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Hyperplastic corneal pannus: An immunohistochemical analysis and review

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ABSTRACT

An exuberant corneal pannus usually develops in adults with a history of surgery or trauma in the anterior central stroma and appears as a glistening, vascularized, moderately elevated, well circumscribed white nodule. We describe a 78–year-old woman with such a pannus, which in the past has typically been referred to as keloidal or hypertrophic. The involved eye had only light perception, and she underwent a penetrating keratoplasty that improved her vision to 20/100. Histopathologic and immunohistochemical evaluations of a the specimen disclosed a reactive spindle cell stromal proliferation of myofibroblasts that were smooth muscle actin positive with a low Ki67 proliferation index. Desmin, caldesmon, and calponin were negative, in keeping with the incomplete myofilamentary differentiation of a myofibroblast. There was a generous admixture of CD68/163-positive histiocytes and dispersed C3/5-positive T-lymphocytes. An absence of CD138- and IgG4-positive plasma cells ruled out an IgG4-related disease. For a lesion to be keloidal, the collagen must have a thick hyaline character, sharp edges, and a sparsity of intervening cells and vessels. A hypertrophic pannus would be composed of large swollen cells not necessarily increased in number. We therefore recommend adoption of the term hyperplastic for lesions like that described here because of the obvious increase in cellularity from proliferating myofibroblasts and the lack of true keloidal collagen.

A corneal pannus nicely conforms to the original Latin word meaning a cloth or carpet—or in biology, a membrane. Two types of thin pannus are generally recognized pathologically: A degenerative avascular fibrous pannus that is interposed between the basal corneal epithelium and an intact Bowman membrane; and a destructive or inflammatory fibrovascular

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pannus that causes dissolution of Bowman membrane.[16,32] A pannus can involve a sector of the cornea or its entirety through 360°, proceeding centrally from the limbus. A pannus associated with a phlyctenule and Herpes zoster ophthalmicus is often sectoral.[25] A neoplastic pannus supports the growth onto the corneal surface of dysplastic squamous cells originating from stem cells at the limbus[35] or from the intraepithelial spread of sebaceous carcinoma arising in the eyelids.[19] A dramatic vascularized pannus simulated an expulsive hemorrhage by creating an elevated epicorneal subepithelial hemorrhagic bulla.[5]

A third type of pannus has been called keloidal[2,4,15,24,26,30,31] or hypertrophic.[22,27] Lowe and Rubinstein-Taybi syndromes include the peculiar feature of a "keloidal" corneal pannus.[23,29] Although the majority of cases of this type of exuberant pannus occurs in men,[2,4,15,24,26,30,31] often in their sixth and seventh decades, infantile and late childhood cases are encountered.[2,11,21,23,26,29] We report detailed histopathologic and immunohistochemical examinations of an upraised, placoid, hypercellular pannus that destroyed Bowman membrane. We propose that instead of a keloidal pannus, a more accurate or descriptive diagnostic term for an exuberant thick pannus would be a hyperplastic pannus, in view of its prominent cellularity.

1. Case report

1.1. *Clinical history*

A 78-year-old woman with a history of hypertension presented with vision of counting fingers in the right eye and light perception in the left. She had a serpiginous corneal ulcer with a descemetocele and corneal melt in the right eye. Her left eye did not display active disease, but the cornea contained a 4.5-mm central leukoma with stromal neovascularization and iridocorneal adhesions, suggesting an old perforation with iridial tissue plugging the corneal wound. The patient herself recalled no such injury. She stated that her left eye had had its unusual appearance since about the age of 7 years. A systemic workup was unrevealing. She was treated with acyclovir and a penetrating keratoplasty in the right eye. Two years later her examination in both eyes was stable with vision of counting fingers OD and light perception OS. She returned a year later at which time the right eye was stable, but the left corneal appearance had changed. The white opacity in the center of the left cornea had become elevated and vaguely nodular, without an increase in circumference (Fig. 1A). Stromal vessels emanated from the limbus circumferentially to the tumor. B scan ultrasonography disclosed a posterior staphyloma with the retina in place, and not patent anterior segment structural abnormalities. Because of the concern that the mass might represent an infiltrative squamous cell carcinoma, a penetrating keratoplasty was performed, with a clear graft the year after surgery and 20/100 vision.

1.2. *Histopathologic findings*

In the middle of the penetrating keratoplasty specimen—on its surface—was an ovoid, semitranslucent, dome-shaped lesion with clear surrounding cornea. Microscopically, the lesion rested on undisturbed underlying stroma (Fig. 1B). The mass measured 0.9 mm in vertical thickness, and the deeper stroma measured 0.5 mm thick. At the lateral edges of the mass were downward extensions of curvilinear epithelium forming collarettes. The surface was covered by a continuous, but attenuated, layer of non-keratinizing squamous epithelium (Fig. 1B, 1C) with focal, finger-like downward extensions (Fig. 1D). Descemet membrane displayed a single healed break (Fig. 1B) with focal reduplication, fibrous metaplasia of the endothelium, and adherent iridial tissue. The cells constituting the mass were spindled or ovoid, with a non-fascicular arrangement. Bundles of collagen separated single cells (Fig. 1D) or sometimes adopted a keloid-like character with frazzled rather than sharp edges (Fig. 1E). Their nuclei were vesicular, oval, or multiple in some cells, with small but clearly visible nucleoli. Mitotic figures were extremely rare. Capillary-size vessels with surrounding lymphocytes were scattered throughout the lesion, but were most prominent at the lesion's interface with the deeper, uninvolved stroma (Fig. 1F). The tumor formed a straight abutment with the deep stroma without infiltration.

1.3. *Immunohistochemical findings*

Immunohistochemical staining with cytokeratin (CK) 14 disclosed strong positivity of the intact surface epithelium and its downward dippings (Fig. 2A); CK7 was negative. The conjunctival epithelium, by contrast, was CK7-positive. CD31 and CD34 for endothelial cells highlighted a concentration of blood vessels in the middle of the lesion and at the deep stromal interface (Fig. 2B). The deep, uninvolved stromal keratocytes were also CD34-positive (Fig. 2B) but cytokeratin-negative. Smooth muscle actin and vimentin immunoreacted with most of the constituent lesional cells (Fig. 2C). Calponin, desmin, and caldesmon, however, were negative. CD68 and CD163 (Fig. 2D) immunostained a generous population of histiocytes. Some S100-positive dendritic stromal cells (Fig. 2D inset) were also present, presumed to be accessory antigen-processing cells. There were also S100-positive intraepithelial melanocytes (also MART-1 positive) and Langerhans cells (also CD1a-positive). The S100-positive dendritic stromal cells were CD1a-negative. CD3 T-lymphocytes were scattered throughout the tumor (Fig. 2E) and especially noticeable around the deep blood vessels, but CD20 B-lymphocytes, CD138 plasma cells, and lymphocytes bearing IgG4 subtype of immunoglobulin were not detected. Ki-67 nuclear staining for cells in the phase of pre-mitotic DNA synthesis was moderate (20% of nuclei) (Fig. 2F), the result of the combined nuclear positivity of the tumor stromal cells (elongated nuclei), lymphocytes, and histiocytes (the latter two displayed staining of round nuclei) (Fig. 2F).

2. Discussion

An exuberant pannus appears as a whitish, vascularized, well-demarcated, shiny, central corneal nodule arising from the anterior stroma, and only in the rarest instance encompasses the cornea's full thickness. These overgrowth lesions