Clinical Notes

Rosette-forming glioneuronal tumor of the fourth ventricle. *A rare neoplasm of the central nervous system*

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Two unusual neoplasms of mixed glioneuronal nature are recognized as novel, distinct entities in the newly updated World Health Organization (WHO) taxonomy of tumors of the central nervous system. These are the papillary glioneuronal tumor and the rosette-forming glioneuronal tumor (RGNT). Histopathologically, the RGNT consists of 2 distinct components: neurocytic rosettes with central anti-synaptophysin immunoreactivity, and astrocytic tumor cells showing features of pilocytic astrocytoma, astrocytoma fibrillare, or oligodendroglioma. In order to better define the clinical and pathological features and therapy of this entity, we report the case of RGNT of the fourth ventricle and review the literature.

This 27-year-old female patient suffered from vertigo, nausea, as well as blurred vision, which had been present for 3 months. The examination of the nervous system was negative, except for the cerebellar ataxia. Head CT and MRI disclosed a heterogeneous mass lesion filling the fourth ventricle with hydrocephalus, which was iso-density on plain CT scan, hypointense in T1-weighted, and hyperintense in T2-weighted MRI, and the enhancement of the tumor was not obvious. Some area of the tumor was cystic, but calcification was absent. The tumor was resected totally via suboccipital craniotomy. The surgical specimen was fixed in 10% buffered formalin, routinely processed for light microscopy, and stained by hematoxylin and eosin (HE). Immunohistochemical studies on the tumor were performed with an avidin-biotin complex and antisera against glial fibrillary acid protein (GFAP; 1:4,000; Dako, Glostrup, Denmark) vimentin (clone V9; 1.50; Dako), S100 protein (1:2,000; Dako), synaptophysin (clone SY 377;1:100; Dako), NEU-N (clone MAB 377; 1:1,000, Chemicon International) and Ki-67 antibody (clone MIB-1; 1:50; Dako). Microscopic examination showed 2 hypocellular neuro-epithelial tumor, composed of 2 distinct cell components. One component displayed aggregates of prominent neurocytic rosettes. The tumor cell nuclei were isomorphic, round and showed homogenous dense chromatin. The nuclei were arranged in ring-like arrays around eosinophilic neuropil cores (**Figure 1**). The second component consisted of analogous oligodendroglioma tumor cells with round to oval and elongated nuclei, which were dispersed diffusely in a fibrillary matrix. The neuropil cores of neurocytic rosettes showed no immunoreactivity for any of the glial markers, but displayed strong immunoreactivity for synaptophysin. Some glial tumor cells had a spindle bipolar shape. Immunohistochemistry for GFAP showed low reactivity of the oligodendroglioma tumor component. The MIB-1 staining of the Ki67 antibody showed a labeling index of 1%. The patient began to suffer from cerebellar mutism 2 days after the operation. Head CT scan indicated the obvious edema around the tumor cavity. After the therapy of dehydration, dilatancy vasodilatation, and drug therapy of bromocriptine, the symptoms recovered gradually 2 weeks later. The follow-up head MRI performed 10 months after the operation indicated no tumor recurrence.

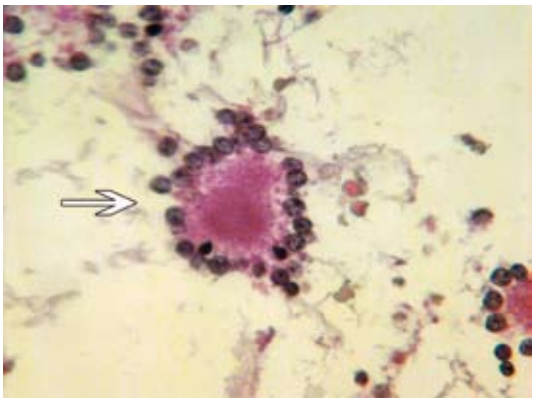

Figure 1 - A typical structure of rosette on hematoxylin and eosin staining (x 400).

The RGNT of the fourth ventricle seems initially to have been described in a 1995 report as a cerebellar form of dysembryoplastic neuroepithelial tumor, but was recognized as an entity *sui generis,* and characterized in a 2002 study of 11 cases by Komori et al.[1] In the newly updated WHO taxonomy of tumors of the central nervous system, RGNT is recognized as a novel and distinct entity. Based on the literature, 24 cases have been reported previously, which indicate that this type of tumor predominantly appears in young adults. The RGNTs, to be midline lesions, generally locate in or near the fourth ventricle, and limited extension into the cerebellar vermis, brainstem and cerebral aqueduct may be seen. Patients usually present with headache, ataxia, or unsteadiness. On many occasions, the patients present incidentally or with apparently unrelated symptoms and no demonstrable neurological signs.[1,2] There is paucity of the imaging data for RGNTs. The RGNTs are relatively circumscribed, may be solid or multicystic, and usually exhibit at least focal contrast-enhancement that may be nodular, linear, ring, or spot-like. However, in our case the enhancement of the tumor is not obvious. On MR assessment, T1WI isohypointensity or hypointensity and T2WI hyperintensity are the rule. Calcification is occasionally seen and may be extensive. There may be associated edema, but this is generally minimal.[3]

Histologically, RGNTs are posited to derive from elements capable of divergent neuronal and glial differentiation, and may have their origin in the pluripotential cells of the subependymal plate.[1] The RGNT is distinctive in its combination of neurocytic and glial components. The former, with their small, uniform round nuclei, can form rosettes, or perivascular pseudo-rosettes structures. The latter component, with elongate to oval nuclei can form areas like pilocytic astrocytoma, astrocytoma fibrillare, or oligodendroglioma. In most previous cases, the glial component of the tumors aggregated pilocytic astrocytoma areas. Immunohistochemistry studies showed positive reactivity of GFAP for the oligodendroglioma tumor component. The neuropil cores of neurocytic rosettes showed no immunoreactivity for any of the glial markers, but displayed strong immuno-reactivity for synaptophysin. The MIB-1 staining of the Ki67 antigen is 0.35-3.07, according to Komori et al,[1] and the mean value is 1.58%.[4] The RGNT must be differentiated from dysembryoplastic neuroepithelial tumor (DNT) and other glioneuronal tumors including the "glioneuronal tumor with neuropil-like islands," "oligodendrogliomas with neurocytic differentiation," and "papillary glioneuronal tumors." In some literature on RGNT, this problem has been explained very distinctly,[5] therefore it will be not discussed here.

As for the literature and our case,[1,5] we know that RGNT is an indolent tumor with a relatively good prognosis, corresponding to WHO Grade l. In our opinion, the most effective therapy is operation, and radiotherapy is not recommended, but can be substituted, if the operation is not suitable. Due to paucity of the prognostic data and reports of tumor recurrence, strict follow-up MRI is necessary.

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