

Venous Hemangioma

An Immunohistochemical and Ultrastructural Study

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We present a case of (arterio)venous hemangioma of 15 years' duration, which arose in a 43-year-old Japanese man on his right infraorbital area. Elastic stain and electron microscopy did not show any evidence for arterial components. Some thick-walled vessels showed mucin deposition and wide intercellular spaces between smooth muscle cells. Several glomoid cells were encountered among these cells. Although the histogenesis of (arterio)venous hemangioma is controversial, the presence of glomoid cells and the mucin deposition, which is occasionally detected in glomus tumors, suggest the relation of this tumor to the Suquet-Hoyer canal. Key words: glomoid cell; mucin deposition; pathogenesis.

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Venous (arteriovenous) hemangioma is a benign acquired vascular tumor, characterized by multiple thick- and thin-walled vascular structures, resembling arteries and veins, respectively. The name "arteriovenous hemangioma" was originally proposed by Girard et al. (1) in 1974. However, the tumor had already been reported by Biberstain & Jessner (2) in 1956 under the name of "cirroid aneurysm". Although this tumor has been known for many years, its pathogenesis is not yet clear and the presence of arterial components is a matter of controversy. We present detailed electron microscopic findings regarding this tumor, which have not been reported before as far as we are aware, together with histochemical and immunohistochemical characteristics.

MATERIALS AND METHODS

A 43-year-old Japanese man had a slowly enlarging asymptomatic nodule on his right infraorbital area with a 15-year history. Examination revealed a soft, dome-shaped, 7 × 6 mm sized, smooth-surfaced, dark red nodule without pulsation (Fig. 1). The nodule was completely excised under local anesthesia.

The specimens were stained with hematoxylin and eosin, periodic acid-Schiff, elastica-Masson and toluidine blue. Immunohistochemical staining with the streptavidin-biotin technique (HISTOFINE SAB kit, Nichirei, Tokyo) was performed according to a standard protocol. Antibodies included factor VIII-related antigen (polyclonal, DAKOPATTS, Carpinteria, CA), alpha-smooth muscle actin (DAKO-Smooth Muscle Actin, 1A4; monoclonal, DAKOPATTS, Denmark) and desmin (monoclonal, BioGenex, Sun Ramon, CA). Lectin-histochemistry was performed using biotinylated Ulex europaeus agglutinin-I (UEA-I; Vector Labo, Burlingame, CA). The reaction was visualized by the avidin-biotin complex technique (Vectastain kit, Vector Labo, Burlingame, CA).

For electron microscopic observation, the tissues were sequentially fixed in half-strength Karnovsky fixative and 1% osmium tetroxide in distilled water. After en bloc staining with uranyl acetate, the tissues

were dehydrated with ethanol and embedded in EPON 812 (Taab, Bershire, U.K.). Ultrathin sections were stained with uranyl acetate and lead citrate.

RESULTS

The lesion revealed a fairly circumscribed vascular tumor, which was composed of numerous thick- and thin-walled vessels lined by a single layer of endothelial cells throughout the dermis (Fig. 2). Some vascular spaces were markedly dilated. No shunt structure was seen. An increased number of capillaries were observed in the stroma. The overlying epidermis appeared normal. Periodic acid-Schiff positive material was present in all vessel walls, and it was diastase-resistant. Elastica-Masson stain did not detect any elastic lamina.

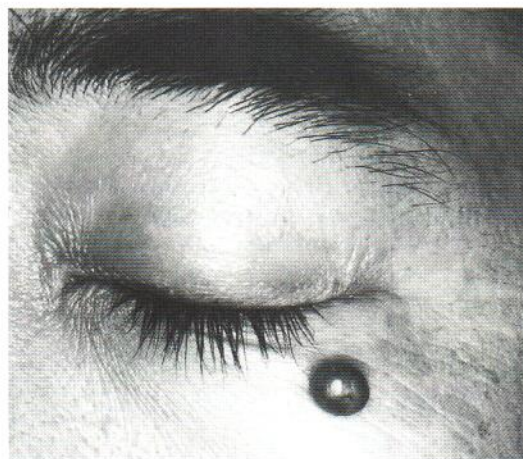


Fig. 1. A dark red nodule on the infraorbital area.

