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Localized amyloidosis of the uterine cervix

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Summary. Localized amyloidosis of the uterine cervix was found in a 56-year-old woman. The firm enlarged cervix showed massive tumorous amyloid deposition. In the amyloid deposits there were foci of ossification and calcification. An infiltrate of multinucleated giant cells, histiocytes, lymphocytes, and plasma cells was seen adjacent to the amyloid deposits. Immunohistochemically, the amyloid reacted with antisera against A-lambda, amyloid protein of immunoglobulin lambda light chain origin. This indicated that the amyloid protein was of immunoglobulin origin in this rare case of localized amyloidosis of the uterine cervix.

Key words: Uterine cervix – Amyloidosis – Amyloid protein

Introduction

Amyloid diseases are largely classified into two categories; systemic and localized forms. Recent advances in the biochemical understanding of amyloid have revealed various types of amyloid proteins (Glenner 1980; Husby and Sletten 1986). For systemic amyloidosis, protein AL of immunoglobulin light chain origin, including kappa chain origin (A-kappa) and lambda chain origin (A-lambda), is usually found in "primary" and myeloma-associated amyloidosis; protein AA in "secondary" amyloidosis and familial Mediterranean fever and prealbumin in familial amyloidotic polyneuropathy and senile systemic (cardiac) amyloidosis. In localized amyloidosis, the origin of the amyloid proteins varies.

In systemic amyloidosis it is common for the uterus to be histologically involved by systemic amyloid deposition, although gynecological symptoms due to amyloid deposition of the uterus have been reported rarely (Copeland et al. 1985). Primary localized amyloidosis of the uterus is rare (Liaras et al. 1984).

We report a patient with localized amyloidosis of the uterine cervix presenting with genital bleeding. The amyloid was of lambda light chain origin, A-lambda.

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Case report

The patient was a 55-year-old woman, mother of two children. Her menopause was at the age of 50. In November 1985, she noted abnormal genital bleeding and visited the gynecologic clinic. Bleeding from the external uterine orifice was observed. The portio vaginalis was swollen and firm. A biopsy from the portio vaginalis revealed amyloid deposition. Systemic investigations including heart, kidney, and gastrointestinal tracts were all normal. Electrophoresis of the serum protein and immunoelectrophoresis of the serum and urine showed no M protein. Bone marrow aspiration was normal. Gastrointestinal biopsies were negative for amyloid. No systemic disease which might be the cause of "secondary" (AA) amyloidosis was detected. Genital bleeding continued. Simple hysterectomy and biopsy of the greater omentum were performed in October 1986.

The resected uterus (Fig. 1a) was 100 g in weight and $93 \times 54 \times 52$ mm in size. The uterine cervix was enlarged ($47 \times 54 \times 52$ mm in size) and firm in consistency. Haemorrhagic erosions were scattered in the portio vaginalis. The wall of the cervix was almost occupied by a circumscribed, grayish, firm mass with haemorrhage and focal calcification. The endocervical mucosa showed haemorrhagic erosions. The uterine corpus was normal.

Histologically (Figs. 1b, c), an amorphous eosinophilic mass occupied almost the entire wall of the cervix. This material showed reactions for amyloid, including positive reactions for Congo red and green birefringence with polarized light. Most portions of the uterine cervix were replaced by this massive, tumorous amyloid deposition.

Part of the cervix was fixed with 2.5% glutaraldehyde and observed by electron microscopy. This showed accumulations of straight nonbranching fibrils in extracellular space (Fig. 1d). Formations of bony trabeculae, containing osteocytes and lined by osteoblastic cells, were frequently found in the amyloid de-

