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Case report

Extradural spinal angiolipoma with secretory activity

An ultrastructural, clinico-pathological study

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Summary. The light and ultrastructural analyses of an extradural intraspinal angiolipoma causing symptoms of spinal cord compression, are reported. The tumour showed morphological evidence of an endocrine-like secretory activity of fat cells, with an apparent mechanism of secretory function that has not previously been described for angiolipomas. The secretory granules, containing a lipid-like material, were covered with a continuous basement membrane originating from the basement membrane of the adipocyte.

Key words: Extradural-intraspinal angiolipoma – Secretory activity

Introduction

Spinal angiolipomas are uncommon benign tumours of mesenchymal origin. This paper presents the histological and ultrastructural features of this neoplasm with morphological evidence for its secretory function.

Case report

The patient was a 46-year-old man with a 2-year history of back pain, numbness, progressive weakness of the lower extremities and paretic gait. During the past year he had also been impotent. Physical examination showed weakness of the legs, bilateral absence of patellar tendon reflex, absence of abdominal reflexes on the left, unilateral absence of Achilles tendon reflex and bilateral contraction of the thigh and leg muscles. There was no response to the Babinski test. The spinal fluid contained 99 mm^3 cells and 141 mg% protein. Roentgenograms showed scoliosis and kyphosis in the lumbosacral region and on computerised tomography a cystic intraspinal mass at Th11–L2 was found. No evidence of abnormal vertebral fusion or other congenital malformation was seen. Myelogram revealed an extradural-intraspinal tumour with a complete block at Th11–L1. A lipomatous, brown, elastic tumor of

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$5.0 \times 3.0 \times 2.0$ cm size with marked adhesion to the dura and complete compression of the spinal cord was found. The postoperative course after complete excision was uneventful and the patient recovered fully.

Histological examination. The tumour was composed of mature adipose tissue and blood vessels (Fig. 1). The vascular component was variable; there were focal collections of small capillaries, usually at the periphery of the tumour. In other areas were groups of large calibre vessels showing thickened walls with smooth muscle hyperplasia. Some cavernous vessels were abnormal with anastomotic branching, similar to an arteriovenous malformation. In some areas of the small capillaries endothelial and pericytic proliferation was found while other areas contained fibrin thrombi. These vascular structures were surrounded by adipose tissue containing deposits of collagen and haemosiderin.

Electron microscopical examination. Ultrastructural examination revealed vascular structures with mature and incompletely matured adipose tissue. The adipocytes contained central, confluent lipid droplets lacking limiting membranes surrounded by a thin rim of cytoplasma, pinocytic vesicles along the cell membrane and a well-formed monolayered basal lamina. Clumped electron-dense material along the cell membrane was frequently seen. The capillaries were lined by more endothelial cells and multilayered, thickened basement membrane with deposits of electron-dense material between the layers (Fig. 2). Morphological evidence of secretory activity of the fat cells was observed.

Mechanism of the exocytosis. Eight phases of the secretory process could be discerned:

1. The granular electron-dense material accumulates along the inner surface of the cell membrane (Fig. 3/1).
2. The cell membrane opens up and the basement membrane begins to spread, surrounding the aggregate (Fig. 3/2).
3. The cell membrane begins to fuse (Fig. 3/3).
4. The basal lamina encloses the aggregate completely and the cell membrane has fused again. Figure 3/4 shows the still observable contact between the fat cell and the granule.
5. The secretory granule, surrounded by basement membrane, separates from the surface of the fat cell (Fig. 3/5).
6. The separated granule is displaced in the direction of the capillary across the interstitium (Fig. 3/6).
7. The basement membrane of the separated granule disintegrates before the granule reaches the basement membrane of the capillary. The transported material is released (Fig. 3/7).
8. The released lipid-like material of the secretory granule scatters between the lamellae of the capillary basement membrane and enters the capillary lumen (Fig. 3/8).

