Is polar spongioblastoma a tumor entity?

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The distribution of cells in a parallel fashion with palisades of nuclei is common in neuroepithelial tumors. The authors have selected 16 such tumors from their series for study, as examples of different neuroepithelial oncotypes containing palisades of nuclei: three ependymomas, three hemispheric pilocytic astrocytomas, three oligodendrogliomas, three medulloblastomas, three cerebellar astrocytomas, and one central neuroblastoma. In two additional tumors, affecting a 12-year-old girl and a 51-year-old woman, this feature was present in the entire surgical specimen and the diagnosis was consistent with a polar spongioblastoma. This diagnosis applies in the literature to rare tumors of childhood and adolescence, both malignant and with embryonal features. In one specimen, a clear ependymomatous feature was found in a remote area of the tumor and in the other there were ultrastructural characteristics of neuroblastoma. Nuclear palisades can be found as local architectural features in many neuroepithelial tumors. The rare tumors diagnosed as polar spongioblastoma, according to published criteria, correspond to ependymomas and neuroblastomas. Polar spongioblastoma does not exist as a tumor entity.

KEY WORDS  • polar spongioblastoma  • nosology  • neuroepithelial tumor

THE so-called  "primitive polar spongioblastoma" has been described as a malignant tumor arising in childhood and adolescence in close proximity to the ventricular system. Only a few examples have been reported, in a variety of locations: these include the cerebellum,

The histological appearance of the tumor is characterized by cells arranged in parallel, like a stepladder, with palisading of nuclei and delicate fibrils between, usually showing areas of calcification and necrosis; Rosenthal fibers are not present. The current interpretation of the tumor is that of a poorly differentiated neoplasm cytogenetically related to primitive spongioblasts. Among primitive neuroectodermal tumors of the central nervous system, it has been interpreted as a primitive neuroepithelial tumor with differentiation along glial cell lines. The same term, "polar spongioblastoma," was employed in the German literature to indicate benign midline and cerebellar glial tumors, which are now called "pilocytic astrocytomas.

In some cases, polar spongioblastomas have been described in association with astrocytomas or oligodendrogliomas. This relationship has been interpreted as an expression of divergent lines of differentiation in a primitive glial tumor. Based on this interpretation, some workers have favored continued inclusion of this tumor in the classification systems as an embryonal tumor while others have suggested that the tumor not be considered a separate entity. Palisading of nuclei, for example, has also been found in neuroblastomas. The nosological significance of the tumor has thus been questioned. In the 1979 tumor classification of the World Health Organization (WHO), this neoplasm was considered an embryonal tumor, whereas in the 1991 edition it was set aside as a tumor of unknown origin.

Since palisading and "stepladder" features can be found in many neuroepithelial tumors, the problem is whether the lesion is a true clinicopathological entity with differentiating capacity or a mere architectural feature of different neoplasias. The question is not easy to answer, because if some kinds of differentiation are accepted it could become simply semantic. In the present paper, the nosological problem is discussed together with the presentation of two cases of so-called "polar spongioblastoma," that is, a tumor where nuclear palisading represents the main histological characteristics.

Materials and Methods

Among a series of 5230 neuroepithelial tumors, 16 examples of different oncotypes were selected for study; these were examples of tumors showing circumscribed areas, composed of cells arranged in parallel fashion with conspicuous palisading of nuclei or stepladder characteristics. There were three ependymomas, three
FIG. 1. Photomicrographs of tumors in this study. H & E, × 135. Left: Section of an ependymoma showing palisading of nuclei around vessels. Center: Section of a pilocytic astrocytoma showing aligned nuclei. Right: Section of a medulloblastoma showing alignment due to rosettes.

hemispheric pilocytic astrocytomas, three oligodendrogliomas, three medulloblastomas, three cerebellar astrocytomas, and one central neuroblastoma.

In two additional cases, the diagnosis of "polar spongioblastoma" was made because the "stepladder" aspect mentioned above was present in all extensions of the tumor, although features indicating some kind of other neuroepithelial tumor were not apparent. The first of these tumors was located between the third ventricle and the depth of the temporal lobe in a 12-year-old girl (Case 1). At operation, the mass appeared necrotic. The girl died 2 years later, and no autopsy was performed. The second tumor was located in the right temporal lobe of a 51-year-old woman (Case 2). She was operated on and died 2 years later. Surgical biopsy specimens were fixed in 10% formalin in Case 1 and in Carnoy's fixative in Case 2. In both cases the specimens were embedded in paraffin and cut in sections 5 μ thick. A specimen of the tumor in Case 2 was fixed in 2% glutaraldehyde, embedded in Epon, and processed for electron microscopy.

