Journal of Neuro-Oncology **15**: 45–49, 1993.

Clinical Study

Diffuse primary leptomeningeal gliomatosis

G. Davila, C. Duyckaerts,* J.P. Lazareth, M. Poisson and J.Y. Delattre
Departments of Neurology (Pr. Brunet) and Neuropathology, Hôpital de la Salpétrière. 47 Bd. de l'Hôpital. 75651 Paris Cedex 13, France*

Key words: leptomeningeal gliomatosis, meningeal metastases, glioma, astrocytoma

Abstract

A 38 year old patient developed multiple cranial nerve palsy, seizures and progressive alteration in consciousness. CSF examination revealed tumor cells and a tentative diagnosis of leptomeningeal carcinomatosis from an unknown primary tumor was made. Treatment with intrathecal methotrexate and cranial radiation therapy was started without effect. At autopsy widespread leptomeningeal gliomatosis originating from a previously unknown astrocytoma of the hippocampus was found.

Introduction

Metastatic seeding of the leptomeninges by gliomatous cells is a well known, generally delayed, complication of CNS gliomas [1–14]. The occurence of a diffuse form of leptomeningeal gliomatosis (LMG) without known primary tumor is rare. Only 6 cases have been previously reported [15–20]. We evaluated an additional case.

Case report

A 38 year old man developed a right sided hearing loss with tinnitus and vertigo in december 1988. Two weeks later, he had a generalized seizure and was admitted to an outside hospital where a CT scan of the head and a lumbar puncture were normal. Over the following month, he complained of a left side hearing loss. He also experienced diffuse pain in the extremities and had a 10 kg loss of weight. He was admitted at the Salpêtrière hospital on February 1989. On examination, he had an unsteady and broad based gait. Multidirectional nystagmus, right facial palsy, and bilateral sensorineural deafness were found. CT scan and MRI revealed contrast enhancement in the cerebello-pontine angles and in the basal cisterns. CSF was sterile and contained 66 WBC/mm^3, 79% of which were lymphocytes; protein was 3,4 g/l; CSF glucose was 16 mg/100 ml (blood glucose 92 mg 100/ml). Repeated lumbar punctures showed the presence of tumor cells. No primary tumor was found despite extensive investigations. A diagnosis of meningeal carcinomatosis from an unknown primary tumor was made. The patient received two intrathecal injections of methotrexate and a course of whole brain radiation therapy (RT) was started. He received 10 Gy in 2 fractions but RT had to be discontinued because of clinical deterioration. The patient developed left ophthalmoplegia, dysarthria, dysphagia and became stuporous. Repeated CT scan showed progression of the contrast enhancing lesions in the basal cisterns and over the cortical sulci. His condition deteriorated rapidly and he died 3 months after the first symptom.

Postmortem examination

Autopsy was performed 24 hours after death. A right bronchopneumonia was found. No others ab-

