Neuropathology 2004; **24**, 336–340

Case Report

Meningioma–primary brain lymphoma association

Anna Maria Buccoliero,[1] Gian Luigi Taddei,[1] Adele Caldarella,[1] Pasquale Mennonna,[2] Franco Ammannati,[2] Antonio Taddei[3] and Furio Mariotti[2]

[1]Department of Human Pathology and Oncology, Medical School, University of Florence, [2]Unit of Neurosurgery, Careggi Hospital and [3]Department of General Surgery, Medical School, University of Florence, Florence, Italy

The authors report a rare meningioma–primary cerebral B cell lymphoma association that occurred in an insulin-dependent type-I diabetic woman. The woman was initially operated on because of meningothelial meningioma of the fronto-basal region, and 2 months later showed a primitive-non-Hodgkin B cell lymphoma, localized in the same area as the meningioma. The published literature on the meningioma–primary cerebral lymphoma association is revised.

Key words: association, intracranial tumor, lymphoma, meningioma, multiple tumors.

INTRODUCTION

Synchronous multiple intracranial tumors especially occur in metastases and in CNS lymphomas where they are observed in 20–50% of the cases.[1] Conversely, only less than 10% of the patients with meningioma or glioma, among the most common primary intracranial tumors, show multiple lesions, whereas, the association of different primary tumors and the association of metastases with primary tumors have rarely been reported.[2–24]

We describe a case of meningioma–primary cerebral lymphoma association that occurred in a patient initially operated on because of meningioma and some weeks later showed an histologically confirmed primitive-non-Hodgkin B cell lymphoma, localized in the same area as the meningioma.

CLINICAL HISTORY

A 67-year-old female was admitted to the Neurosurgical Service (Careggi Hospital, Florence, Italy) with a 2 to 3-week history of progressive memory impairment and confusion. At admission, neurological and motor examination did not show evidence of additional important signs. The patient was hypertensive and affected by insulin-dependent type-I diabetes. Cerebral computed tomography (CT) revealed a mid-line 4-cm lesion in the fronto-basal region involving the olfactory grooves, and particularly extending in the left frontal lobe. The lesion showed slight perilesional edema and moderate and homogeneous contrast enhancement. Two small infiltration-like areas were recognised (Fig. 1). Preoperative diagnosis was meningioma. The lesion was surgically removed. A distinct cleavage plane from nervous parenchyma was identified. Surgical excision was pronounced as macroscopically complete by the surgeon.

Histopathological examination of the entire surgical specimens revealed a meningothelial meningioma. The tumor was composed of uniform round-oval cells occasionally forming lobules and having oval nuclei with frequent clear inclusions. Some psammoma bodies were visible. Necrosis was absent and the mitoses were exceptional (Fig. 2). At the immunohistochemistry (standard streptavidin-biotin peroxidase method) the lesion was epithelial membrane antigen (clone PGM1 Dako, Glostrup, Denmark; 1:50 dilution; microwave antigenic enhancement) and vimentin (clone V9 BioGenex, San Ramon, CA, USA; 1:2000 dilution; microwave antigenic enhancement) positive.

The patient's postoperative course was uneventful with complete neurological recovery. Because of the histological diagnosis of benign meningioma and because of the gross total surgical resection, no further therapy was recommended and no immediate postoperative radiological controls were planned. Neurological examination 1 month after the surgery was negative.

One month later the patient was again admitted to the hospital because of severe neurological deterioration. CT and MRI showed two contiguous lesions localized in the same area as the first tumor: a bigger lesion at the cerebral falx level adherent to the left orbital roof associated with

Correspondence: Anna Maria Buccoliero, MD, Department of Human Pathology and Oncology, Medical School, University of Florence, Viale GB Morgagni, 85, 50134 Florence, Italy. Email: ambuccoliero@unifi.it

Received 27 January 2004; revised and accepted 25 March 2004.