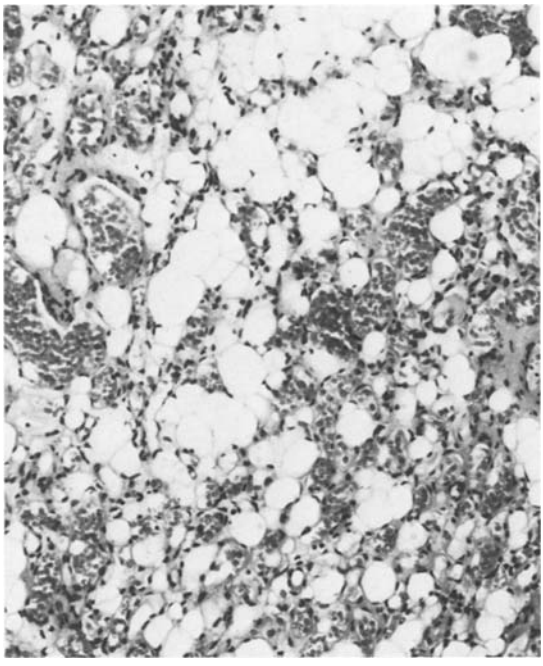

Fig. 1. Peripheral part of the tumour with prominent vascular component. (H&E, ×135)

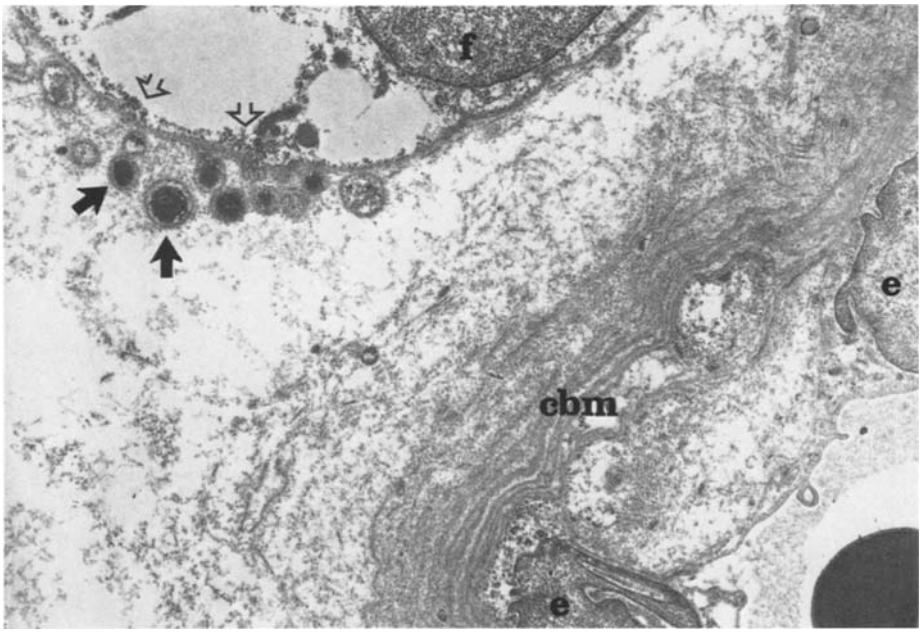

Fig. 2. The multilayered basement membrane of the capillary (*cbm*) and part of the adipocyte (*f*) with the aggregated electron-dense material along the cell membrane (*open arrows*). Some grouped secretory granules covered by basal lamina (*arrows*). e, capillary endothelial cells. (×9,580)

