

## CLINICAL REPORT

## Papillary Endothelial Hyperplasia and Dilated Lymphatic Vessels in Bullous Pilomatricoma

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**This is a report of papillary endothelial hyperplasia in a 9-year-old girl with a pilomatricoma showing bullous appearance. Histologically, papillary proliferation of endothelial cells was found within dilated lymphatic endothelium-lined vascular channels overlying a pilomatricoma. The endothelial cells covering the papillae were of a lymphatic endothelial cell nature proved by immunohistochemistry and electron microscopy. Abundant fibrous long-spacing collagen was observed in the connective tissue and fibroblasts within papillae. Key words: papillary endothelial hyperplasia; pilomatricoma; lymphatic vessels.**

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Bullous pilomatricoma is an uncommon lesion and only a few cases of this variant exist in the literature (1–3). The bullous appearance was attributable to lymphatic obstruction that resulted in the dilation of lymphatic vessels. The occurrence of papillary endothelial hyperplasia (PEH) lesions overlying a pilomatricoma showing bullous appearance appears to be very rare. Julian & Bowers (4) described one variant of pilomatricomas where the area between the pilomatricoma and the overlying epidermis was filled with dilated lymphatic vessels and numerous small blood vessels. However, the detailed nature of these small blood vessels was not available in their clinical review and other reports. We herein report an unusual case with pathological changes of PEH within dilated lymphatic vessels overlying a typical pilomatricoma. The clinicopathologic, immunohistochemical and ultrastructural features of this lesion are presented.

## CASE REPORT

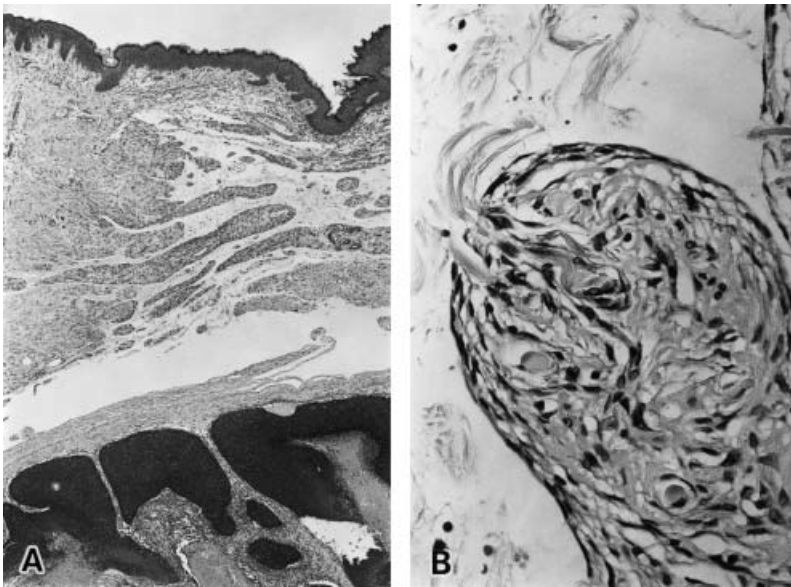
The patient, a 9-year-old girl, suffered from a tender nodule on her right scapular region that had developed about 6 months earlier and gradually enlarged. There was no history of particular local trauma or chronic irritation at the site of the lesion. Physical examination

revealed stalk-shaped, pink skin covering a hard nodule measuring 24 × 22 mm in size, and part of the surface showed telangiectasia (Fig. 1). The tumour resembled a flaccid, thick-walled bulla in appearance. It was well defined from the subcutaneous tissue. Laboratory studies, including blood cell count, urinalysis and serum biochemistry, were all within normal limits. The total lesion was surgically removed under general anaesthesia. When the lesion was bisected immediately after removal, a serum-like liquid was shed from the cut surfaces of the dermis portion between the tumour and epidermis.