The following histological methods were carried out for all tumor specimens: hematoxylin and eosin, luxol fast blue B stain for myelin, Gomori stain for reticulin, and periodic acid-Schiff reaction. Immunohistochemical methods included the use of peroxidase-antiperoxidase complex or Strept-avidin-biotin complex for the following antigens: glial fibrillary acidic protein (GFAP) (antiserum, 1:400), vimentin (monoclonal antibody (MoAb), 1:20), neurofilaments (SMI31 and SMI32, 1:500), factor VIII/R antigen (RAg) (MoAb, 1:800), and synaptophysin (MoAb, 1:20).

FIG. 2. Photomicrographs of the "polar spongioblastoma" in Case 1. Left: Section showing a typical "stepladder" appearance. H & E, × 135. Center: Section showing the distribution of small vessels. H & E, × 270. Right: Section showing an area with features typical of ependymoma. H & E, × 135.
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Fig. 3. Photomicrographs of the "polar spongioblastoma" in Case 2. *Left* and *Center*: Sections showing typical appearance, H & E, ×135 (left), ×270 (center). *Upper Right*: Section showing cells with neuronal features (arrows). H & E, ×165. *Lower Right*: Section with positive staining for Synaptophysin. PAP-DAB, ×165.

**Results**

*Photomicrographic Appearance*

The areas in the 16 neuroepithelial tumors showing "stepladder" characteristics had the following histological features. The ependymoma specimens showed palisading of nuclei immersed in a combed fibrillary matrix, containing vessels in longitudinal or transverse sections (Fig. 1 left). The fibrils were only occasionally GFAP- and vimentin-positive. In the adjacent areas, the fibrillary matrix was transformed into perivascular pseudorosettes that were definitely GFAP-positive.

In the oligodendroglioma specimens, palisading of nuclei was observed in both the gray and white matter. In the gray matter there was a parallel disposition of satellite perineuronal cells, and in the white matter palisading was due to the alignment of infiltrating tumor cells among myelin fibers.

Hemispheric pilocytic astrocytoma specimens exhibited nuclei that were either aligned in palisades or amassed in small groups, and immersed in a slightly GFAP- and vimentin-positive fibrillary matrix (Fig. 1 center). Vessels were small, scarce, and unevenly distributed. In the adjacent areas the appearance was of a classical astrocytoma.

In the cerebellar pilocytic astrocytomas, there were either one to two rows only of nuclei or coupled nuclei with the appearance of coffee beans. The fibrillary matrix was GFAP-negative or slightly GFAP-positive. These areas were usually found peripherally or in proximity to areas with oligodendrogial features.

The medulloblastomas showed palisading formed by closely packed nuclei, with mitoses. No vessel was visible among the rows of nuclei, and in the adjacent areas the fibrillary matrix continued in that many Homer-Wright rosettes were visible (Fig. 1 right). The specimen was GFAP- and vimentin-negative.

The one example of neuroblastoma showed palisading of small, round, and isomorphic nuclei. In the fibrillary matrix many vessels were visible, thickened, and variously sectioned. The matrix was negative for every antigen. Many rosettes were found in the surrounding areas.

In the "polar spongioblastoma" found in Case 1, palisading of nuclei was regular, with an undulating course (Fig. 2 left). The fibrillary matrix was GFAP-negative and slightly vimentin-positive. Neurofilaments and synaptophysin were negative. Gomori staining for reticulin and factor VIII/RAg testing revealed a rich network of small vessels (Fig. 2 center), regularly distributed, with no cell process terminating on them. Scattered mitoses, abundant calciospheres, and large necroses were present. The entire surgical specimen was sectioned serially. In a limited marginal area of the specimen, in proximity to a large necrotic area, the histological appearance progressively changed. The fibrillated areas between the palisading became wider and less regular. They were arranged around vessels on which GFAP- and vimentin-positive processes, either scattered or amassed, progressively converged. Mitoses were more abundant and large areas of necrosis persisted. This area clearly showed features of ependymoma (Fig. 2 right).