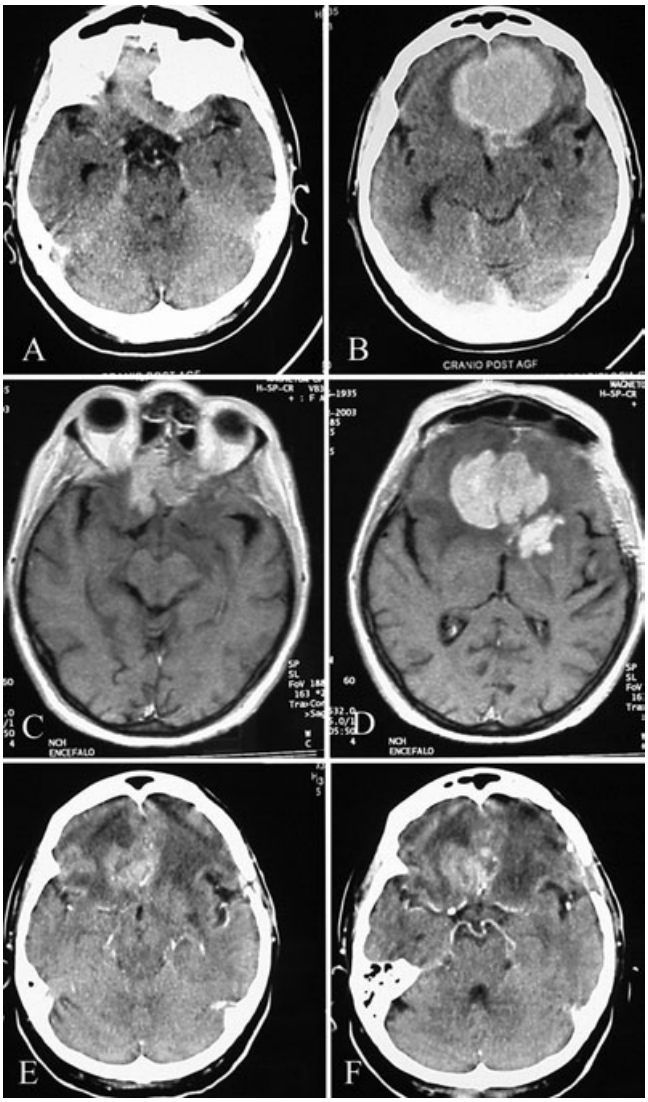

Fig. 1 (A,B) Meningioma, CT with administration of contrast medium. Mid-line 4 cm lesion of the fronto-basal region showing two small infiltration-like areas. (C,D) Lymphoma, MRI with administration of contrast medium. A bigger lesion at the cerebral falx level and a smaller lesion in the left capsular area shoving a more intense contrast enhancement. (E,F) Control during steroid and chemo therapy, CT with administration of contrast medium; reduction of the lesions is appreciable.

hyperostosis of the sphenoid ridge, and a smaller lesion in the left capsular area showing a more intense contrast enhancement (Fig. 1). A stereotactic biopsy of the bigger lesion was obtained.

Histopathological examination revealed a B-cell lymphoma. A proliferation of pleomorphic large centroblast-like cells showing mitoses, necroses, and hemorrhagic infiltrate was present. Frequently, the neoplastic cells were organized in an angiocentric pattern forming pseudopapillary structures (Fig. 3). Immunohistochemistry showed a

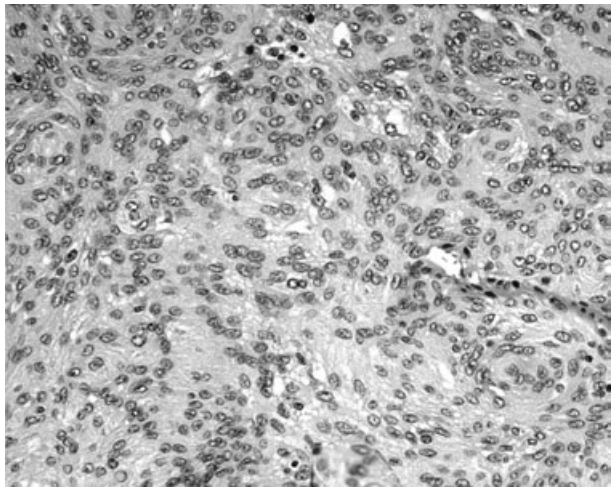

Fig. 2 Meningothelial meningioma, uniform round-oval cells having oval nuclei with frequent clear inclusions.

prevalent CD45 (clone 2B11, PD7/26 Dako; 1:400 dilution; microwave antigenic enhancement) and CD20 (clone L26 Dako; 1:400 dilution; microwave antigenic enhancement) positive cells (Fig. 3). Occasionally, CD3 (polyclonal, Dako; 1:50 dilution; microwave antigenic enhancement) positive cells were also visible (Fig. 3).

Steroid and chemo therapy (methotrexate) were given and consequent reduction of the lesion was documented (Fig. 1). Clinical and radiological examinations didn't reveal any abnormal findings in other systems, in particular no lymphadenopathy.