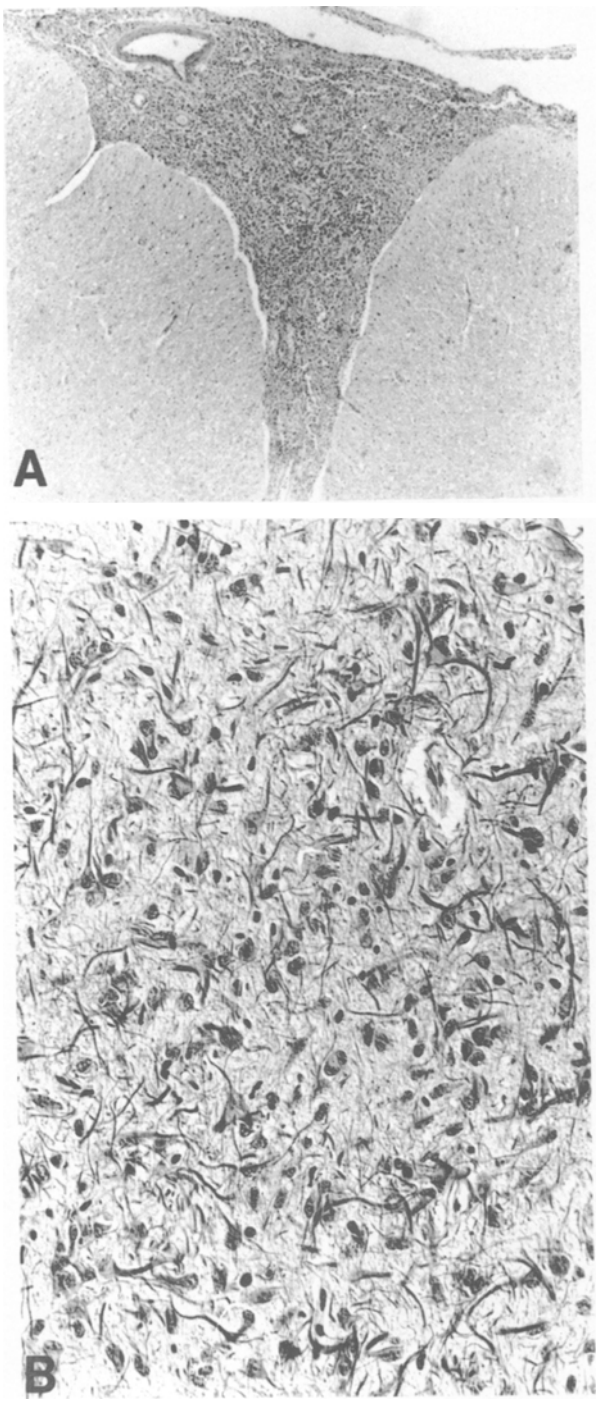

Fig. 1. A. Spinal cord. Cervical level (C7). Haematein-Eosin × 45. Diffuse infiltration of the subarachnoid space by tumoral astrocytes. B. Right hippocampus. Mallory. Phosphatungstic-Haematoxylin × 130. Numerous glial filaments in the tumor invading parenchym.

normalities were noticed outside the nervous system.

The leptomeninges of the cerebrum, cerebellum, and spinal cord were diffusely thickened. The third, seventh and eighth cranial nerves, as well as the roots of the cauda equina were irregularly swollen. On section, infiltration of the right hippocampus and fornix was noted.

Microscopically, the right Ammon's horn was invaded by protoplasmic and fusiform astrocytes (Fig. 1B). There was no vascular proliferation, necrosis nor hemorrhage.

The cerebral and spinal subarachnoid spaces were diffusely infiltrated by the same tumor (Fig. 1A). Fusiform, GFAP positive, tumoral cells were also found along the Virchow-Robin spaces, sometimes invading the superficial cortical layers. The oculomotor nerves and the dorsal roots of the spinal cord were widely infiltrated. Occasionally, the glioma cells were large, with a high nuclear-cytoplasmic ratio, and a few monstrous nuclei.

Based on these findings, a final diagnosis of right hippocampus astrocytoma with diffuse meningeal dissemination was made.

Discussion

Leptomeningeal gliomatosis (LMG) occurs in three different settings. In 20 to 25% of patients suffering from extensive recurrence of intracerebral gliomas, meningeal dissemination is an accessory event during the terminal phase of the disease or an autopsy finding [6, 8, 21]. More rarely (less than 3% of the cases) fatal meningeal dissemination occurs in the absence of recurrence of a known primary glioma [14]. The rarest condition is primary LMG during which there is not known parenchymatous tumour [15]. The meningeal tumor may arise from early meningeal seed of an asymptomatic intraparenchymal glioma or from a heterotopic glioma [22]. Russel and Rubinstein [23] emphasized that the diagnosis of LMG from primary heterotopic glioma should be viewed with skepticism since it is difficult to sample the entire CNS to exclude the presence of a small intraparenchymatous glioma responsible for the subarach-

Table 1. Characteristics of patients with a diffuse primary leptomeningeal gliomatosis