The "polar spongioblastoma" in Case 2 was characterized by regular palisading of isomorphic nuclei throughout the entire specimen (Fig. 3 left). No mitosis
was visible. The vessels were slightly less regularly distributed and slightly thicker than in Case 1, and the cells were less elongated and less regularly distributed (Fig. 3 center). Scattered among the tumor cells were some larger cells with clear neuronal features (Fig. 3 upper right) that stained positive for neurofilaments. Synaptophysin was irregularly positive (Fig. 3 lower right). This appearance was seen throughout the serial sections of the tumor. In some areas the palisading was less evident and some GFAP-positive cells were present, interpreted as local reactive astrocytes. Calciospheres and circumscribed areas of necrosis were present.

Electron Microscopy

Electron micrographs of the tumor in Case 2 showed that most cells had elongated features without evidence of differentiation (Fig. 4 upper left). Some cells showed a neuron-like aspect, with large, round, vesicular nuclei and processes rich in microtubules (Fig. 4 upper right). In some instances, dense core granules were found within the cytoplasm (Fig. 4 lower left). Large areas of the specimen were composed of small cell processes rich in microtubules. No synaptic-like densities could be found. The diagnosis was that of neuroblastoma.

Discussion

Areas with a "stepladder" appearance of nuclei can be clearly observed in many neuroepithelial tumors, as was demonstrated and confirmed in the 16 tumors examined in this study. In these tumors, which were chosen as representative and do not exhaust all the tumors with "stepladder" appearance in our series, the particular histological feature appears like a secondary structure, probably due to pathocontemporary influences; for example, it may be due to pressure of growth on crowded tumor cells, anchored at one of their poles to perivascular pseudorosettes or rosettes. This mechanism can be invoked in ependymomas or medulloblastomas. Also, peculiar modalities of cell division (as in astrocytomas) or the adaptation to pre-existing structures (as in oligodendrogliomas) could have played a role. In neuroblastomas, the richness and regular distribution of the vasculature together with abundant rosettes might be the responsible influences.

There are really very few tumors completely composed of palisading of nuclei, the so-called "polar spongioblastoma," with the two presented in this study, there are less than 20 published cases. In these cases, the palisading pattern is so diffuse that it can hardly be interpreted as secondary architecture, and no other contemporary formal genetic factor can be identified in the tissue. It is the nature of these tumors that needs discussion and clarification. Obviously, there is no reference to the term "spongioblastoma" used in the German literature to indicate pilocytic astrocytomas of the hemispheres and midline. An analysis of the clinico-biological features of all of the cases that have appeared in the literature to date
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might furnish a clue to interpret the peculiar distribution of cells in this tumor. However, there are no common characteristics among the tumors, not even the young age of the patients. The tumors are found in different locations, from the cerebral hemispheres to the spinal cord and from the brain stem to the cerebellum. The clinical behavior is variable: some patients had a rapid and fatal outcome\(^4\)^ and were associated with long\(^5\)^\(^\text{17}\)^ or intermediate\(^5\)^\(^\text{15}\)^ survival times. It must be added that metastasis via the cerebrospinal fluid is an inconstant feature.

The "polar spongioblastoma" was claimed to derive cytogenetically from radial gliia\(^5\) and was considered, therefore, as a primitive glial tumor\(^6\) or as a poorly differentiated neuroepithelial tumor in the WHO classification of 1979.\(^7\) In the new WHO classification,\(^8\) this lesion has been set aside as a neuroepithelial tumor of uncertain origin, because of its undefined nosological characteristics and nature.

In our experience, even cases with diffuse distribution of the "stepladder" features do not represent "polar spongioblastoma." Palisading of nuclei may represent primary features of other neuroepithelial tumors such as neuroblastomas and ependymomas. In the former, neuronal characteristics such as granules, microtubules, positivity for synaptophysin, and synapses\(^6\)^\(^\text{8}\) confirm the nature of the tumor. It is only a semantic question to call these tumors "neuroblastomas" or "undifferentiated tumors with neuronal differentiation." In one case described in the literature,\(^9\) there were neuroendocrine characteristics. There is no evidence favoring the concept that the ependyomatosus area represents differentiation of an undifferentiated tumor. The distribution of tumor cells in palisades may in fact be typical of nondifferentiation and thus it is not surprising to see this in tumors such as ependymomas and neuroblastomas.

In conclusion, whereas a difference can be accepted between a simple alignment of cells in a tumor due to pathoelastic influences and a diffuse alignment representing an architectural feature, it is not possible to differentiate the latter from a true and primitive distribution of cells of specific ontotypes. Therefore, we consider the "stepladder" appearance as a characteristic of some neuroepithelial tumors, mainly neuroblastomas and ependymomas, and we do not regard "polar spongioblastoma" as a separate tumor entity.

References


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