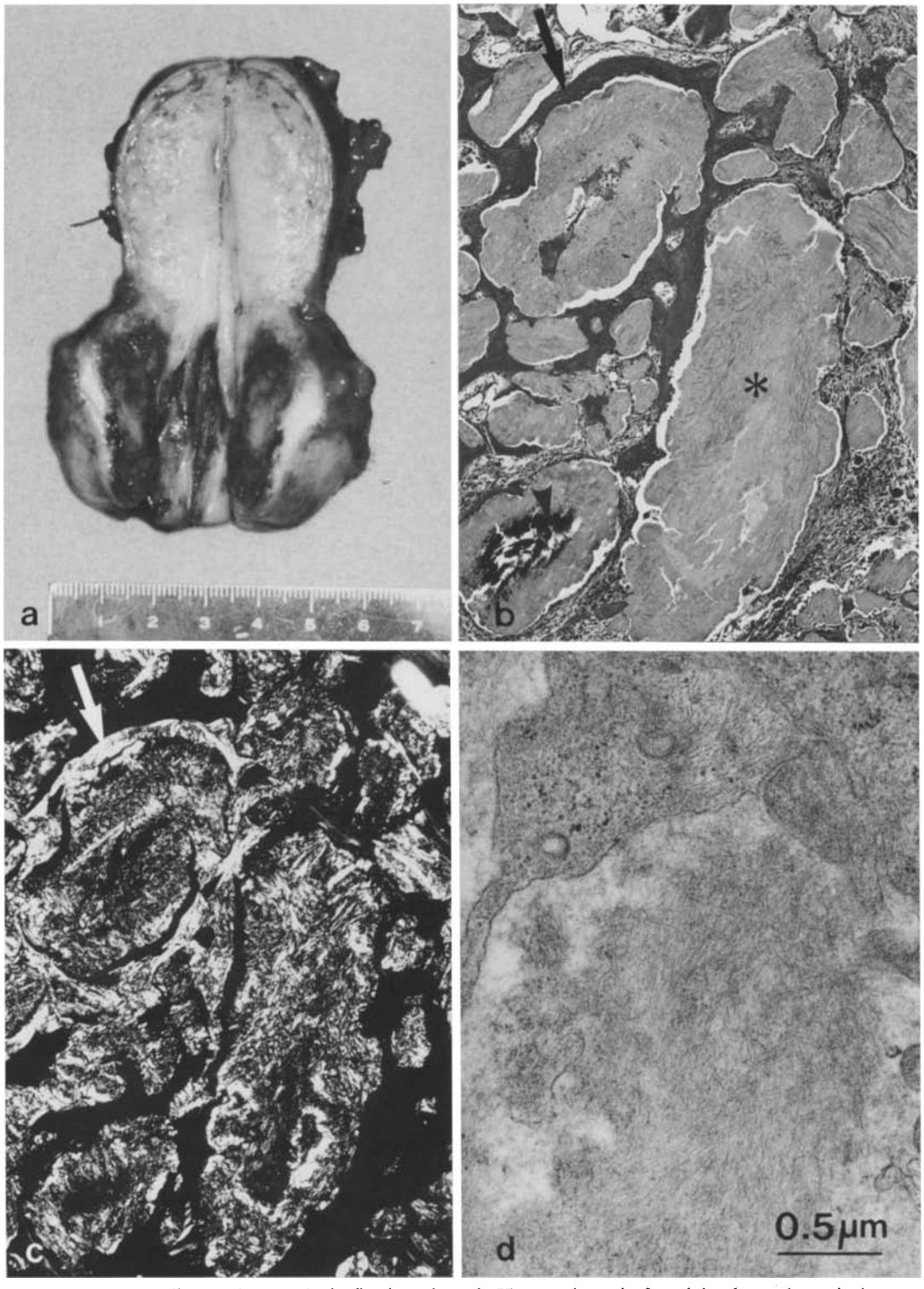

Fig. 1. (a) uterus. The uterine cervix is firmly enlarged. Haemorrhage is found in the endocervical mucosa and cut surfaces of the cervix. **(b)** low power view of amyloid deposition. Formation of bony trabeculae (*arrow*) and calcification (*arrow heads*) are observed in the massive amyloid deposits (*). (Haematoxylin-eosin stain, ×52). **(c)** the same section as **(b)** stained with Congo red and observed under polarized light. Amyloid deposits show green birefringence. Bony trabeculae (*arrow*) are white in color and distinguished from amyloid. (×52). **(d)** an electron micrograph of amyloid deposition. Amyloid fibrils are deposited adjacent to a giant cell. (×32400)

