Brain Pathology 7: 1027-1028 (1997)

CASE OF THE MONTH

March 1997 - 4 Year Old Girl with Ring Chromosome 22 and Brain Tumor

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Clinical history

The patient is a four year old Caucasian girl with a constitutional ring chromosome 22 abnormality. The patient has the phenotypic features and developmental delay characteristic of ring chromosome 22 abnormality (1). She developed some morning emesis, a week of lethargy and some neck pain for six weeks prior to the onset of severe ataxia prompting imaging studies.

Imaging studies

T1 weighted image after gadopentetate dimeglumine contrast injection shows an irregularly shaped mass occupying the third ventricle, with apparent involvement of the septum. There is signal heterogeneity with intermediate and high signal and irregular enhancement after contrast injection (Figure 1).

Microscopic

Microscopic examination revealed a cellular neoplasm with multiple foci of geographic necrosis. The majority of the cells had large, vesicular nuclei with open chromatin and prominent nucleoli and variable amounts of cytoplasm, ranging from abundant to scarce. Some cells showed the classic rhabdoid appearance with

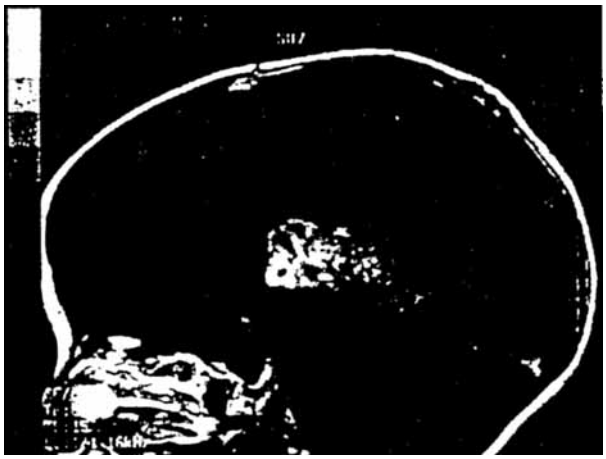

Figure 1.

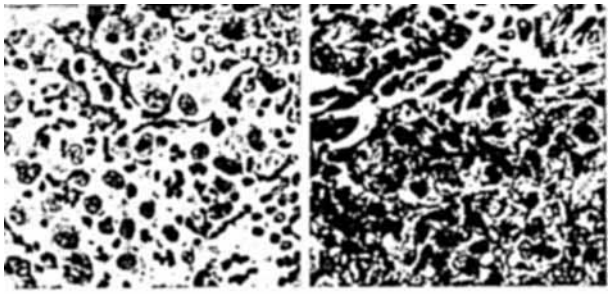

Figure 2.

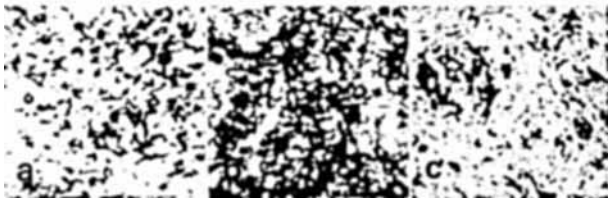

Figure 3. a. Vimentin **b.** EMA **c.** GFAP

globular cytoplasm and peripheral nuclei (Fig 2a). Mitotic figures were common. There were small areas of primitive appearing cells with high nuclear-to-cytoplasmic ratio arranged in sheets. The majority of the neoplasm was similar to that seen in Figure 2B. Most cells in the touch preparation have abundant pink cytoplasm. Areas similar to that represented in the second micrograph (Fig 2b) composed the majority of the tumor which consisted of rhabdoid cells in sheets, without any architectural organization. (400 x original magnification).

A special stain for reticulin demonstrated abundant staining around individual cells as well as bundles of reticulin dispersed throughout the tumor. A panel of immunohistochemical stains demonstrated diffuse strong positivity for vimentin, epithelial membrane antigen and GFAP (Figs 3A, B, C, respectively). S-100 also showed multifocal strong positivity. Weakly or focal positivity was seen with PGP9.5, Synaptophysin and muscle specific actin. Immunostains for Desmin, Neurofilament, CEA and transthyretin were negative. Ki-67 proliferation index was 24%.

Diagnosis

Atypical Teratoid/Rhabdoid tumor of the central nervous system in a child with ring chromosome 22 abnormality.

Additional treatment and clinical progress

The patient had a good postoperative course. Following chemotherapy there was a 20% reduction in tumor. She received a second course, but her follow-up MRI revealed further progression of the disease and dissemination of the tumor seven months after the diagnosis.

Discussion

Atypical teratoid/rhabdoid tumor of the central nervous system (ATRT) is an aggressive childhood neoplasm sharing histopathologic features with both central primitive neuroectodermal tumors (cPNET) and peripheral malignant rhabdoid tumors (MRT). While the most common cytogenetic abnormality in cPNETs involves chromosome 17 i(17q), both ATRT and MRT share monosomy of chromosome 22 (2), or at least genetic losses in the distal part of the long arm of chromosome 22 (3). The putative mechanism of tumorigenesis is inactivation of a still to be defined tumor suppressor gene (TSG) distinct from the NF-2 gene, located in the distal long arm of chromosome 22. The same, or a different but closely placed, TSG may be responsible for the development of meningiomas (4). Of special interest in this case is the presence of a constitutive ring chromosome 22 abnormality in this child. Ring chromosome 22 generally involves loss of the distal part of the long arm of the chromosome, including the locus for the putative TSG. In fact, childhood meningiomas and multiple meningiomas have been previously described in patients with constitutional ring chromosome 22 (5,6). To my knowledge, this is the first case of ATRT presenting in a patient with ring chromosome 22. Studies by Ota et al., (7) suggest a neural crest origin and they propose to classify MRT as a subtype of cPNET.

The most extensive and recent review of ATRT with detailed clinical, radiologic and pathologic description of 52 cases is that of Rorke et al. (8) Histopathologically, all tumors contain groups of rhabdoid cells in differing proportions along with cPNET, mesenchymal and/or epithelial components. The immunohistochemical pattern of staining varies among the different components, but the rhabdoid cells are almost uniformly positive for epithelial membrane antigen. Desmin is immunoreactive in the rhabdoid component of a minority of tumors.

The admixture of different histologic patterns in the majority of ATRT of the CNS is a subject of much interest. Unlike teratomas, the other type of tumor composed of cells of mixed embryologic origin in which the cell of origin is a germ cell, the cell of origin in ATRT is unknown.

References

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Case Abstract

A four year old Caucasian girl with a constitutional ring chromosome 22 abnormality and developmental delay presented with increasing ataxia and a six week history of non-specific symptoms. Imaging studies demonstrated a large third ventricular tumor with apparent involvement of the septum. Microscopic and immunohistochemical studies demonstrated an atypical teratoid/rhabdoid tumor. This tumor is compared and contrasted to peripheral malignant rhabdoid tumors and central primitive neuroectodermal tumors. The role of a putative tumor suppressor gene on the long arm of chromosome 22 in the pathogenesis of these tumors is also discussed.

For a more complete discussion of this case and additional micrographs please access this case on the WWW at: http://path.upmc.edu/divisions/neuropath/bpath/cases/case12.html. We welcome comments about these or similar cases our readers may have encountered.
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