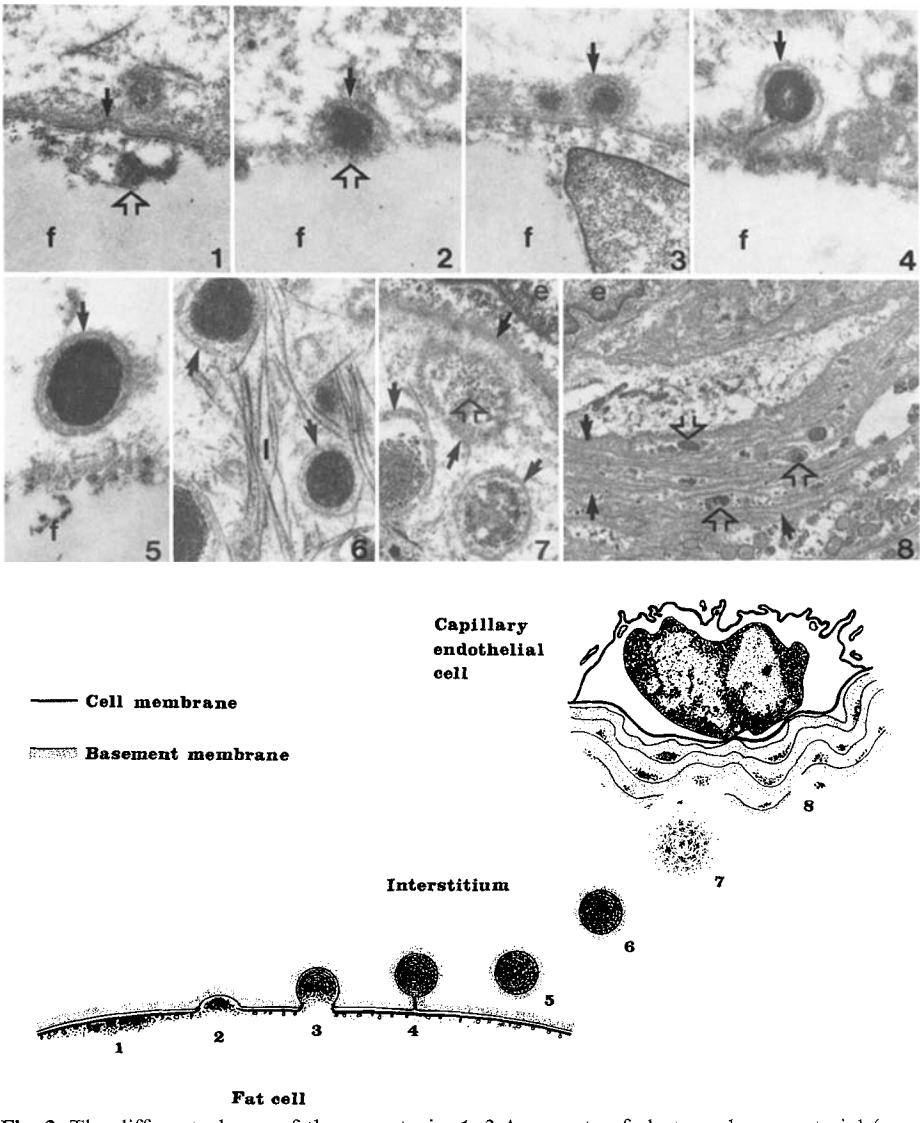

Fig. 3. The different phases of the exocytosis. *1, 2* Aggregate of electron-dense material (*open arrows*) along the cell membrane of the fat cell (*f*). The basement membrane begins to spread out (*arrow*). *3, 4* The secreted lipid-like material covered by basement membrane (*arrow*) breaks off from the surface of the adipocyte. *5, 6* Transporting secretory granules (*arrows*) in the interstitium (*I*). *7* The granules break down into small subunits (*open arrow*) near the capillary basement membrane (*arrows*). (*1–7* ×19,000; *8* ×5,100)

The cytoplasma of the endothelial cells contained no Weibel-Palade bodies. Many pinocytic vesicles were present along the inner surface of the cell membrane. Many single or clustered secretory granules surrounded by basement membrane were observed in the interstitium among the collagen fibres. These granules were seen mostly near the fat cells adjoining the