Authors year	Age sex	Clinical picture	CSF					Myelography or spinal MRI	Ventriculography cranial CT scan	Clinical diagnosis	Tumor treatment	Time between first symptoms and death	Pathology
			Opening pressure mm H_2O	Protein mg/dl	Glucose mg/dl	Cytology	Malignant cells						
Korein *et al.* 1957 [15]	16, M	S, H, C, P. Hemiparesis Nystagmus Hemianopia	500	54	ND	ND	Negative	ND	Hydrocephalus	Serous meningitis	ND	9 years	Anaplastic oligodendro-glioma
Sumi *et al.* 1968 [16]	61, H	S, H, C, P. Hemiparesis III palsy	240	248	36	14 WBC	Negative	ND	Hydrocephalus	Unknown	ND	6 months	Astrocytoma
Bhrany *et al.* 1974 [17]	46, F	S, H, C. Tetraparesis Multiple cranial nerve palsies	430	1060	49	No WBC	Negative	Normal	Hydrocephalus	Unknown	ND	16 months	Astrocytoma
Simonati *et al.* 1981 [18]	19, F	Headache VI palsy Sphincterial incontinence Paraplegy Bulbar palsy	ND	'High'	ND	ND	ND	D7–D10 block	Hydrocephalus	Unknown	Radiation therapy	5 years	Astrocytoma
Ho *et al.* 1981 [19]	55, M	H, C, S, P. Loss of coordination	150	1150	60	58 WBC 80% lympho-cytes	Negative	ND	Hydrocephalus	Tuberculous meningitis	ND	3 months	Astrocytoma
Kitahara *et al.* 1985 [20]	15, F	H, P. Unsteadiness of gait Nystagmus Gaze palsy Tetraparesis	ND	99	79	3 WBC	Positive	ND	Hydrocephalus Enhancement of basal cisterns	Meningeal tumor of unknown origin	ACNU (Intrathecal) Radiation therapy 60 Gy	3.5 years	Astrocytoma
Present case 1992	38, H	Deafness Seizures Unsteadiness of gait Nystagmus VII palsy	ND	340	16	66 WBC 79% lympho-cytes	Positive	ND	Enhancement of basal cisterns	Meningeal carcino-matosis	Methotrexate (Intrathecal) Radiation therapy 10 Gy	3 months	Astrocytoma

S = Seizure; H = Headache; C = Confusion; P = Papilledema; ND = Not done.

noid spread. Furthermore, it may be difficult, even at autopsy, to differentiate a primary intraparenchymatous glioma with secondary meningeal seeding from primary LMG with secondary invasion of the brain [16]. In contrast with meningeal carcinomatosis, the clinical picture of primary leptomeningeal gliomatosis is most often that of a focal progressively expanding mass of the brain or spinal cord and the meningeal location of the tumor is an unexpected surgical or pathological discovery [15]. This finding indicates that glioma cells generally do not have the ability to detach from the primary focus, to seed the meninges and to grow in multiple sites, possibly because a desmoplastic reaction limit the risk of dissemination. However, a diffuse form of primary LMG has been rarely reported (Table). The clinical presentation is then similar to leptomeningeal carcinomatosis with a mixture of cerebral, cranial nerves and spinal signs of a subacute progression [19], as illustrated by our patient. In the 7 reported cases (including ours), radiological and laboratory studies showed non specific abnormalities. On CT scan, hydrocephalus was the most common finding (6/7 patients) sometimes associated with contrast enhancement of the basal cisterns (2/4). The CSF was always abnormal during the course of the disease: increased opening pressure (3/4 patients); increased protein concentration (7/7 patients); low glucose concentration (2/5); increased number of lymphocytes (3/5). Only 2/7 patients had tumor cells in the CSF and their glial origin was not identified.

GFAP immunostaining is sometimes useful to identify the glial origin of tumoral cells in the CSF [24]. This staining should be performed when tumor cells are identified in the CSF in the absence of a known primary tumor. Whether earlier diagnosis will improve the prognosis remains to be seen. The prognosis of the diffuse type of primary LMG is poor but the course of the disease varies widely (Table 1). In our case, the duration of survival was only 3 months after the first symptoms. On the other hand, Korein *et al.* [15] reported a patient who had a diagnosis of petit mal epilepsy related to an oligodendroglioma in temporal subarachnoid space for 9 years prior to death from LMG. None of the reported patients had a highly malignant glioma. There was no correlation between the course of the disease and the histological features of the tumor. For example, the patient reported by Sumi *et al.* [16] deteriorated rapidly despite the histological features of a slow growing 'benign' tumor. The reason why the cells of a few and often low grade gliomas have a propensity to seed and to invade the meninges diffusely and massively while the parenchyma is relatively spared, remains unknown.

