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CLINICAL INVESTIGATIONS

Phakomatous Choristoma of the Eyelid: Immunohistochemical Observation

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Abstract: This article reports the first case of phakomatous choristoma of the eyelid in Japan. The tumor occurred in a 2-week-old boy and was located in the left lower lid near the inner canthus. An immunohistochemical study of this rare, congenital tumor was performed. The immunohistochemical analysis revealed that the epithelial cells of this tumor showed positive staining for vimentin, S-100 protein, and neuron-specific enolase, while they had no immunoreactivity for cytokeratin, glial fibrillary acidic protein, epithelial membrane antigen, or a macrophage marker. Both the epithelial cells and the central contents of the islands in this tumor showed positive staining with anti-human alpha crystallin monoclonal mouse IgG. These results strongly indicated that a phakomatous choristoma was of a lenticular origin. **Jpn J Ophthalmol 1998;42:41–45** © 1998 Japanese Ophthalmological Society

Key Words: Congenital tumor, crystallin, eyelid, phakomatous choristoma.

Introduction

The term *phakomatous choristoma* was coined by Zimmerman in 1971 to describe a congenital tumor of presumed lenticular anlage in three cases.[1] Since then, 10 additional cases of this extremely rare tumor have been reported.[2–11] Electron microscopy has previously revealed that the features of the tumor cells in phakomatous choristoma share characteristics of the epithelial cells in the human crystallin lens.[4,5,7,8,10] These features strongly suggested that this tumor is of lenticular anlage. Furthermore, three cases of this tumor have accumulated in the aspect of immunohistochemical study.[7,10,11]

This article reports the first case of a phakomatous choristoma in the Orient. The purpose of this study is to document a case of phakomatous choristoma including immunohistochemical observation.

Case Report

A 2-week-old male infant was seen by an ophthalmologist with a history of a mass visible in the inferomedial aspect of the left lower eyelid. The lesion had been noted by the mother shortly after his birth. He was referred to the Department of Ophthalmology at Aoto Hospital of the Jikei University School of Medicine. A smoothed-edged, firm mass was palpable near the inner canthus. The lesion was nonmobile, nonfluctant, and not attached to the overlying skin. The left tear duct was syringed with free passage of fluid to the nasopharynx. The remainder of the ocular examination, as well as the general physical examination, had no abnormality. The infant was the product of a full-term pregnancy. Delivery was normal, and the baby was in good health. Computed tomography demonstrated a discrete, well-circumscribed, homogeneous, solid mass inferomedial to the left eyeball. Calcification and fatty accumulation were not noticed in the mass.

At operation, a very firm tumor, measuring 12 × 7 mm, was removed via an infraorbital incision (Figure 1). The tumor was adherent to the tarsus and the

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Figure 1. A very firm tumor, measuring 12 × 7 mm, was removed via an infraorbital incision. The tumor was adherent to the tarsus and the palpebral conjunctiva of the lower fornix, but it was otherwise easily freed from other tissues.

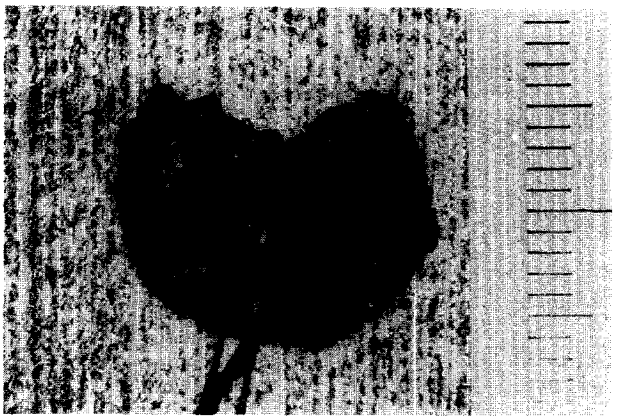

Figure 2. The cut surface of the tumor had a reticulated appearance.

palpebral conjunctiva of the lower fornix but was otherwise easily freed from the tissues. The cut surface of the tumor had a reticulated appearance (Figure 2).

