

Istvan Vajtai · Marlene Arnold · Erik Vassella

Oligodendroglioma with neurocytic differentiation and characteristic loss of heterozygosity on chromosomes 1p and 19q

Received: 29 August 2005 / Revised: 6 September 2005 / Accepted: 6 September 2005 / Published online: 13 October 2005
© Springer-Verlag 2005

Neuronal differentiation in neoplasms of the central nervous system (CNS) has been known to occur either as a polyphenotypic trait of primitive neuroectodermal tumors (PNET) or in the form of composite lesions incorporating well-defined neuronal and glial elements (e.g., ganglioglioma).

Interest in the pathology of neoplasms with mixed neuronal-glial properties has been revived in particular by studies on the differentiation potential of central neurocytomas [4]. On the one hand, so-called “oligodendroglioma mimics”—among them extraventricular neurocytomas—came to be appreciated; on the other, the issue of neuronal differentiation in bona fide oligodendrogliomas has been further elaborated [2]. The latter aspect recently resulted in a report by Perry et al. [6] on four supratentorial infiltrative gliomas of adults with oligodendroglial histology, evidence of neuronal immunophenotype, and demonstration of co-deletions on chromosomes 1p and 19q by fluorescent in situ hybridization (FISH) analysis. A similar case was subsequently published by Mrak et al. [5].

We recently had the opportunity to observe an additional example of the above constellation by studying the brain tumor from a 66-year-old female presenting with seizures. This contrast-enhancing and partially calcified left temporal mass of 5×5×4 cm (Fig. 1a) was removed by surgery. Histology revealed characteristic features of an oligodendroglioma complete with “secondary structures” of Scherer (i.e., perineuronal satellitosis, subpial accumulation of tumor cells).

Focally brisk mitotic activity with a mean MIB-1 labeling index of near 25%, as well as microvascular proliferation, qualified this tumor as anaplastic (WHO grade III). Rhythmic palisades or “marching files” were a prominent feature; these occasionally coalesced to form vague neurocytic type (Homer Wright-like) rosettes (Fig. 1b–d). Throughout the tumor strong immunoreactivity for synaptophysin was noted (Fig. 1e, f). Staining for chromogranin-A and neurofilament protein, as evidence of more advanced neuronal (gangliocytic) maturation, was absent in tumor cells.

Polyacrylamide gel electrophoresis of PCR-amplified microsatellite markers revealed loss of heterozygosity (LOH) on both chromosome 1p36 (D1S468, D1S228, D1S214) and 19q13 (D19S412) in DNA extracted from tumor tissue as compared with non-tumorous somatic DNA obtained from a prior tonsillectomy specimen (Fig. 1g, h).

The genotype documented here is considered a characteristic “molecular signature” of oligodendrogliomas, and adds further support to the existence of neuronal differentiation within tumors that otherwise fulfill accepted clinicopathological criteria of oligodendroglioma. These include, among others: occurrence in adults, supratentorial location, overtly infiltrative growth and a propensity to recur for both low- and high-grade lesions, in contradistinction from extraventricular neurocytomas, which are essentially, if not exclusively, low-grade [2, 6]. Notably, the latter

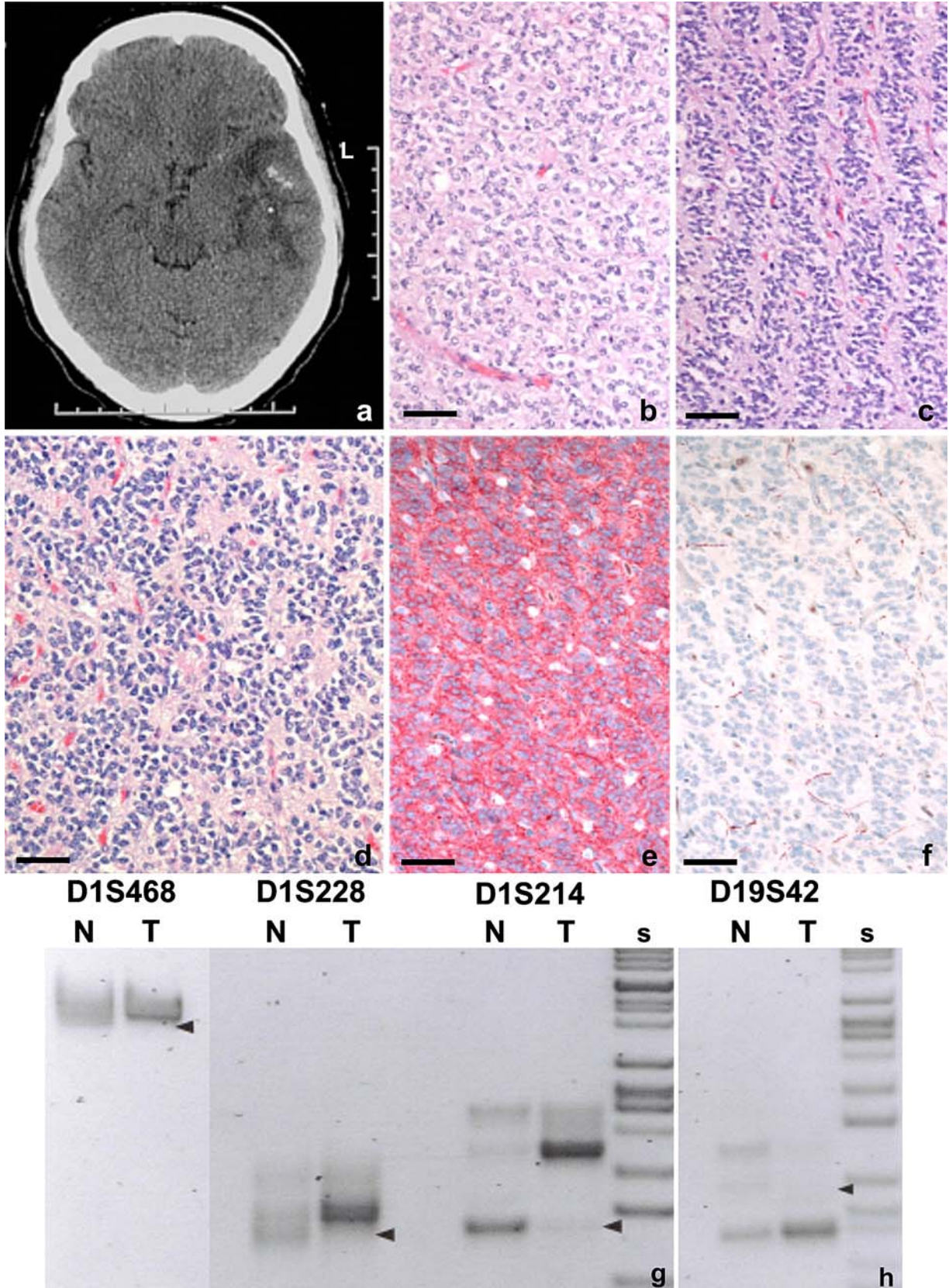
I. Vajtai (✉) · M. Arnold
Department of Clinical Pathology, Institute of Pathology,
University of Berne, Murtenstrasse 31, Postfach 62,
3010 Berne, Switzerland
E-mail: istvanvajtai@yahoo.com
Tel.: +41-31-6323210
Fax: +41-31-6329938

