Phenotypic characteristics of GFAP-positive oligodendroglial tumours
Part II: Ultrastructural study

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Five cases of anaplastic oligodendrogliomas containing numerous GFAP-positive cells have been analysed by electron microscopy to establish the fine structural characteristics of neoplastic cells. Ultrastructurally, all tumours have revealed monotonous appearance typical of oligodendrogliomas, however some structural variability, particularly with reference to astrocytic differentiation, has been observed. The majority of neoplastic cells have shown the fine structural features of oligodendrocytes, accompanied by various numbers of intermediate cytoplasmic filaments. These filaments have been usually distributed in the perinuclear, less often in the peripheral, parts of the cytoplasm. The cells exhibiting features common to both oligodendroglial and astroglial cells might be regarded as an intermediate morphological form between these two cell types. True neoplastic astrocytes could be encountered only sporadically. The present electron microscopic study supports the opinion that GFAP-positive oligodendroglial tumours contain heterogeneous neoplastic cell populations with the transitional cell types between oligodendroglial and astroglial lineage.

key words: anaplastic oligodendroglioma, ultrastructure, intermediate filaments

INTRODUCTION

Oligodendrogliomas represent tumours derived from oligodendrocyte lineage but the histogenesis and differentiation of oligodendroglial cells in the developing central nervous system (CNS) and brain tumours is not fully understood. In recent years great attention has been paid to the cellular heterogeneity displayed by brain tumours including oligodendrogliomas. This heterogeneity, reflected in morphological differences between individual cells and in considerable variation in the expression of immunohistochemical markers, indicates the possibility of various patterns of cell differentiation [13, 21, 25]. In particular, the evidence of a varying degree of astrocytic differentiation in oligodendrogliomas has been a subject of debate [9, 11, 19]. The variability in expression of immunohistochemical markers of some oligodendroglial tumours results in significant diagnostic and nosological problems. Thus, in specific cases of the primary CNS tumours, electron microscopic studies are necessary to establish a correct differential diagnosis [15, 17]. In our immunohistochemical study of anaplastic oligodendroglial tumours, the GFAP expression occurs in morphologically different tumour cells responding to typical neoplastic oligodendrocytes with perinuclear accumulation of glial filaments, small gemistocytes and neoplastic or reactive astrocytes [18].

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The present study has been performed to evaluate the fine structural characteristics of tumour cells in GFAP-positive anaplastic oligodendroglial tumours. The electron microscope analysis has been centred mainly on the observation of intermediate filament production in heterogeneous neoplastic cell populations.

MATERIAL AND METHODS
Tissues from 5 biopsy specimens of oligodendrogliomas, constituted by a large number of GFAP-positive neoplastic oligodendroglial cells evidenced by immunohistochemistry, were processed for electron microscopy. The representative samples fixed in 10% formalin were postfixed in 2% cold glutaraldehyde for 1 hour, washed in cacodylate buffer, pH 7.2–7.6, postfixed in 2% osmium tetroxide, dehydrated in graded alcohols and embedded in Epon 812. Semithin sections were stained by toluidine blue to select the areas exhibiting marked variability of the cells. Ultrathin sections were counterstained with uranyl acetate and lead citrate and examined in a JEOL 1200 EX electron microscope.

RESULTS
By electron microscopy, most tumour cells showed monotonous appearance characteristic of oligodendrogliomas (Fig. 1). The plasmalemmal membrane of the tumour cells and intracytoplasmic organelles were sometimes artifically destroyed and the cytoplasm was partly empty, corresponding to the perinuclear halo seen in the light microscope. The majority of neoplastic cells exhibited round to oval nuclei lacking indentation, surrounded by a scant, electron lucent cytoplasm (Fig. 2). Cells with more or less irregular nuclei and delicate chromatin granules or peripheral clumping of chromatin were seen sporadically. The cytoplasm contained various quantities of small, often elongated mitochondria, few short channels of granular endoplasmic reticulum, free ribosomes and cytoplasmic microtubules. Some cells showed an abundance of lisosomes filled with electron-dense, granular material. Occasionally, polygonal crystalline bodies or arrangements of tubular structures were seen (Fig. 3). The concentric arrays of cytoplasmic membranes were detected only sporadically, whereas the rows of folding cell processes were frequently observed. The myelin-like bodies or concentric laminar structures arranged around other organelles were also found.

Among uniform oligodendrogial cells with scanty, electron-lucent cytoplasm, numerous cells exhibiting

Figure 1. Oligodendroglioma composed of neoplastic cells exhibiting regular nuclei and scanty, electron-lucent cytoplasm, × 6000.
the presence of intermediate filaments were seen (Fig. 4). The intermediate filaments were usually accumulated in the perinuclear areas or distributed in the whole cytoplasm. The cells with bundles of filaments encircling the nucleus were most commonly observed (Fig. 5). These neoplastic cells responded to
gliofibrillary oligodendrocytes-GFOC and showed ultrastructural features common to both oligodendroglial and astroglial cells.