The patient was alive 6 months after the first admission.

DISCUSSION

Multiple primary brain tumors of different histogenesis can be found in the setting of phacomatosis or cranial radiotherapy.[11,16,24] In contrast, the association of two (or more) different primary intracranial tumors not related to phacomatosis or radiotherapy is rare with an annual incidence in the general population that has been calculated as much less than one per million.[16]

Specific definitions are used to indicate the insurgence of more tumors: collision or combined tumors are those with infiltration of a tumor by a different tumor; tandem or coincidental tumors are synchronous tumors of different histogenesis in contiguous or far areas.[3,18–20]

Several hypotheses have been suggested to explain the presence of different multiple primary intracranial tumors in patients without phacomatosis and radiotherapy. A locally acting oncogenic factor or an irritative effect of a tumor inducing the growth of another neoplasm have been suggested as possible explanations.[11,16] Nevertheless, the observation that the most common association of primary

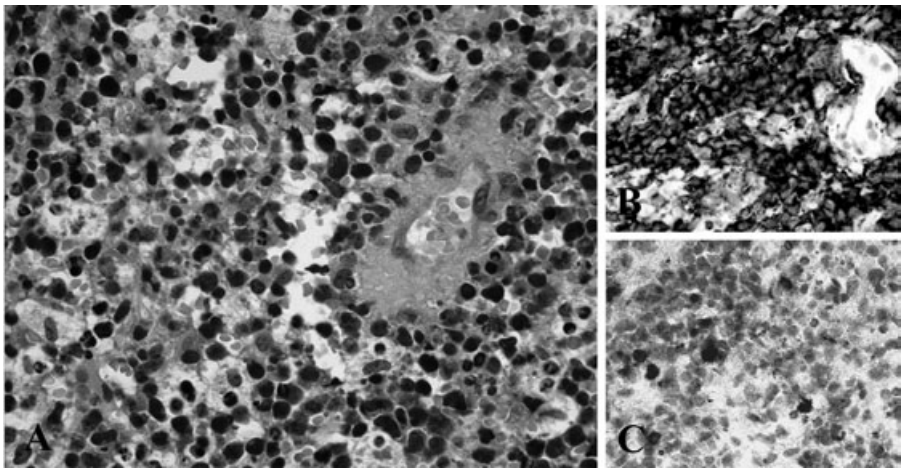

Fig. 3 B-cell lymphoma, pleomorphic large cells proliferation frequently showing an angiocentric pattern (A). The majority of the cells were CD20 positive (B). Rare CD3 positive cells were present (C).

tumors of different types is between meningioma and glioma, two of the most frequent intracranial tumors, has been suggested as a purely coincidental event.[11]

Meningioma is a common and generally benign slow-growing tumor. The majority of meningiomas are intracranial or spinal, although ectopic cases have been exceptionally reported in almost all organs. Radiation exposure, genetic factors, particularly neurofibromatosis-2 (NF2), and hormonal factors have been implicated in its development and growth. Meningiomas exhibit a wide range of histologic patterns, besides meningothelial, fibrous and transitional meningiomas (the most common subtypes), many variants, inclusive of the lymphoplasmacyte-rich meningioma, have been identified. Multiple meningiomas are frequently observed in NF2-affected patients, whereas they occur in less than 10% of sporadic cases.[1] The most common associations comprising the meningioma are meningioma-glioma and meningioma-pituitary adenoma that are reported 41 and 36 times, respectively, in the published literature.[3,11,25–34]

Intracranial lymphoma is a relatively rare disease including secondary involvement of the nervous system in systemic lymphoma and primary central nervous system lymphoma (PCNSL). PCNSL commonly belongs to the group of the non-Hodgkin B cell lymphomas. People in a immunosuppressive state have a higher risk of contracting this tumor but an increased incidence has also recently been reported in the immunologically normal population.[1] EBV, a human gamma herpes virus, has been implicated in the genesis of cerebral lymphoma in immunodeficent as well as in some immunocompetent people.[13]

Primary intracranial lymphomas might show singular or multiple lesions but it is rare that they are described in concurrence with other intracranial tumors. To the best of our knowledge only eight cases of primitive intracranial lymphoma in association with other intracranial malignancies have been reported.[6,7,10,13,15,22,23,35] In three of these cases lymphoma was associated with a glioma (one oligodendroglioma, one astrocytoma, one glioblastoma) and in five with a meningioma.