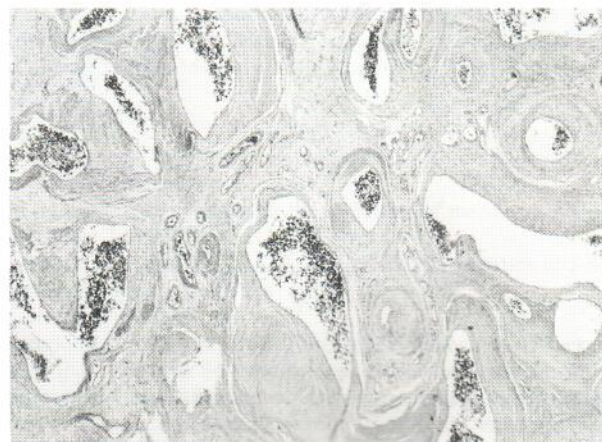


Fig. 2. The tumor shows multiple thick- and thin-walled vessels. An increased number of capillaries are observed in the stroma (hematoxylin and eosin, × 30).

Toluidine blue stain (pH 7) revealed a significant amount of metachromatic material in some vessel walls. Many mast cells were also observed in the stroma. The metachromatic staining in the vascular walls was markedly diminished by toluidine blue at pH 2.5 and was completely digested by testicular hyaluronidase, suggesting the presence of hyaluronic acid.

Immunohistochemistry and lectin-histochemistry

The endothelial cells of large and dilated vessels were almost negative for factor VIII-related antigen, while those of medium- and small-sized vessels were positive. The endothelial cells of all vessels were positively labelled with UEA-I lectin.

All vessel walls were positive for alpha-smooth muscle actin. Some positive cells had round shapes, resembling glomus cells.

Electron microscopy

The vascular walls were composed of one layer of endothelial cells and several layers of smooth muscle cells. They were surrounded by a basal lamina and collagen fibers. No elastic fiber was observed.

There were many Weibel-Palade bodies within the endothelial cells of medium- and small-sized vessels, while only a few were found in those of dilated large vessels. Low electron dense amorphous material in the wide intercellular spaces between the smooth muscle cells of thick vascular walls suggested mucin deposition (Fig. 3). Several glomoid, round or oval-shaped smooth muscle cells were found in thick-walled vessels (Fig. 4). Some of them were closely spaced and interdigitated with each other along their short processes. These cells contained many cytoplasmic myofilaments with dense bodies and pinocytotic vesicles lining the plasma membrane. The cells were surrounded by a basal lamina.

DISCUSSION

Arteriovenous hemangioma usually appears as a solitary, asymptomatic, red to blue papule or nodule, which frequently occurs on the face and four extremities (3). Cure is usually obtained by simple excision (4, 5).

This vascular tumor shows a circumscribed mass of proliferating thick- and thin-walled vessels without capsule formation throughout the dermis (6). Enzinger & Weiss (3) classified this hemangioma into "deep form" and "superficial form". The "deep form" usually occurs in young people and shows distinct shunts. The "superficial form" occurs in adults, and shunt is absent or insignificant. Our case as well as the original cases of Girard et al. (1) correspond to the latter type.

Despite the name "arteriovenous" hemangioma, most cases so far reported have failed to show the presence of true arterial components. Many authors concluded that thick-walled vessels, resembling arteries, actually represent veins, since no elastic lamina has been detected. We could not find any elastic lamina histologically or electron microscopically in the thick-walled vessels in our case, either. Lever & Schaumburg-Lever (6) and Wade et al. (7) proposed the name of "venous hemangioma" for this tumor. Our case supports their proposal.

The pathogenesis of this vascular tumor remains unknown. Girard et al. (1) suggested that this tumor represents hamartomas with numerous arteriovenous shunts and that it arises from the subpapillary vascular plexus. Carapeto et al. (8),