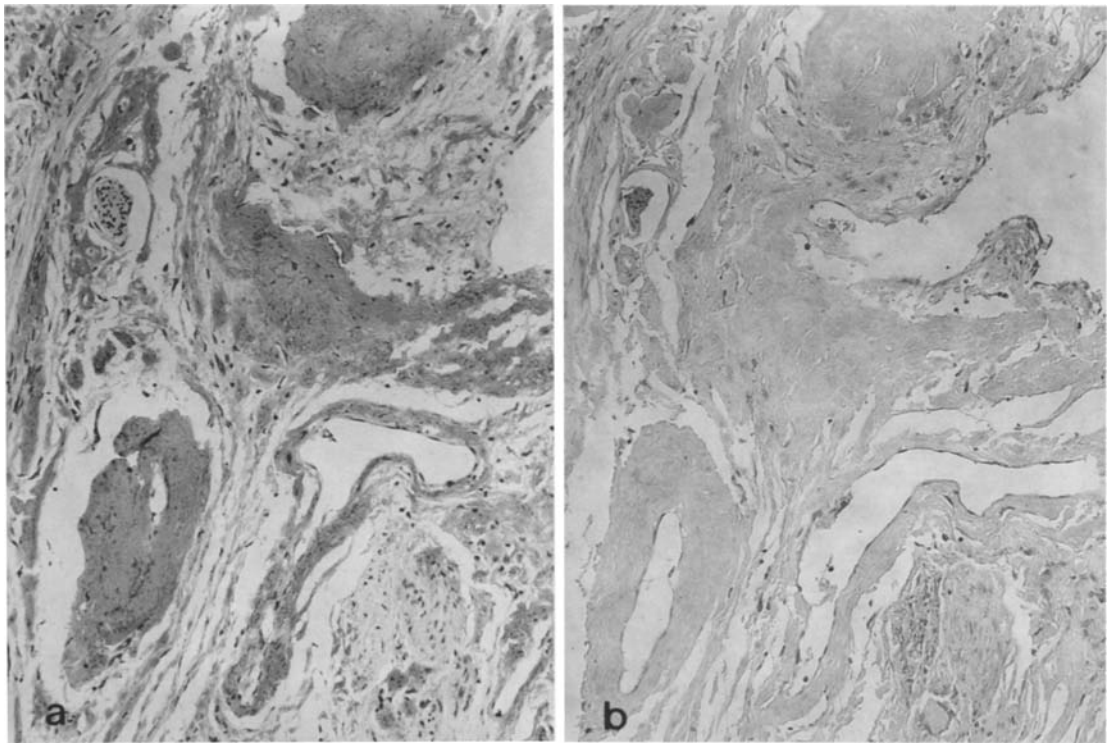

Fig. 2. Amyloid deposits react with anti-A-lambda sera **(a)** and not with antisera to A-kappa, prealbumin, and AA **(b)**. **(a)** anti-A-lambda, PAP technique, ×130; **(b)** anti-AA, PAP technique, ×130

posits. Small foci of calcification were also scattered in the amyloid deposition. Multinucleated foreign body type giant cells, histiocytes, and some lymphocytes and plasma cells were found adjacent to the amyloid deposits. In the marginal areas of the amyloid mass of the cervix, vascular involvement by amyloid was seen. Amyloid deposits were also found between the smooth muscle cells. Amyloid was occasionally found in the nerve fascicles in the wall of the cervix and beneath the endocervical mucosa, with focal loss of the mucosal columnar epithelium.

The amyloid was resistant to potassium permanganate treatment before Congo red staining (Wright et al. 1977). The formalin-fixed, paraffin-embedded sections were immunostained with anti-A-kappa (Fujihara et al. 1980), anti-A-lambda (Fujihara et al. 1980), anti-human AA (Kyowa Medex, Tokyo), and anti-human prealbumin (Behring, Marburg), using the peroxidase-anti-peroxidase (PAP) technique (Fujihara et al. 1980). The amyloid reacted positively with anti-A-lambda and not with the other anti-sera (Fig. 2). In addition to positive staining with anti-A-lambda, most of the infiltrating plasma cells were also stained with anti-A-lambda.

The uterine corpus was histologically normal, and no amyloid was found in it. The biopsy of the greater omentum was negative for amyloid.

Discussion

Amyloid deposition in our case was localized to the uterine cervix. No systemic or other uterine disease was found. Amyloid deposition in the uterine cervix was massive, tumour-forming, and accompanied by ossification, calcification, and an infiltrate of giant cells, histiocytes, lymphocytes, and plasma cells.