Materials and Methods

The tumor was fixed by immersion in 10% neutral-buffered formaldehyde and embedded routinely in paraffin for histopathologic examination. Sections were stained with hematoxylin-eosin (HE), periodic acid Schiff (PAS), Alcian blue, Masson trichrome, and Elastica van Gieson stains. After the diagnosis of phakomatous choristoma was established by conventional histology, paraffin block was sectioned serially and 3-μm sections were mounted on polylysine-coated slides for immunochemistry. Immunohistochemical analysis was performed with the streptoavidin-biotinylated immunoperoxidase method using diaminobenzidine as the chromogen. Commercially available monoclonal antibodies against vimentin (Amersham, Little Chalsontboks, UK), S-100 protein (Nichirei, Tokyo, Japan), cytokeratin (Becton Dickinson, San Jose, CA, USA, CAM5.2), glial fibrillary acidic protein (Nichirei), neuron specific enolase (Nichirei), epithelial membrane antigen (DAKO, Glostrup, Denmark, E29), and a macrophage marker (DAKO, KP1) were used. Mouse monoclonal IgG against human alpha crystallin was purified and used for this study.

Pathologic Findings

Histological examination showed the tumor to be composed of cuboidal cells occurring in tubular structures and solid islands embedded in a dense collagenous stroma (Figure 3). The epithelial structures were surrounded by thick, irregular, PAS-positive basement membranes (Figure 4). Very swollen epithelial cells resembling "bladder-like cells" or "Wedl cells," observed in certain cataractous human lenses, were identified (Figure 4). Small foci of dystrophic calcification and an amorphous eosinophilic material were present in the center of some of these epithelial islands (Figure 3). The surrounding connective tissue stroma stained positively with Masson trichrome stain and were rich in acid mucopolysaccharide.

The epithelial cells in the tumor showed intense immunoreactivity for vimentin (Figure 5). Intense staining for S-100 protein was noted in the epithelial cells including the Wedl cells (Figure 6). Positive immunoreactivity for neuron-specific enolase was observed in the epithelial cells (Figure 7). There was no immunoreactivity observed using antibodies against the following antigens: cytokeratin, glial fibrillary acidic protein, epithelial membrane antigen, or a macrophage marker.

Both the epithelial cells and the center of the islands in this tumor showed positive staining with anti-human alpha crystallin monoclonal mouse IgG (Figures 8**A**, 8**B**).

Discussion

Zimmerman first reported three cases of phakomatous choristoma of the eyelid.[1] Up to the present, a total of 13 cases of an unusual congenital eyelid tumor have been reported (Table 1).[2–11] This article reports the 14th case of phakomatous choristoma. Nine of the cases were reported in the United States, two in Australia, one in Europe, one in South Africa, and this case in Japan. Eleven patients were males and three were females. Each patient had a firm tu-

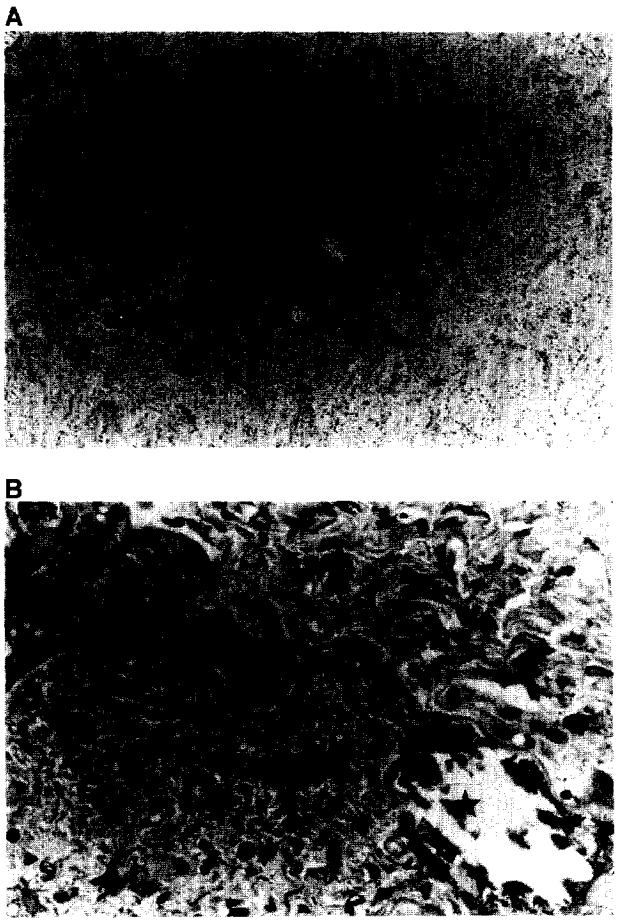

Figure 3. Histological examination showed the tumor to be composed of a dense collagenous tissue and epithelial structures (arrow) with cuboidal cells arranged in cords and islands. Calcification (star) was observed in the epithelial structure. Stained with hematoxylin-eosin: (**A**) low magnification (×40); (**B**) high magnification (×200).