References

1. Spiller WG: Gliomatosis of the pia and metastasis of glioma. J Neurol Mental Dis 34: 297–302, 1907
2. Cairns H, Russell DS: Intracranial and spinal metastases in gliomas of the brain. Brain 54: 377–419, 1931
3. Russell DS, Cairns H: Spinal metastasis in a case of cerebral glioma of the type known as astrocytoma fibrillare. J Path 33: 383–391, 1930
4. Eade OE, Urich H: Metastasising gliomas in young subjects. J Path 103: 245–256, 1971
5. McLaughlin JE: Juvenile Astrocytomas with subarachnoid spread. J Path 118: 101–107, 1976
6. Erlich SS, Richard LD: Spinal subarachnoid metastasis from primary intracranial glioblastoma multiforme. Cancer 42: 2854–2864, 1978
7. Kowano N, Miyasaka Y, Yada K, Atari H: Diffuse cerebrospinal gliomatosis. J Neurosurg 49: 303–307, 1978
8. Yung WKA, Horten BC, Shapiro WR: Meningeal gliomatosis: A review of 12 cases. Ann Neurol 8: 605–608, 1980
9. Vincent FM: Spinal leptomeningeal invasion from intracranial glioblastoma multiforme. Arch Phys Med Rehabil 64: 34–36, 1983
10. Packer RJ, Allen J: Brainstem glioma: Clinical manifestations of meningeal gliomatosis. Ann Neurol 14: 177–182, 1983
11. Awad I, Bay JW, Rogers L: Leptomeningeal metastasis from supratentorial malignant gliomas. Neurosurgery 19: 247–251, 1986
12. Choucair AK, Levin VA: Development of multiple lesions during radiation therapy and chemotherapy in patients with gliomas. J Neurosurg 65: 654–658, 1986
13. Vries EP, Visser M, Troost D: Supratentorial meningeal spread from brainstem glioma. J Neurol Neurosurg Psychiatry 1011–1013, 1989
14. Delattre JY, Walker RW, Rosenblum MK: Leptomeningeal gliomatosis with spinal cord or cauda equina compression: a complication of supratentorial gliomas in adults. Acta Neurol Scand 79: 133–139, 1989
15. Korein J, Feigin I, Shapiro M: Oligodendrogliomatosis with intracranial hypertension. Neurology 7: 589–594, 1957
16. Sumi SM, Leffman H: Primary intracranial leptomeningeal

glioma with persistent hypoglycorrhachia. J Neurol Neurosurg Psychiatry 31: 190–194, 1968
17. Bhrany D, Murphy M, Horenstein S, Silbert S: Diffuse periventricular and meningeal glioma. Acta Neuropath (Berl) 30: 243–249, 1974
18. Simonatti A, Mazza C, Rizzuto N: An unusual case of meningeal gliomatosis. Acta Neuropathol (Berl) Suppl VII 97–100, 1981
19. Ho KL, Hoschner JA, Wolfe DE: Primary leptomeningeal gliomatosis. Symptoms suggestive of meningitis. Arch Neurol 38: 662–666, 1981
20. Kitahara M, Katakura R, Wada T, Namiki T, Suzuki J: Diffuse form of primary leptomeningeal gliomatosis. J Neurosurg 63: 283–287, 1985
21. Polmeter FE, Hernohan JW: Meningeal gliomatosis. Arch Neurol Psych 57: 593–616, 1974
22. Cooper I, Kernohan J: Heterotopic glial nests in subarachnoid space: Histopathologic characteristics, mode of origin and relation to meningeal gliomas. J Neuropath Exp Neurol 10: 16–29, 1951
23. Russel DS, Rubinstein LJ. Pathology of tumors of the nervous system. Arnold, London, 4th ed, 1977, p 26–27, 341–347
24. Wechsler LR, Gross RA, Miller DC: Meningeal gliomatosis with negative CSF cytology: The value of GFAP staining. Neurology 34: 1611–1615, 1984

Address for offprints: J.Y. Delattre, Hôpital de la Salpétrière, Service de Neurologie, Division Mazarin, 47 Bd. de l'Hôpital, 75651 Paris Cedex 13, France