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Immunohistochemical study of intracranial cysts

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Summary. We present the immunohistochemical study of 11 cases of intracranial cysts: two extraventricular ependymal cysts, three colloid cysts of the third ventricle, four extraventricular choroidal cysts and two Rathke's cleft cysts. Antibodies against glial fibrillary acidic protein (GFAP), cytokeratins (AE1, CK5D, AE3), S-100 protein, epithelial membrane antigen (EMA), vimentin, neuron specific enolase (NSE), neurofilaments protein (NF) and prealbumin, were used. The epithelium of choroidal cysts, showed strong immunoreactivity for Prealbumin and cytokeratins, similar to the normal choroid plexus epithelium. The ependymal cysts showed epithelial immunoreactivity for GFAP and S-100, both glial markers expressed by the normal ependymal epithelium. On the contrary, the epithelial wall of colloid cysts and Rathke's cleft cyst, expressed epithelial markers (cytokeratins and EMA) but no neuroepithelial markers, with a immuno-phenotype similar to that of other cysts of endodermal nature. This finding supports the neuroepithelial origin for choroid and ependymal cysts, and an endodermal nature for colloid and Rathke's cleft cysts. We conclude that these immunohistochemical markers are useful in the differential diagnosis of intracranial cysts.

Key words: Immunohistochemical study, Intracranial cysts

Introduction

The intracranial epithelium-lined cysts are uncommon lesions in the Central Nervous System (CNS). The origin of these cysts is from simple folding of neuroepithelium into or out of the primitive ventricular system during the embryogenesis of CNS (choroidal and ependymal cysts), (Shuangshoti and Nestki, 1966; Shuangshoti et al., 1965, 1970, 1988; Ciricillo et al., 1990; Odake et al., 1990) from remains of endodermal epithelium (Rathke's cleft cysts, enterogenous and respiratory epithelial cysts) (Ho and Chason, 1989; Russel and Rubinstein, 1989; Shuangshoti et al., 1989; Macdonald et al., 1991) or controversial (colloid cysts) (Jan et al., 1989; Kondziolka and Bilbao, 1989; Lach et al., 1993). In spite of this, the covering epithelium of the cysts are frequently similar and thus their final diagnosis can be difficult. In this communication we present the findings of a histological study with immunohistochemical markers for epithelium of neural and non-neural origin, in four types of intracranial epithelial cysts (choroidal, ependymal, colloid and Rathke's cleft). The embryological origin of these cysts and the usefulness of the immunohistochemical markers in their differential diagnosis are discussed.

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Materials and methods

We have studied two extraventricular ependymal cysts, three colloid cysts of the third ventricle, four extraventricular choroidal cysts and two Rathke's cleft cysts. All tissues were fixed in 10% formalin and were processed routinely for light microscopy. Sections cut at 5 to 6 μm were stained with Haematoxylin and Eosin, reticulin impregnation (Willder) and PAS. Immunohistochemical stains were performed for glial fibrillary acidic protein (GFAP), cytokeratins AE1 (40, 48, 50, 56, 5 KD), CK5D (40, 45, 52, 5 KD), S-100 protein, epithelial membrane antigen (EMA) and vimentin (monoclonals, prediluted, Biogenex); cytokeratins AE3 (52-67 KD) (monoclonal, prediluted, Signet), neuron specific enolase (NSE), (polyclonal, prediluted, Immunotech); neurofilaments protein (NF) that included the subunits of 70, 160 and 210 kd (monoclonal, 1/50, Eurodiagnostic); and prealbumin, (monoclonal, 1/25, Dako). Primary antibodies were visualized with a streptavidin-biotin-peroxidase universal kit with AEC chromogen (Biomeda, USA).

Results

The wall of the choroidal epithelial cysts was composed of a single cuboidal epithelial layer resting on a well-defined basement membrane. The epithelial cells showed occasional intracellular vacuolization, without PAS-positive material. No ciliated or goblet cells were seen. Histological examination of the ependymal cyst wall revealed a single layer of nonciliated cuboidal epithelium resting on a glial stroma. The basement membrane was absent. In case 6, a small part of the wall was covered by epithelium similar to the normal choroid plexus. The wall of the colloid cysts was lined by simple or pseudostratified cuboidal or columnar epithelium with ciliated and nonciliated cells as well as scattered goblet cells. The lumen of the cysts was filled by an eosin- and PAS-positive material with frequent microcalcifications. The wall of the Rathke's cleft cysts was lined by pseudostratified or simple columnar or cuboidal epithelium with frequent ciliated cells and scattered goblet cells. Both cysts contained areas of squamous differentiation.

