.
- [11] Wenning GK, Luginger E, Sailer U, *et al.* Postoperative parkinsonian tremor in a patient with a frontal meningioma. *Mov Disord* 1999; 14: 366-8.
- [12] Salvati M, Frati A, Ferrari P, *et al.* Parkinsonian syndrome in a patient with a pterional meningioma: case report and review of the literature. *Clin Neurol Neurosurg* 2000; 102: 243-5.
- [13] Pramstaller PP, Salerno A, Bhatia K, *et al.* Primary central nervous system lymphoma presenting with a parkinsonian syndrome of pure akinesia. *J Neurol* 1999; 246: 934-8.
- [14] Sanchez-Guerra M, Cerezal L, Leno C, *et al.* Primary brain lymphoma presenting as Parkinson's disease. *Neuroradiology* 2001; 43: 36-40.
- [15] Vhora S, Kobayashi S, Okudera H. Pineal cavernous angioma presenting with parkinsonism. *J Clin Neurosci* 2001; 8: 263-66.
- [16] Ertan S, Gulcin B, Tanriverdi T, *et al.* Parkinsonism caused by cavernoma located in basal ganglion. *Parkinsonism Relat Disord* 2005; 11: 517-9.
- [17] Voermans NC, Bloem BR, Janssens G, *et al.* Secondary parkinsonism in childhood: a rare complication after radiotherapy. *Pediatr Neurol* 2006; 34: 495-8.
- [18] Skimming JA, McDowell HP, Wright N, *et al.* Secondary parkinsonism: an unusual late complication of craniospinal radiotherapy given to a 16-month child. *Med Pediatr Oncol* 2003; 40: 132-134.
- [19] Pranzatelli MR, Mott SH, Pavlakis SG, *et al.* Clinical spectrum of secondary parkinsonism in childhood: a reversible disorder. *Pediatr Neurol* 1994; 10: 131-40.

Received: January 18, 2009

Revised: February 28, 2009

Accepted: March 12, 2009

© Yasuhara *et al.*; Licensee *Bentham Open*.

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.