Histochemistry of hydrolytic enzymes in cerebral tumors

The relationship between the different cytotypes and cell regression

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The histochemical behavior of hydrolytic enzymes of human cerebral tumors has been widely investigated. Very recently some observations were reported on rat tumors induced by nitrosourea derivatives. Interpretation of the results is quite difficult, however, due to both general and technical problems of enzyme demonstration.

Our experience concerns mainly acid phosphatase, nonspecific esterases, and beta-glucuronidase. The distribution of these enzymes, acid phosphatase in particular, is associated with two fundamental factors: intensity of regressive or catabolic events, and cell differentiation. Acid phosphatase is confined to pericytial and scattered parenchymal cells in fibrillary astrocytoma, while it is more abundant in protoplasmic and anaplastic astrocytoma, and reaches its highest intensity in glioblastoma. Perivascular and phagocytosing cells, perinecrotic palisadings, and most tumor cells from anisomorphic areas show strong positive reactions. Malignant cerebral tumors, such as medulloblastomas, and isomorphic areas of glioblastomas are poorly endowed with acid phosphatase, while very atypical tumors, such as monstrouscellular sarcomas, are very rich in enzymatic activity. For this reason, the appearance of high levels of acid phosphatase may be interpreted as an expression of regression rather than malignancy.

As far as cellular localization of acid phosphatase is concerned, Gomori and diazo methods reveal most frequently a corpuscular reaction product. However, in some cytotypes, especially in malignant gliomas, a diffuse staining of the cytoplasm with or without corpuscular reaction is observed using diazo methods. This phenomenon appears only in large cells, such as gemistocytic astrocytes, giant cells of glioblastoma, and mostrocellular sarcoma. Intermediate stainings between corpuscular, diffuse, and completely negative reactions may be observed. Different interpretations may be given. If the diffuse staining may be regarded as a sign of progressive modification of the cell, the association of corpuscular and diffuse reactions may suggest cell regression, as in early necrotizing cells or perinecrotic palisadings.

In other cells, e.g., gemistocytes, a morphological transformation is accompanied by central accumulation of reaction product and subsequently by the complete disappearance of the enzyme activity. The existence of intermediate patterns indicates that many cell types have a reactive origin and may subsequently regress. This is also confirmed in nitrosourea-induced brain tumors in the rat, where a good example is provided by the gemistocytes observed in oligodendroglioma, which is originated by oligodendroglia and accompanies the onset of necrosis.

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mors are also related to cell differentiation. In some mature tumors, e.g., ependymomas, whose corresponding normal tissues are endowed with abundant acid phosphatase, there is a strongly positive histochemical response. In oligodendrogliomas, on the contrary, the pattern is not constant, since enzyme activity may be very high in parenchymal cells or limited to perivascular cells and included neurons. Normal white-matter oligodendroglia has practically no enzyme activity, while activated oligodendroglia is strongly positive to all the enzymes considered here. Probably oligodendrogliomas are endowed with more than one histoenzymatic pattern. The two histochemical pictures may be well observed in surrounding areas of the experimental brain tumors in the rat. Cell differentiation and reaction seem to be closely associated in these tumors.

Histochemically, the affinity between cell reaction, differentiation, and regression is strikingly apparent in cerebellar spongiblastomas. The highest enzyme activity is observed in cells of the cystic areas, while many astrocytic cells with an enzyme reaction similar to that of hypertrophic reactive astrocytes, as well as intermediate forms of reaction between these cells and elongated spongiblasts, may be observed. Signs of regression may be noted in areas of cystic degeneration of some astrocytes.

Among the other enzymes studied, E-600 resistant naphthyl esterase, indoxyl-esterase, and beta-glucuronidase are generally distributed as described for acid phosphatase with some exceptions. We wish to underline that the corpuscular reaction of naphthyl-esterase observed in perinecrotic palisadings of glioblastoma is partly E-600 sensitive and that autofluorescent PAS-positive material is associated with acid phosphatase, betaglucuronidase, E-600 resistant naphthyl esterase, but not with indoxyl esterase, in microglial differentiation and in adventitial sarcomas.

Various interpretations of these and other conflicting findings may be suggested, including the possible heterogeneous role of lyosomes in their hydrolase content. A precise interpretation of the enzyme pictures observed in different cell types is hampered by lack of definitive information concerning their exact function in cell metabolism. In brain tumors, acid hydrolase reactions may be interpreted as an expression of cytotic processes. In general our findings are related to three cell events: reactivity, differentiation and regression. The first two phenomena may be closely associated and may involve the same cells. If atypical deviation or anaplasia occur, cell regression becomes more evident and it is the most common consequence of the first two events, unlike in other types of tumor.

References

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