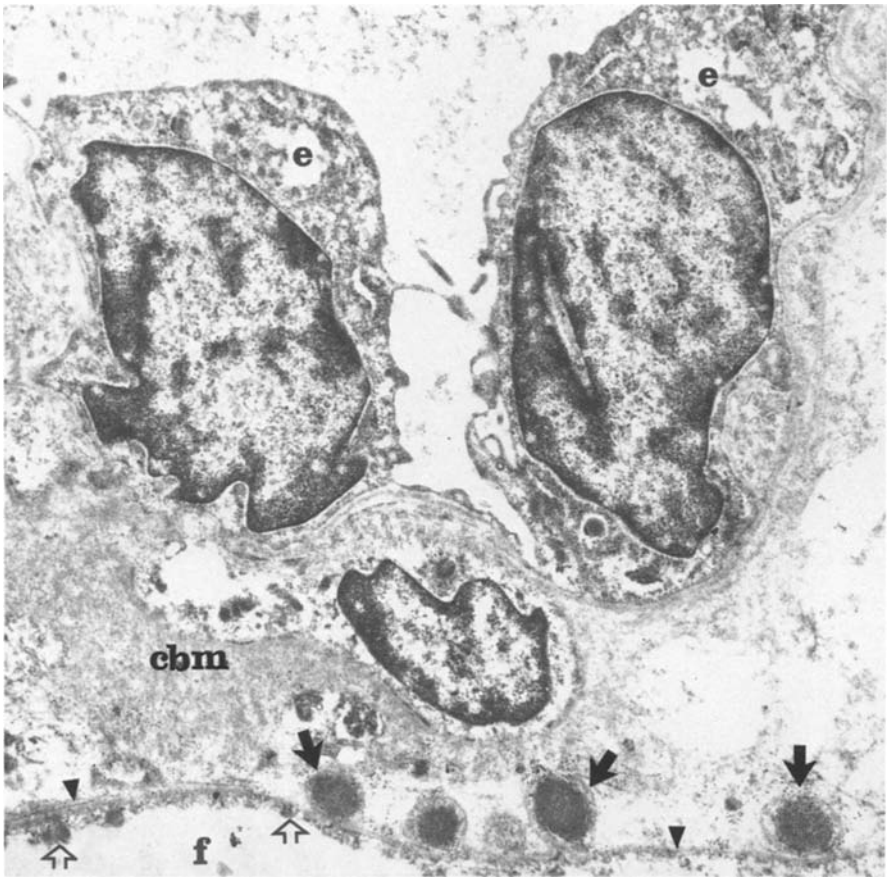

Fig. 4. Adipocyte (*f*) covered with simple basal lamina (*arrow heads*). Some secretory granules with lamellated internal structure (*arrows*). The basal lamina (*cbm*) of the capillary is thickened. e, capillary endothelial cell. (c 15,000)

capillaries (Fig. 4). All granules were covered by a basal lamina. The sizes of granules ranged between 0.5–1.0 μm, with some variation in interior structure (Fig. 5A–F). Some had an interior structure of concentric layers of double-membranes with periodic densities (Fig. 5B). Some of these densities may have been calcium but we have no data to support this. The homogenous density of the greater part of the granules seems to be from other material. In others, the symmetrical lamellae were broken into fragments near the capillaries (Fig. 5C–E). A few granules were also observed containing two concentric structures covered by a common basement membrane (Fig. 5F).