The results of the immunohistochemical study (Figs. 1-6) are summarized in Table 1.

The majority of the epithelium of an ependymal cyst, case 6, showed immunoreactivity for GFAP, but there was a zone with strong cytoplasmatic expression of prealbumin; this epithelium was histologically similar to the normal choroidal plexus (Fig. 4).

Discussion

The epithelium of choroidal cysts presented here expressed cytokeratins, especially the cytokeratins of low molecular weight. This marker has been described in the epithelium of normal choroid plexus (Kasper et al., 1986; Kondziolka and Bilbao, 1989; Lach et al., 1993) but, to our knowledge, has not been reported in the epithelium of choroidal cysts. Immunoreactivity for prealbumin was found in the epithelial wall of all cysts studied here. This marker is expressed by the epithelial cells of normal choroidal plexus (Herbert et al., 1986; Inoue et al., 1987, 1988; Lach et al., 1993) and has also been reported in the epithelium of choroidal cysts (Herbert et al., 1986; Inoue et al., 1987, 1988).

The epithelium of our two ependymal cysts showed strong positivity for S-100 protein and GFAP (Shuangshoti et al., 1988), both glial markers expressed

Table 1. Immunohistochemical features of intracranial epithelial cysts.

CASE	PRE	AE3	AE1	CK5	GFAP	EMA	NF	S100	VIM	NSE
Choroidal epithelial cyst										
1	+	±	+	±	-	-		-	-	
2	+	±	+	±	-	±		±	-	
3	+	-	+	±		-		+	-	
4	+	±	±	-		-		+	±	
Ependymal cysts										
5	-								±	
6	±								-	
Rathke's cleft cysts										
7				±		±		+		
8				±		±		±		
Colloidal cysts										
9			±	+	-	+				
10			-	±	-	±		-	-	
11			±	±	-	±		-	-	

+, positive immunostain in more than 50% of epithelial cells; ±, positive immunostain in less than 50% of epithelial cells; -, negative. PRE, prealbumin; AE3, cytokeratin AE3; AE1, cytokeratin AE1; CK5, cytokeratin AE5D; VIM, vimentin.

Fig. 1. Choroid cyst. Prealbumin immunoreactivity of epithelial wall. x 400

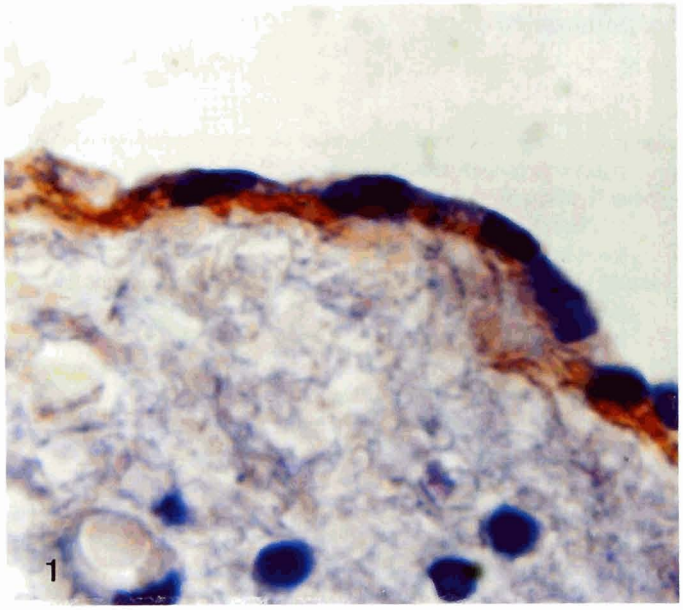
Fig. 2. Choroid cyst. Cytokeratin AE1 expression in epithelial cells. x 100

Fig. 3. Immunoreactivity for GFAP in epithelium and glial stroma in an ependymal cyst. x 250

Fig. 4. Case 6, positive immunostain for GFAP in ependymal cells of the cyst wall. The epithelium with choroidal differentiation is negative (arrow). x 100