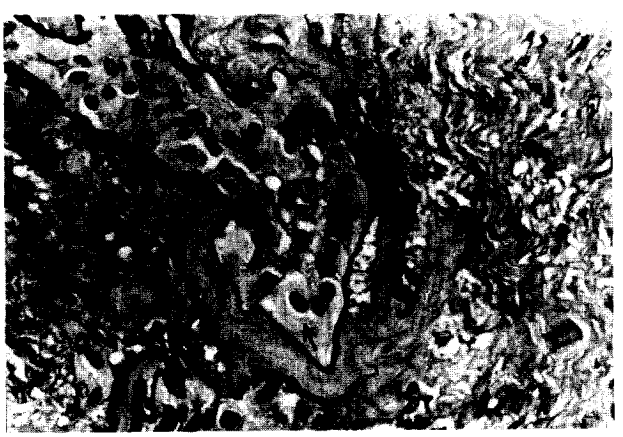

Figure 4. The epithelial structures were surrounded by thick, irregular, periodic acid Schiff (PAS) positive materials (large arrow) interpreted as basement membranes. The small arrow shows the Wedl's bladder cell (PAS, ×200).

Figure 5. The epithelial cells in the tumor showed intense immunoreactivity for vimentin (×200).

mor localizing in the nasal portion of the lower eyelid—eight cases in the right eyelid and six cases in the left eyelid.

Light microscopical features of the tumor in our case are similar to those of the previously reported cases (Figures 3, 4).[1–11] Therefore, we diagnosed the tumor in our case as phakomatous choristoma.

Immunohistochemical observation on a phakomatous choristoma was reported in three previous cases.[7,10,11] We also performed immunohistochemical analysis on our case. There were some differences in the immunoreactivities for some kinds of antigens among the cases of phakomatous choristoma. (Table 2). In the previous reports, the epithelial cells of the tumor showed negative staining (Sinclair-Smith et al[7]) and positive staining (Rosenbaum et al[10] and Ellis et al[11]) for vimentin. The epithelial tumor cells in our case had intense immunoreactivity for vimentin (Figure 5). Vimentin is the most primitive among the

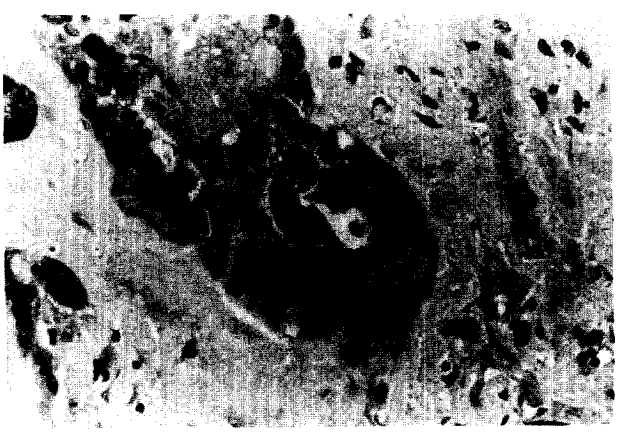

Figure 6. Intense staining for S-100 protein was obtained in the epithelial cells (×200).

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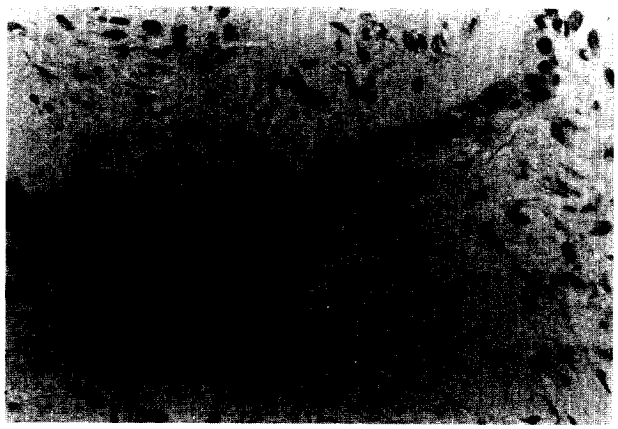

Figure 7. Positive staining for neuron-specific enolase was obtained in the epithelial cells (×200).

