Immunohistochemical demonstration of glial markers in retinoblastomas

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Summary. Twenty retinoblastomas were studied immunohistochemically in order to visualize glial cells. In the retina, the glial cells in the ganglion cell layer and the Müller cells were GFAP positive, while only the glial cells of the ganglion cell layer expressed S-100 reactivity. In the tumours S-100/GFAP positive glial cells were found in areas near the retina and along many tumour vessels. Some S-100 reactive cells previously interpreted as tumour cells were refound in a few tumours. In areas with Flexner-Winterstein rosettes and in areas with light cells showing photoreceptor-like differentiation, glial cells reactive for both S-100 and GFAP were demonstrated. The latter findings may represent differentiation in a glial direction in the more mature parts of retinoblastoma.

Key words: S-100 protein - GFAP - Glia - Immunohistochemistry - Retinoblastoma

Introduction

The histogenesis of the retinoblastoma has often been debated and both a glial and a neuronal origin has been proposed (Dunphy 1964; Tso 1980). The histology of this tumour presents a varying degree of differentiation ranging from areas with photoreceptor-like differentiation to entirely anaplastic areas, even within a single tumour. Immunohistochemical studies have contributed to further characterization of the tumour. Neuronal markers have been demonstrated in the bulk of cells (Tegenghi et al. 1984; Molnar et al. 1984; Messmer et al. 1985) and recently the photoreceptor specific antigen S has been visualized in these tumours (Mirshahi et al. 1986). However, populations of cells with a glial character have also been described (Tegenghi et al. 1984; Molnar et al. 1984; Messmer et al. 1985; Lane and Klintworth 1983).

The presence of glial elements in the retinoblastomas has prompted a discussion whether these cells are part of the tumour or a proliferation of glial cells from the retina. With regard to the glial fibrillary acidic protein (GFAP) containing cells, a non neoplastic nature has generally been suggested (Tegenghi et al. 1984; Molnar et al. 1984; Messmer et al. 1985; Lane and Klintworth 1983). Among the S-100 reactive cells, however, a population of primitive, neoplastic cells have been found (Tegenghi et al. 1984).

Our results are of interest in the discussion about the existence of more mature glial elements as part of retinoblastomas.

Materials and methods

Paraffin embedded material from 20 eyes with retinoblastomas was investigated. Sections were stained with haematoxylin and eosin and immunohistochemically with the PAP technique (Sternberger 1979) for the presence of GFAP (antibody supplied by Dr. Elisabeth Bock) and S 100 (DAKO pattern Z 311). Controls included cerebral tissue and peripheral nerves. As previous investigations (Schroder and Johannsen 1986) have shown that enzyme digestion did not improve the immunohistochemical results, this step was not included in the staining procedure.

Results

In most of the studied cases areas of tumour free retina were present. The GFAP-stained sections showed positive reaction in the glial cell in the ganglion cell layer and around vessels as well as in the Müller cells (Fig. 1c). S-100 immunoreactivity was restricted to the glial cells in the ganglion cell layer and around vessels (Fig. 1b).
In the parts of retina invaded by tumour both GFAP positive Müller cells and S-100 and GFAP containing astroglial cells were seen (Fig. 1). In several areas where no remnants of the retina were observed in haematoxylin and eosin stained sections immunohistochemistry visualized remnants at the glial framework. Moreover, the parts of the tumours close to normal retina contained stellate cells of astroglial type with no apparent organization except for perivascular clustering. This population was characterized immunohistochemically by strong S-100 reactivity and moderate GFAP