Light microscopic examination showed that a well-circumscribed, rounded tumour existed in the dermis. Two types of cells, basophilic cells and shadow cells, composed the irregular tumour nests in a fibrotic stroma. These findings were consistent with pilomatricoma. The dermis was oedematous and contained a small amount of mixed inflammatory infiltrate. Dilated endothelium-lined vascular channels were found, which were identified as lymphatic vessels. Pronounced papillary formations were observed within these extremely dilated lymphatic vessels. The papillary projections were either attached to the wall of the vascular space or appeared to float in the lumen (Fig. 2A). These papillae were lined by a single layer of flattened endothelial cells (Fig. 2B) and consisted of a connective tissue core of



Fig. 1. A hard nodule on the right scapular region (approx. 2 cm in diameter) showing bullous appearance.



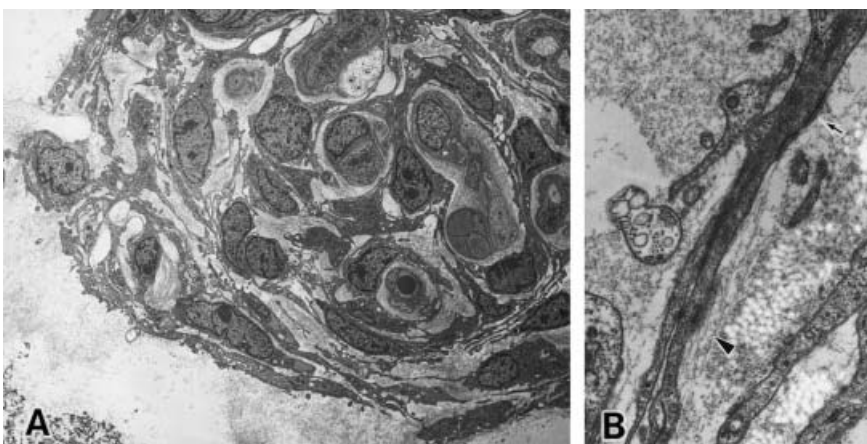
*Fig. 2.* Histological features. (A) A dilated lymphatic vessel structure with irregular papillary stalks. A pilomatricoma nest can be seen in the lower right corner (haematoxylin and eosin stain). (B) Close-up view; papillae are covered by a layer of endothelial cells.

varying thickness and cellularity, with or without small capillaries. There was no evidence of necrosis or prominent cytological pleomorphism of endothelial cells. The appearance was similar to the characteristic changes in PEH.

Using standard immunoperoxidase techniques on formalin-fixed and paraffin-embedded sections, the small proliferating vessels within the connective tissue cores of papillae were strongly labelled with antibodies to CD34 (Becton Dickinson) and Factor VIII-related antigens (Dako). Many subendothelial cells also exhibited a weak reaction to these antibodies within some papillae. However, the endothelial cells covering papillae showed no reaction to them.

Electron microscopic study revealed that the cells lining the surface of papillae had features including an extremely attenuated endothelium, a thin and discontinuous basal lamina and subendothelial anchoring filaments (Fig. 3). No Weibel-Palade body was found. The

principal cells were fibroblasts in the papillae stroma. These fibroblasts had oval or convoluted nuclei and irregular cytoplasmic projections. They contained well developed Golgi complex, rough endoplasmic reticulum and mitochondria. Intracytoplasmic filaments 6–8 nm thick and a few pinocytotic vesicles were also present. Capillaries were interspersed in the intercellular spaces in some papillae. Individual endothelial cells typically had bulky cytoplasm that did not show fenestration. A major portion of the cytoplasm was occupied by pinocytotic vesicles, mitochondria, rough endoplasmic reticulum and microfilament bundles. Weibel-Palade bodies were present in some mature endothelial cells. A few intercellular junctions of various lengths united adjoining cells. Intercellular lumens were formed by reflexive overlapping between the protrusions of one or two cells. Intracytoplasmic lumen formation was evident, with some lumina being occupied by degenerated cell