Fig. 5. Cytokeratin AE1 in a colloid cyst. x 100

Fig. 6. Cytokeratin CK5 in a Rathke's cleft cyst. x 100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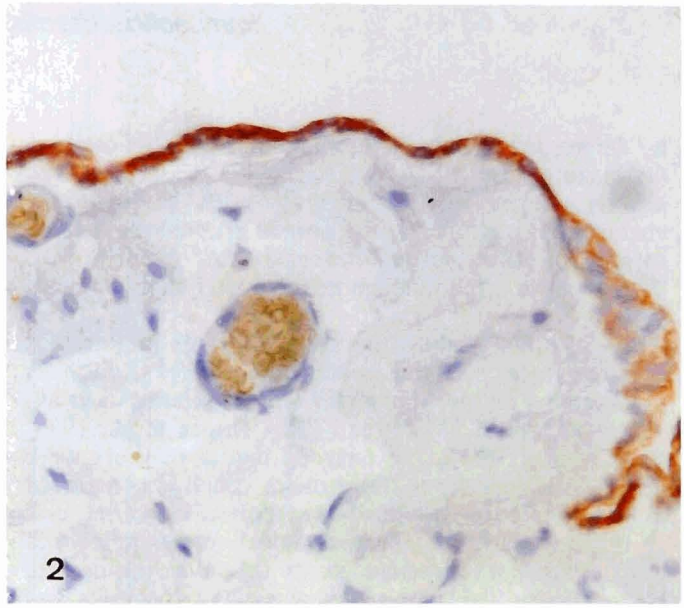
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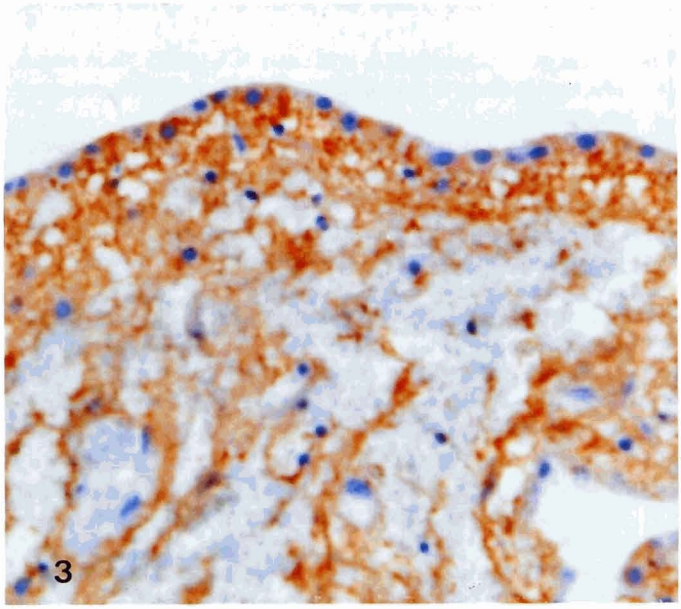
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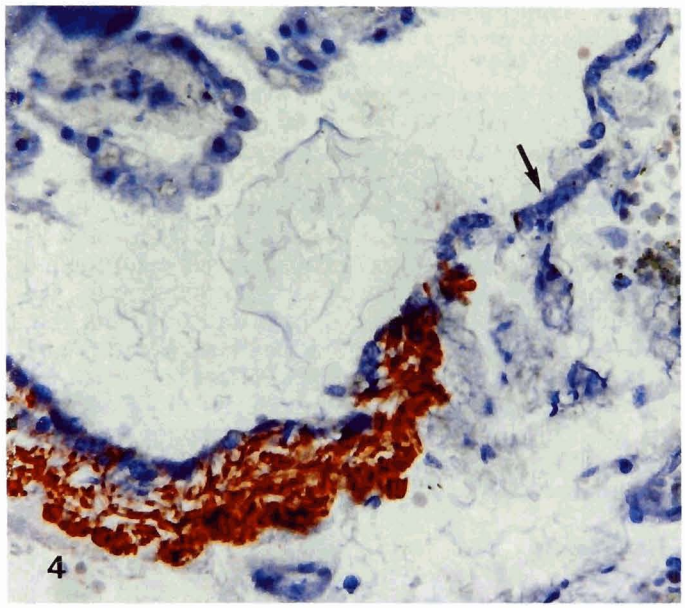
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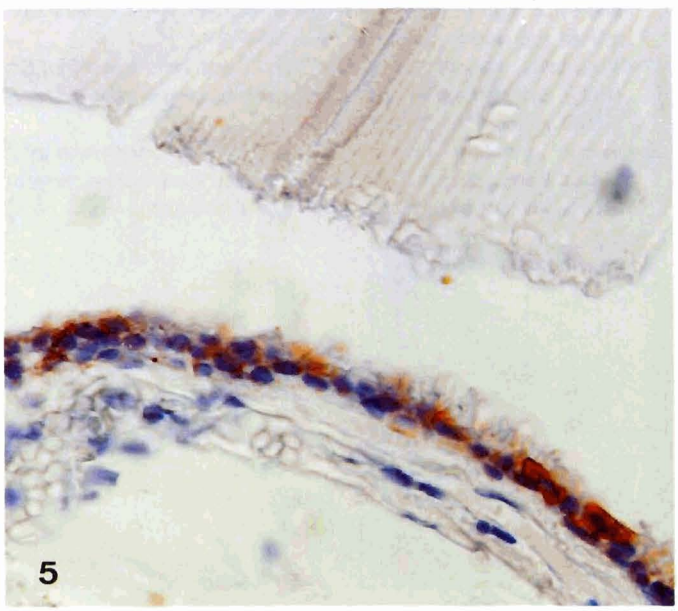
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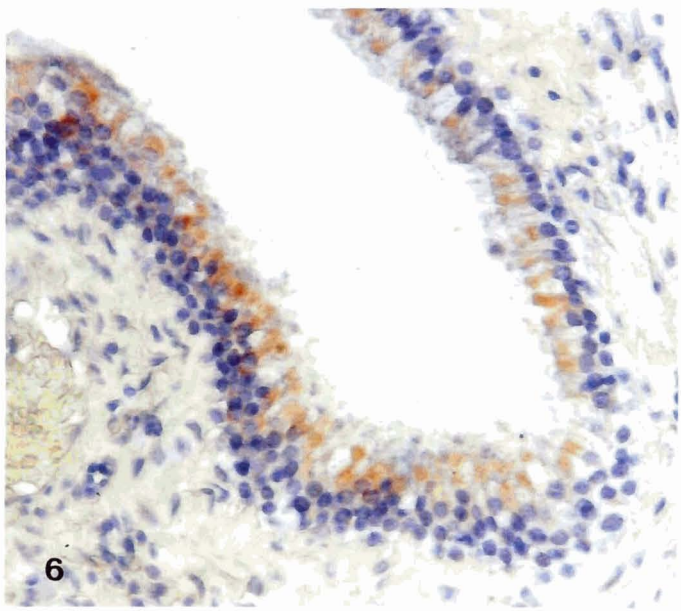
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by the normal ependymal epithelium. Epithelial markers (cytokeratins and EMA) were negative. Case 6 showed a part of the epithelial wall with histological characteristics similar to the normal choroid plexus and immunohistochemical expression of prealbumin. Therefore we think this is a mixed ependymal-choroidal cyst.

