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LETTER TO THE EDITOR

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

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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 a 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

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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

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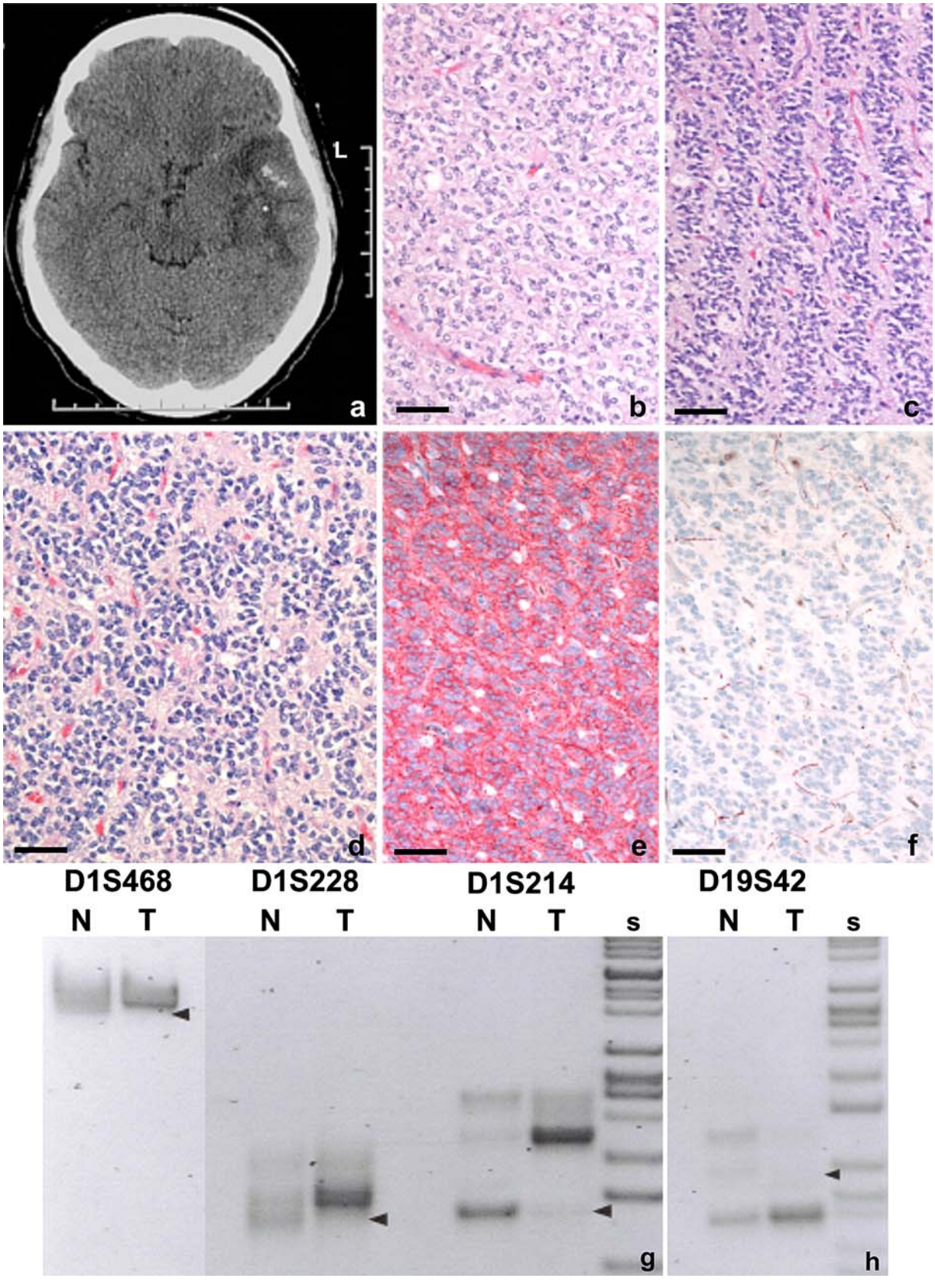
only seldom harbor LOH 1p/19q [7]. Although obviously rare, the ''oligodendroglioma with neurocytic differentiation'' may evolve to a paradigm with histological and genetic features that will eventually prove reproducible enough to warrant consideration as an emerging entity [3].



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].

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