Discussion

The infiltrating and noninfiltrating angiolipomas are frequently located in the subcutaneous tissue of the trunk and extremities, salivary glands and in bone. They occur more frequently in children than in adults (Dixon

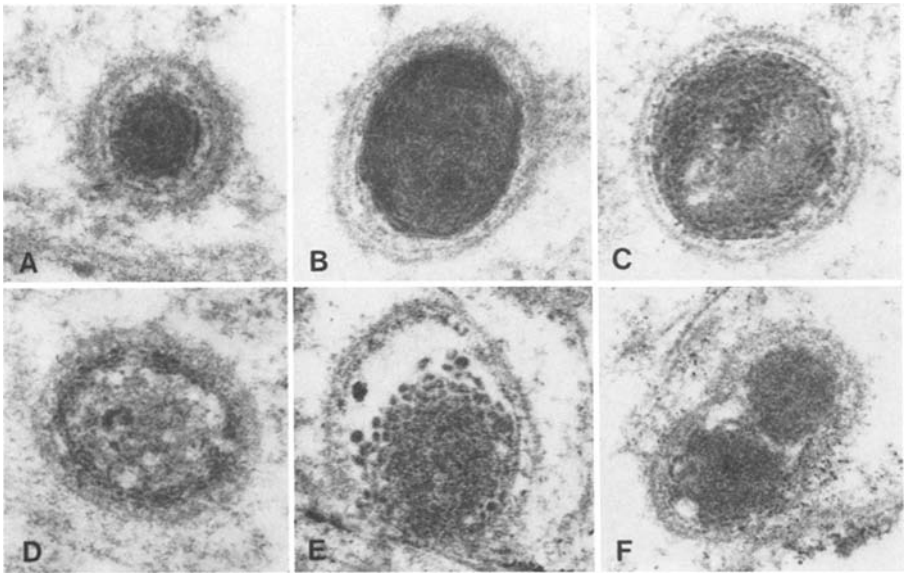

Fig. 5A–F. The different types of secretory granules. (**A, B** ×54,000; **C** ×61,000; **D, C** ×48,000; **F** ×40,500)

et al. 1981; Lin and Lin 1974). They are seldom found intraspinally, where they cause severe neurological symptoms, such as spastic paraparesis, sensory disturbances or urinary and sexual dysfunction (Ehni and Love 1945; Bender et al. 1974; Lin and Lin 1974; Miki et al. 1981). Electron-microscopical examination showed that some capillary endothelial cells in angiolipomas have decreased numbers of Weibel-Palade bodies in contrast to normal endothelial cells. We found no Weibel-Palade bodies. This suggests that the vessels in the tumour are neoplastic, not normal components of the lesion (Dionne and Seemayer 1974). The basal lamina of the capillaries was multilayered and thickened, having anastomotic branching similar to that in arteriovenous malformations. These morphological features and the coexistence with other vascular malformations support the theory that congenital vascular abnormalities may serve as a possible origin for the tumour.

The adipocytes in the present tumour showed secretory activity with exocytosis in the direction of capillary lumen. Allegra et al. (1983) described endocrine activity in a hibernoma with endoplasmacrine lipid granule secretion, rows of pedunculated plasmalemmal granules in the perisinusoidal cells and periodic plasmalemmal densities (Dixon et al. 1981). Similar endocrine activity was observed in the present angiolipoma but the mode of exocytosis seen here has not been described previously. Eight different phases of the transport process differing from the exocytosis in the hibernoma were observed. The ultrastructural features of transported material suggest a lipid-like secretion with a typical lamellated concentric structure. The material produced in the adipocytes was not secreted directly into the

sinus, but it was transported across the interstitium as granules covered with a single basement membrane. These granules broke into small subunits near the capillary and the lipid-like material freed of basal lamina was apparently released into the sinus across the multilayered basement membrane of the capillary. To the best of our knowledge, this form of exocytosis has not yet been described in the literature.

The pathogenesis of angiolipomas is unclear. Some authors propose repeated trauma or other irritating agents or dysembryogenesis as causes of the vascular and adipocytical differentiation of the so-called "bipotential, perivascular reticular cell" (Ehni and Love 1945; Gould et al. 1979; Lin and Lin 1974; Pearson et al. 1970). Our observations on an unusual type of secretory activity in the tumour cells support the concept that it derives from pluripotential stem cells having secretory capacities not normally found in the mature fat cell.

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