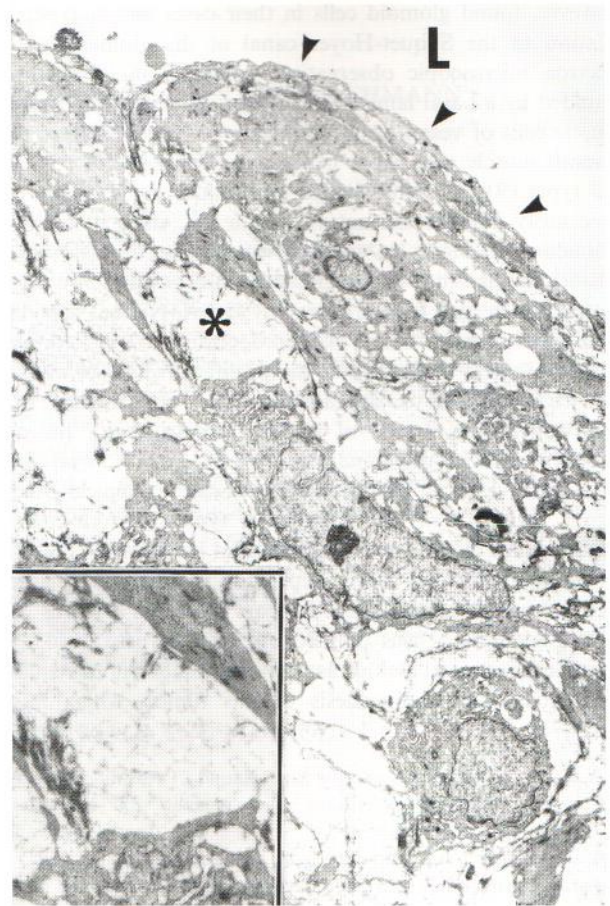


Fig. 3. A large dilated vessel. The endothelium is flattened (arrowheads) and contains a few Weibel-Palade bodies. Wide intercellular spaces among the smooth muscle cells of this vessel wall suggest mucin deposition. Inset, high magnification of wide intercellular spaces (asterisk) L: lumen ($\times 2450$, inset, $\times 5000$).

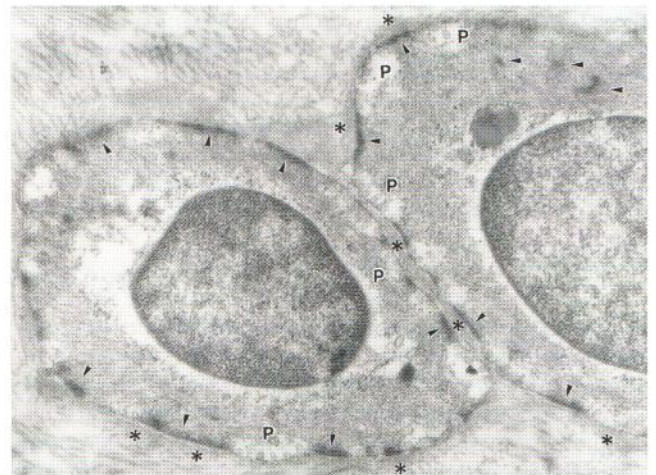


Fig. 4. The glomoid cells are observed in a vessel wall and contain many cytoplasmic myofilaments, with dense bodies and peripheral condensation (arrowheads). Pinocytotic vesicles line the plasma membrane. The cells are surrounded by a basal lamina (asterisk). p: pinocytotic vesicle ($\times 24500$).

however, found glomoid cells in their cases and suggested a relation to the Suquet-Hoyer canal of the glomus. In our electron microscopic observation, round glomoid cells surrounded by a basal lamina were observed among the smooth muscle cells of vessel walls. True glomus cells, pericytes, and smooth muscle cells most likely represent three interrelated cell types (9). A round-shaped appearance per se might not necessarily indicate the nature of the cell, since it might be secondarily induced by widening of the intercellular spaces. Besides the presence of the glomoid cells, however, we found another interesting feature shared by (arterio)venous hemangioma and glomus tumor; mucin deposition. Deposition of hyaluronic acid was noted in the proliferative vessel walls of our case. Mucinous degeneration has occasionally been described in the stroma of solitary glomus tumor (myxoid form) (9, 10). Our preliminary analysis has detected hyaluronidase-sensitive mucin deposition in most cases of typical glomus tumor and in 4 of our 5 cases of typical (arterio)venous hemangioma. Although the relationship between the presence of glomoid cells and mucin deposition remains unexplained, (arterio)venous hemangioma appears to reveal features suggesting glomus, as was pointed out by Carapeto et al. (8). Further histological and ultrastructural studies will be required to establish the pathogenesis of this tumor, which might

be regarded as a hamartomatous angioma with glomus-like cells.

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