*Fig. 3.* (A) Ultrastructure of a papilla shows many small vessels and fibroblasts within the core surrounded by a single layer of flattened endothelial cells ( $\times 2000$ ). (B) Part of a layer of endothelial cell covering papillae. Note the incomplete basal lamina (arrows) and subendothelial anchoring filaments (arrowhead) linking the endothelium to the surrounding connective tissue ( $\times 16,000$ ).

fragments, occasionally by a single erythrocyte. The abluminal surface of the endothelial cells was surrounded by basal lamina. However, some capillaries could be distinguished between blood vessels and lymphatic vessels due to lack of Weibel-Palade bodies and basal lamina. A capillary-like structure and the surrounding fibroblasts occasionally formed a whirling pattern. A few mast cells, macrophages and lymphocytes were seen. The interstitial space included large numbers of collagen fibres and abundant fibrous long-spacing collagen within papillae. However, the collagen was predominantly observed in the vicinity of the capillary at the mature stage. It was seen close to the capillary basal lamina, and some of the fibres appeared to be continuous with the basal lamina; their orientation was usually parallel to cell extension. Intracytoplasmic long-spacing collagen was occasionally seen in fibroblasts.

## DISCUSSION

Almost any vessels in the body may be affected by PEH, including haemangiomas, pyogenic granuloma and hamartoma (5, 6). The occurrence of PEH-like lesions in dilated lymphatic vessels is exceedingly rare; only five cases with cystic and cavernous lymphangiomas have been reported (7–9). Clearkin & Enzinger (10) stated that the occurrence and development of PEH are associated with a slowing of blood flow, stasis and thrombus formation, representing a peculiar process of thrombi undergoing organization of blood vessels. Kuo & Gomez (7) suggested that this process could also take place in the lymphatics, and equally be interpretable as PEH within dilated lymphatic vessels.

Dilated lymphatic vessels surrounding the papillae could be distinguished. Therefore, we conclude that the localized endothelial proliferation processes affected a lymphatic collecting vessel and not a venous one. At least part of the newly formed capillaries within the cores of papillae displayed characteristics of blood vessels, which were demonstrated by strong expression of factor VIII-related and CD34 antigens, and the occurrence of Weibel-Palade bodies and continuous basal lamina. This raises a question concerning the origin of endothelial cells in the papillary structures in our case. The endothelial cells covering papillae probably represent the earliest stage in papillary proliferation, while the papillae core represents more recent organization (6). Microvascular endothelial cells are a cell type with high potential to adapt to changes in the environment (11). It is possible that some lymphatic endothelial cells with continued maturity in proliferation acquired features characteristic of blood vessels, including the production of Weibel-Palade bodies (12). Therefore, the endothelial cells

within the papillae core may also be of lymphatic endothelial cell origin.

It is hypothesized that a hard pilomatricoma probably causes the obstruction of lymphatic vessels and congestion of lymphatic vessels following their dilatation and leakage of lymphatic fluid. As a result of oedema in the dermis, the bullous appearance occurs. Lymph contains fibrinogen and other coagulation factors and has the ability to form a coagulation thrombus during lymph stasis (11, 13). The PEH in our case might also have resulted from peculiar organization of a thrombus, which is similar to the process occurring in blood vessels. Therefore, we agree with Kuo & Gomez (7) that benign proliferation of endothelial cells can also occur within dilated lymphatic vessels.

The presence of fibrous long-spacing collagen has not been reported in PEH. In an *in vitro* study, these structures were formed by degrading collagen fibres in the presence of collagenase (14). On the other hand, reduction in collagenase activity can reduce endothelial cell proliferation (15). It is possible that the occurrence of fibrous long-spacing collagen in our case represented preparation of tissue suitable for endothelial cell proliferation and migration, reflecting part of the remodelling process.

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