As in other studies, the epithelial cells of Rathke's cleft cysts expressed epithelial markers, such as cytokeratins of low molecular weight (Uematsu et al., 1990; Lach et al., 1993) and EMA (Inoue et al., 1988; Lach et al., 1993). The neuroepithelial markers were negative, except the S-100 protein, which is considered to be a nonspecific immunohistochemical marker.

In previous immunohistochemical studies of colloid cysts, epithelial immunoreactivity for epithelial markers has been reported, such as cytokeratins (Konziolka and Bilbao, 1989; Uematsu et al., 1990; Lach et al., 1993) or EMA (Inoue et al., 1988; Konziolka and Bilbao, 1989; Lach et al., 1993). In our cases we have found epithelial expression for cytokeratins of low molecular weight (AE1, CK5) and EMA, but not for AE3 cytokeratin. The neuroepithelial markers were all negative.

In conclusion, the epithelium of choroidal and ependymal cysts, shows immunoreactivity for markers of normal neuroepithelial structures of CNS, such as choroid plexus epithelium (prealbumin and cytokeratins) or ependymal epithelium (GFAP). On the contrary, the epithelial wall of colloid cysts and Rathke's cleft cyst, only expressed epithelial markers (cytokeratins and EMA) but no neuroepithelial markers, with an immunophenotype similar to other cysts of endodermal nature. This finding supports the neuroepithelial origin for choroid and ependymal cysts, and an endodermal nature for colloid and Rathke's cleft cysts.

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