In the literature, only two patients with amyloid deposition in the uterine cervix have been briefly described, with colposcopic findings (Liaras et al. 1984). Those two cases were characterized by cervial polyps. Keratin-related amyloid deposition has been reported in a squamous cell carcinoma of the uterine cervix (Gondou et al. 1987).

In immunohistochemical studies, the amyloid of this localized amyloidosis of the cervix reacted with anti-A-lambda (Fujihara et al. 1980). Although AL amyloid is generally found in systemic amyloidosis (primary or myeloma-associated type), several cases with AL amyloid have been reported in localized amyloidosis of the respiratory tract (Fenoglio and Pascal 1970; Page et al. 1972), urinary tract (Fujihara and Glenner 1981), and skin (Husby et al. 1981; Kitajima et al. 1986). Page et al. (1972) purified amyloid fibril protein from localized nodular pulmonary amyloidosis with plasmacytic infiltration and showed that it was derived from lambda light chain. These localized pulmonary amyloid deposits were often accompanied by ossification, calcification, and local cellular infiltrates, including plasma cells, as was found in

our case (Glenner 1980). Fujihara and Glenner (1981) demonstrated that amyloid deposits immunoreacted with anti-A-lambda in nine of eleven cases of primary localized amyloidosis of the genitourinary tract. Infiltrates of chronic inflammatory cells, including plasma cells and lymphocytes, were commonly associated with these amyloid deposits, and the plasma cells reacted with anti-A-lambda as in our case. The A-lambda-positive plasma cells might produce the lambda light chain precursor of the amyloid fibrils. Chronic inflammation of the uterine cervix might pre-exist and induce monoclonal secretion of the "amyloidogenic" lambda light chain of the plasma cells as discussed in localized amyloidosis of the genitourinary tract by Fujihara and Glenner (1981).

Finally, the clinical manifestation in this patient was genital bleeding. This is similar to the presentation of patients with localized amyloidosis of the urinary bladder, where haematuria is a common clinical manifestation (Fujihara and Glenner 1981).

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References

Copeland W, Hawley PC, Teteris NJ (1985) Gynecologic amyloidosis. Am J Obstet Gynecol 153:555–556

Fenoglio C, Pascal RR (1970) Nodular amyloidosis of the lungs. Arch Pathol 90:577–582

Fujihara S, Balow JE, Costa JC, Glenner GG (1980) Identification and classification of amyloid in formlain-fixed, paraffin-embedded tissue sections by the unlabeled immunoperoxidase method. Lab Invest 43:358–365

Fujihara S, Glenner GG (1981) Primary localized amyloidosis of the genitourinary tract. Immunohistochemical study on eleven cases. Lab Invest 44:55–60

Glenner GG (1980) Amyloid deposits and amyloidosis. The beta-fibrilloses. N Engl J Med 302:1283–1292, 1333–1343

Gondou S, Ishihara T, Takahashi M, Yokota T, Kawano H, Nagasawa T, Yamashita Y, Uchino F, Iwata T, Kamei T, Okuzono Y (1987) Amyloid in squamous cell carcinoma of the uterine cervix. Tr Soc Pathol Jpn 76:77 (in Japanese)

Husby G, Sletten K, Blumenkrantz, Danielsen L (1981) Characterization of an amyloid fibril protein from localized amyloidosis of the skin as lambda immunoglobulin light chains of variable subgroup I (A-lambda I). Clin Exp Immunol 45:90–96

Husby G, Sletten K (1986) Chemical and clinical classification of amyloidosis 1985. Scand J Immunol 23:253–265

Kitajima Y, Seno J, Aoki S, Tada S, Yaoita H (1986) Nodular primary cutaneous amyloidosis. Isolation and characterization of amyloid fibrils. Arch Dermatol 122:1425–1430

Liaras J, Conti C, Marien M, Beurlet J, Frappart L (1984) Aspects colposcopiques d'un dépôt de substance amyloïde au niveau du col utérin. Arch Anat Cytol Path 32:374

Page DL, Isersky C, Harada M, Glenner GG (1972) Immunoglobulin origin of localized nodular pulmonary amyloidosis. Res Exp Med 159:75–86

Wright JR, Calkins E, Humphrey RL (1977) Potassium permanganate reaction in amyloidosis. A histologic method to assist in differentiating forms of this disease. Lab Invest 36:274–281

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