Some cells exhibited more abundant cytoplasm, which was almost totally filled with filaments arranged in parallel bundles. They exhibited ultrastructural sim-
Similarity to small gemistocytes and were characterised by eccentrically situated nuclei and ovoid cytoplasm lacking cell processes but densely filled with filaments (Fig. 6). Moreover, the cells with intermediate ultrastructural features between GFOC and minigemistocytes containing a large number of intertwined bundles of

Figure 6. A typical minigemistocyte with eccentrically situated nucleus and abundant cytoplasm, lacking cell processes but almost totally filled with filaments, × 12 000.

Figure 7. The cell with intermediate ultrastructure features between GFOC and minigemistocyte exhibiting cytoplasm containing a large number of filaments, × 10 000.
filaments could be occasionally detected (Fig. 7). Some cells with perinuclear accumulation of filaments revealed the osmophylic condensation characteristic of the structure of Rosenthal fibres (Fig. 8).

Classical neoplastic astrocytes, characterised by more or less irregular nuclei and abundant cell cytoplasm filled with bundles of gliofilaments, were rarely found (Fig. 9).
DISCUSSION

In recent years many studies have indicated that the presence of GFAP-expression in neoplastic oligodendroglial cells, both in pure oligodendrogliomas and in mixed gliomas, is more frequently detected than was originally assumed [6, 9, 25, 26]. The immunohistochemical expression of intermediate glial filaments has been demonstrated in various oligodendroglial cells exhibiting morphological features of typical oligodendrocytes named “gliofibrillary oligodendrocytes” (GFOC) and/or miniature form of gemistocytes called “minigemistocytes” [9, 19].

It has been suggested that some heterogeneity of these tumour cells exists and that oligodendrogliomas can display a spectrum of histological, immunohistochemical and fine structural features. It has been demonstrated that even isomorphic oligodendroglioma is not quite homogeneous [1].

Electron microscope analysis can provide the more detailed morphological features necessary to distinguish particular cell types. There are a lot of ultrastructural characteristics frequently found in cells of the oligodendroglial line including oval cell shape, round nuclei lacking nuclear indentation, scanty cytoplasm containing abundance of mitochondria, cytoplasmic microtubuli and myelin-like membranous structures or atypical polygonal crystalline structures [2, 3, 7, 8, 16, 20, 24]. However, individual ultrastructural characteristics cannot be considered as pathognomic for the oligodendrogliomas and only the rows of folding cell processes are thought to represent a fundamental structural principle of oligodendroglia [2]. Concentric lamination, considered a specific feature of oligodendrogliomas, has been found in fibrillary astrocytomas, mixed gliomas and glioblastomas [12].

This electron microscopic study has proved that the majority of anaplastic GFAP-positive oligodendrogliomas are composed of heterogeneous cell populations. A lot of neoplastic cells have shown the fine structural features of oligodendrocytes, accompanied by the presence of intermediate filaments. The majority of intermediate filaments have been accumulated around the cell nuclei corresponding closely to the strong perinuclear rim of GFAP—immunoreactivity on immunohistochemical studies. Some cells exhibiting abundant, highly fibrillated cytoplasm, ought to be regarded as neoplastic astrocytes, intermixed with other neoplastic cells of oligodendrogial origin. A few cells, rich in cytoplasmic filaments, could be identified either as persisting astrocytes intermixed with the other neoplastic cells or as a form of immature neoplastic cells of the oligodendrocyte line. Thus, confirming our previous studies [18], these electron microscope findings are evidence that many tumour cells exhibit ultrastructural features common to both oligodendrogial and astroglial cells, and might be regarded as an intermediate form between these two cell types. Some of these cells revealed the presence of microtubules, which is considered as a conspicuous component of oligodendrocytes. It is noticeable that cytoplasmic filaments as well as microtubules are not the specific morphological markers for oligodendrocytes or astrocytes and only the predominance of one of these structures established their cytogenic identifications [3]. The interpretation of accumulation of filaments in oligodendrogliial tumours at the ultrastructural level is controversial [14, 25]. It has been postulated that tumours of CNS often recapitulate the development during normal ontogeny. The progenitor cells of oligodendrocytes named “glioblasts” derive from multipotential neuroepithelial cells. It has been suggested that oligodendrocytes during the development of CNS arise from astroglial precursors [4, 5]. This hypothesis was confirmed by in vitro study, which documented that the progenitor cells in rats might develop into astrocytes or oligodendrocytes depending on the contents of culture medium [22, 23]. It has also been suggested that characteristic microscopic features of oligodendrocytes can be taken by various types of cells under certain circumstances [10].

The data of the current ultrastructural findings and of our previous immunohistochemical studies support the opinion that the GFAP-positive oligodendrogial tumours contain the heterogeneous population of neoplastic cells representing the various transitional cell types between oligodendrogial and astroglial lineage.

REFERENCES