These five cases of meningioma–primary cerebral lymphoma association affected adult people (38, 49, 56, 62, and 80 years old) with a female predominance (female, four cases; male, one case). In four cases, meningioma and primary cerebral lymphoma were simultaneously diagnosed and arose in different areas. In the remaining case a left frontal lobe meningioma was diagnosed and surgically excised first and, successively, in the same area a second tumor, which proved to be a brain lymphoma, was operated.

The cause and the pathogenesis of associated meningioma–lymphoma is unclear. However, as meningiomas are common and slow-growing intracranial neoplasms, the possibility of their concurrence with a second brain tumor might increase.[23] In contrast, an irritative effect of meningioma facilitating the insurgence of lymphoma cannot be excluded in cases in which the two lesions occurred in succession in the same area.[22]

The recognition of multiple intracranial tumors and their clinical presentation might depend on the sensitivity of the diagnosts used.[21] An early radiological identification of multiple cerebral tumors in the same patient is important for the correct therapy. MRI, because of its sensitivity, can be decisive in recognizing smaller lesions or lesions located in the posterior fossa that are not visible on CT. Nevertheless, there can be difficulty, especially when the lesions are adjacent.

Regarding our current case, even if some unclear radiological aspects (the two infiltration-like areas) were already present in the first CT scan, the adjacent localization of the two lesions could be the cause of the retardation of the radiological recognition of lymphoma. However, the surgeon and pathologist did not note, macroscopically or histologically, any pathological tissue in

addition to meningothelial meningioma. Therefore, it remains unclear if the lymphoma was already present at the time of the diagnosis and of the surgical excision of the meningioma.