Table 1. Summary of Studies of Phakomatous Choristoma of the Eyelid

Study	Sex	Laterality
Zimmerman (1971)[1]	Male	Right
Zimmerman (1971)[1]	Male	Right
Zimmerman (1971)[1]	Male	Right
Filipic and Silva (1972)[2]	Female	Right
Greer (1975)[3]	Male	Left
McMahon et al (1976)[4]	Male	Left
Baggesen and Jensen (1977)[5]	Female	Left
Tripathi et al (1981)[6]	Male	Left
Sinclair-Smith et al (1989)[7]	Male	Right
Eustis et al (1990)[8]	Male	Left
Leatherbarrow et al (1992)[9]	Female	Right
Rosenbaum et al (1992)[10]	Male	Right
Ellis et al (1993)[11]	Male	Right
Kamada et al (this study)	Male	Left

intermediate filaments and is found in nonepithelial cells at the embryonic stage. It has been demonstrated that vimentin is a major intermediate filament in human lens epithelial cells.[12,13]

As for cytokeratin, the focal cytoplasmic staining of the epithelial cells with a keratin cocktail was reported (Rosenbaum et al[10]). However, negative staining was shown using antiserum to cytokeratin (Sinclair-Smith et al[7]), 903, 904, or CAM5.2 (Ellis et al[11]). The tumor cells in our case were negative for CAM5.2. Cytokeratins present in the lens during the early stage of development and disappear after the 8th week in the human embryo.[14] The bovine lens-forming cells have abundant intermediate-size filaments of the vimentin type, but they do not contain cytokeratins or desmin filaments.[15] The epithelial cells of phakomatous choristoma might be differentiated, because they were negative for cytokeratin.

Intense immunoreaction to S-100 protein was noted in the epithelial cells of our case as well as in the previously reported cases (Figure 6). The S-100 protein was originally isolated from the nervous system. Recently, the detection of S-100 immunoreactivities in the cornea, iris, and lens of the rabbit has been demonstrated.[16]

We present the first evidence that the epithelial cells of a phakomatous choristoma showed positive staining for neuron-specific enolase, an enzyme that distributes in neuronal cells and paraneurons (Figure 7). It was reported that the lens epithelium showed moderate neuron-specific enolase activity during early development in the chicken embryo.[17]

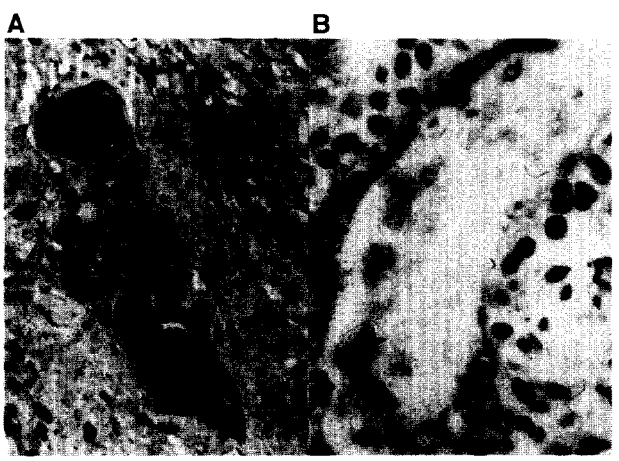

Figure 8. Positive staining with monoclonal antibody agonist human alpha crystallin in the epithelial cells (**A**; ×200) and the homogenous material (star) in the islands (**B**; ×250) was obtained.

Table 2. Immunohistochemical Analysis of Phakomatous Choristoma

	Sinclair-Smith	Rosenbaum	Ellis	Kamada
Vimentin	−	+	+	+
Cytokeratin	−	+	−	−
GFAP	−			−
S-100 protein	+	+	+	+
NSE	−			+
EMA	−			−
Mϕ marker	−			−
CEA	−			
Crystallin			α,β,γ; polyclonal	α; monoclonal

GFAP = glial fibrillary acidic protein; NSE = neuron-specific enolase; EMA = epithelial membrane antigen; CEA = carcinoembryonic antigen.

The mammalian lens has three main classes of water-soluble proteins: alpha, beta, and gamma crystallins. Ellis et al reported on the immunohistochemical analysis of a phakomatous choristoma using rabbit polyclonal antibodies against lens-specific proteins.[11] The anti-alpha crystallin polyclonal antibodies stained the epithelial cells, but they stained the central contents much less intensely. The antibody to beta crystallin stained the central contents positively, but it did not stain the peripheral epithelial cells. We demonstrated that both the epithelial cells and the center contents of the epithelial islands in a phakomatous choristoma showed positive staining with monoclonal antibody against human alpha crystallin (Figure 8**A**, 8**B**).

These results strongly indicate that a phakomatous choristoma is of a lenticular origin.

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