E. Vassella
Laboratory of Molecular Pathology, Institute of Pathology,
University of Berne, Berne, Switzerland

Fig. 1 Native axial CT scan to show focally calcified tumor in left temporal lobe (a). Histologically, beside classic “honeycomb” pattern (b) and rhythmic palisades (c), some scattered groups of neurocytic type rosettes (d) were occasionally seen. Most tumor cells show intense positivity for synaptophysin (e). On a consecutive section (f), the corresponding area reveals only scant residual neurofilament-positive axons in infiltrated brain parenchyma. SYBR gold-stained electrophoresis gels (Spreadex®) to show loss of microsatellite markers on chromosome 1p36 (g) and 19q13 (h) in tumor-derived DNA versus normal somatic control (T tumor, N normal control, S length standard). b–d Hematoxylin and eosin; e, f immunohistochemistry. Bars 50 µm

only seldom harbor LOH 1p/19q [7]. Although obviously rare, the “oligodendroglioma with neurocytic differentiation” may evolve to a paradigm with his-

tological and genetic features that will eventually prove reproducible enough to warrant consideration as an emerging entity [3].



From a practical standpoint, it is important for the pathologist to become aware of the existence of “oligodendrogliomas with neurocytic differentiation” so as not to intuitively bias interpretation of synaptophysin-immunoreactive “honeycombing” CNS tumors towards either low-grade oligodendroglioma mimics, or the highly malignant PNET.

In a more general context of CNS tumor biology, the “oligodendroglioma with neurocytic differentiation” further substantiates the variously perceived occurrence of neuronal characteristics in diffusely infiltrating gliomas [8]. With ostensibly “composite” lesions (e.g., ganglioglioma, dysembryoplastic neuroepithelial tumor, etc.) on one end of the spectrum, and an infiltrating glioma of hybrid glial-neuronal phenotype on the other, speculation about a purported pluripotential cell of origin (e.g., the N-O cell) thus comes full circle [9]. Although the very existence of the latter is only supported by circumstantial evidence, neoplastic transformation of adult neuroectodermal precursors with stem cell properties is currently being entertained as a possible source of at least a subset of gliomas [1].

References

1. Berger F, Gay E, Pelletier L, Tropel P, Wion D (2004) Development of gliomas: potential role of asymmetrical cell division of neural stem cells. *Lancet Oncol* 5:511–514
2. Brat DJ, Scheithauer BW, Eberhart CG, Burger PC (2001) Extraventricular neurocytomas. Pathologic features and clinical outcome. *Am J Surg Pathol* 25:1252–1260
3. Cenacchi G, Giangaspero F (2004) Emerging tumor entities and variants of CNS neoplasms. *J Neuropathol Exp Neurol* 63:185–192
4. Deimling A von, Kleihues P, Saremaslani P, Yasargil MG, Spoerri O, Sudhof TC, Wiestler OD (1991) Histogenesis and differentiation potential of central neurocytomas. *Lab Invest* 64:585–591
5. Mrak RE, Yasargil MG, Mohapatra G, Earel J, Louis DN (2004) Atypical extraventricular neurocytoma with oligodendroglioma-like spread and an unusual pattern of chromosome 1p and 19q loss. *Hum Pathol* 35:1156–1159
6. Perry A, Scheithauer BW, Macaulay RJB, Raffel C, Roth KA, Kros JM (2002) Oligodendrogliomas with neurocytic differentiation. A report of 4 cases with diagnostic and histogenetic implications. *J Neuropathol Exp Neurol* 61:947–955
7. Perry A, Fuller CE, Banerjee R, Brat DJ, Scheithauer BW (2003) Ancillary FISH analysis for 1p and 19q status: Preliminary observations in 250 gliomas and oligodendroglioma mimics. *Front Biosci* 8:1-9
8. Varlet P, Soni D, Miquel C, Roux FX, Meder JF, Chneiweiss H, Daumas-Duport C (2004) New variants of malignant glioneuronal tumors: a clinicopathological study of 40 cases. *Neurosurgery* 55:1377–1392
9. Williams BP, Read J, Price J (1991) The generation of neurons and oligodendrocytes from a common precursor. *Neuron* 7:685–693