REFERENCES

1. Kleihues P, Cavenee K. World Health Organization Classification of tumors. *Pathology and Genetics of Tumours of the Nervous System*. Lyon: IARC Press, 2000.
2. Barnard RO, Geddes JF. The incidence of multifocal cerebral gliomas. A histologic study of large hemisphere sections. *Cancer* 1987; **60**: 1519–1531.
3. Brennan TG, Rao CV, Robinson W, Itani A. Tandem lesion: chromophobe adenoma and meningioma. *J Comput Assist Tomogr* 1977; **1**: 517–520.
4. Bucciero A, Del Basso A, De Caro M *et al.* Metastasis of breast carcinoma to intracranial meningioma. Case report and review of the literature. *J Neurosurg* 1992; **36**: 169–172.
5. Djalilian HR, Shah MV, Hall WA. Radiographic incidence of multicentric malignant gliomas. *Surg Neurol* 1999; **51**: 554–558.
6. Ederli A, Lo Russo F, Vesentini G. Glioblastoma of the brainstem associated with Hodgkin lymphoma. *Ital J Neurol Sci* 1983; **4**: 349–356.
7. Fewings PE, Bhattacharyya D, Crooks D, Morris K. B-cell non-Hodgkin cerebral lymphoma associated with an anaplastic oligodendroglioma. *Clin Neuropathol* 2002; **21**: 243–247.
8. Gardiman M, Altavilla G, Marchioro L, Alessio L, Parenti A, Piazza M. Metastasis to intracranial meningioma as first clinical manifestation of occult primary lung carcinoma. *Tumori* 1996; **82**: 256–258.
9. Geuna E, Pappada G, Regalia F, Arrigoni M. Multiple meningiomas. Report of nine cases. *Acta Neurochir (Wien)* 1983; **68**: 33–43.
10. Giromini D, Peiffer J, Tzonos T. Occurrence of a primary Burkitt-type lymphoma of the central nervous system in an astrocytoma patient. *Acta Neuropathol (Berl)* 1981; **54**: 165–167.
11. Goyal A, Sing AK, Sinha S, Tatke M, Sing D, Gupta V. Simultaneous occurrence of meningioma and glioma in brain: report of two cases. *J Clin Neurosci* 2003; **10**: 252–254.
12. Honma K, Hara K, Sawai T. Tumor to tumor metastasis. A report of two unusual autopsy cases. *Virchows Arch Pathol Anat* 1989; **416**: 153–157.
13. Ildan F, Bagdatoglu H, Boyar B, Haciyakupoglu S, Gonlusen G, Tunali N. Combined occurrence of primary cerebral lymphoma and meningioma. *Neurosurg Rev* 1995; **18**: 45–48.
14. Koh YC, Yoo H, Whang GC, Kwon OK, Park HI. Multiple meningiomas of different pathological features: case report. *J Clin Neurosci* 2001; **1** (Suppl. 8): 40–43.
15. Kuroiwa T, Ohta T, Kobata H, Yamamoto H, Kimura N. Coexistence of intracranial meningioma and primary malignant lymphoma-case report. *Neurol Med Chir (Tokyo)* 1990; **30**: 268–271.
16. Lee EJ, Chang CH, Wang LC, Hung YC, Chen HH. Two primary brain tumors, meningioma and glioblastoma multiforme, in opposite hemispheres of the same patient. *J Clin Neurosci* 2002; **9**: 589–591.
17. Matyja E, Kuchna I, Kroh H, Mazurowski W, Zabek M. Meningiomas and gliomas in juxtaposition: casual or causal coexistence? Report of two cases. *Am J Surg Pathol* 1995; **19**: 37–41.
18. Muzumdar DP, Goel A, Desai KI. Pontine glioma and cerebellopontine angle epidermoid tumor occurring as collision tumours. *Br J Neurosurg* 2001; **15**: 68–71.
19. Perry A, Sceithauer BW, Szczesniak DM, Atkinson JL, Wald JT, Hammak JE. Combined oligodendroglioma/pleomorphic xantoastricytoma: a probable collision tumor: case report. *Neurosurgery* 2001; **48**: 1358–1361.
20. Prayson RA, Chowdhary S, Woodhouse S, Hanson M, Nair S. Collision of a syncytial meningioma and malignant astrocytoma. *Ann Diagn Pathol* 2002; **6**: 44–48.
21. Sheehy JP, Crockard HA. Multiple meningiomas: a long term review. *J Neurosurg* 1983; **59**: 1–5.
22. Shigemori M, Tokunaga T, Miyagi J *et al.* Multiple brain tumors of different cell types with an unruptured cerebral aneurysm-case report. *Neurol Med Chir (Tokyo)* 1991; **31**: 96–99.
23. Slowik F, Jellinger K. Association of primary cerebral lymphoma with meningioma: report of two cases. *Clin Neuropathol* 1990; **9**: 69–73.
24. Shirabe T, Higashi Y. A 25-year-old woman with multiple brain tumors who died after a course of 1 year and 6 months. *Neuropathology* 2003; **23**: 364–366.
25. Honneger J, Buchfelder M, Schrell U, Adams EF, Fahlbusch R. The coexistence of pituitary adenomas and meningiomas: three case reports and a review of the literature. *Br J Neurosurg* 1989; **3**: 59–69.
26. Cano A, Roquer J. Association of intracranial meningioma and hypophysial adenoma. *Neurologia* 1995; **10**: 139.
27. Canda T, Sengiz S, Canda MS, Acar UD, Erbayraktar RS, Yilmaz HS. Histochemical and immunohistochemical features of a case showing association of meningioma and prolactinoma containing amyloid. *Brain Tumor Pathol* 2002; **19**: 1–3.
28. Inagawa S, Yamakawa H, Nishikawa M. Triple primary brain tumors of different histological types: case report. *Surg Neurol* 1994; **41**: 52–55.

29. Abstract R, Parizel PM, Willems PJ *et al.* The association of meningioma and pituitary adenoma: report of seven cases and review of the literature. *Eur Neurol* 1993; **33**: 416–422.
30. Uno M, Ohshima T, Matsumoto K, Sano T. A case report of adjiacent tumor of sphenoid ridge meningioma and GH producing pituitay adenoma. *No Shinkei Geka* 1991; **19**: 583–587.
31. Jaskolski DJ, Jakubowski J. Association of suprasellar meningioma with pituitary adenoma. *Zentralbl Neurochir* 1990; **51**: 229–231.
32. Mathuriya SN, Vasishta RK, Dash RJ, Kak VK. Pituitary adenoma and parasagittal meningioma: an unusual association. *Neurol India* 2000; **48**: 724.
33. Laun A, Lenzen J, Hildebrant G, Achchenmayr W. Tuberculum sellae meningioma and hypophyseal adenoma in a woman. *Zentralbl Neurochir* 1993; **54**: 119–124.
34. Gorge HH, Poll W, Gers B. Para and suprasellar meningioma coincident with a hormonally active intrasellar hypophyseal adenoma – case report. *Zentralbl Neurochir* 1993; **54**: 190–196.
35. Cannavo S, Curto L, Fazio R *et al.* Coexistence of growth hormone-secreting pituitary adenoma and intracranial meningioma: a case report and review of the literature. *J Endocrinol Invest* 1993; **16**: 703–708.