Clinical Reports

Systemic amyloidosis and ovarian carcinoma

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Summary: A case of ovarian carcinoma and systemic amyloidosis in a 64 year old woman with nephrotic syndrome is reported. Immunohistochemical study of renal and rectal biopsy specimens revealed the presence of amyloidosis AA antigens, consistent with secondary amyloidosis. The absence of chronic inflammatory or infectious disease suggested the presence of a neoplasm. The gynaecological sonogram showed a solid mass located behind the uterus. Laparotomy confirmed a poorly differentiated ovarian carcinoma. The association of systemic amyloidosis and ovarian carcinoma has not to our knowledge been described previously.

Introduction

Amyloidosis has been described in association with chronic diseases and infections, and in a small percentage with malignant disease, primarily haematological tumours and renal carcinomas. We report a patient with ovarian carcinoma and systemic amyloidosis presenting with the nephrotic syndrome. Immunohistochemical studies showed the presence of amyloidosis AA antigens, consistent with secondary amyloidosis.

Case report

A 64 year old woman was admitted complaining of anorexia, malaise, progressive weight loss and leg oedema for one year. There was no family history of familial Mediterranean fever. Haemoglobin was 7.3 g/dl, ESR 137 mm/hour, C-reactive protein 14.3 mg/dl (normal <0.8 mg/dl), serum creatinine 100 µmol/l, serum proteins 6.5 g/dl, albumin 2.05 g/dl, and gammaglobulin 3.2 g/dl. Blood and urinary immunoelectrophoresis did not demonstrate the presence of paraprotein. Twenty-four hour urinary protein exceeded 7 g. Chest X-ray was normal. Renal biopsy demonstrated amyloid deposits. A gastroduodenoscopic and rectoscopic examination showed no abnormality but rectal biopsy confirmed the systemic nature of the amyloidosis. Immunohistochemical study was performed with the avidin–biotin–peroxidase com-

plex method on formaldehyde-fixed and paraffin-embedded tissue with the monoclonal antibody anti-amyloid AA clone mcl (Dako, Glostrup, Denmark) diluted 1:10. This antibody reacts with amyloid fibrils in paraffin-embedded tissue and shows no reaction with antigens such as human serum proteins (albumin, transferrin, IgG) or non-AA amyloid fibril proteins.² A biopsy of proven secondary amyloidosis was used as a positive control. As a negative control the primary antibody was replaced by non-immune mouse serum. Renal and rectal biopsy specimens revealed the presence of amyloidosis AA antigens, consistent with secondary amyloidosis (Figure 1).

Figure 1 Rectal mucosa with amyloid in small vessel wall stained by peroxidase reaction (arrow) with monoclonal antibody anti-amyloid AA (× 400).

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Accepted: 29 October 1993

The absence of chronic inflammatory or infectious disease suggested the existence of a neoplasm. Gynaecological ultrasound revealed a 10 cm solid mass located behind the uterus. Laparotomy confirmed a tumour in the left ovary, adhering to the sigmoid colon and infiltrating locally. The tumour was partially extirpated and revealed poorly differentiated ovarian carcinoma (Figure 2).

Figure 2 Ovarian carcinoma poorly differentiated (hematoxylin and eosin, $\times 400$).

The patient suffered from postoperative renal insufficiency and died on the 10th day after surgery. An autopsy could not be performed.

Discussion

Amyloid substance deposition in malignant diseases may be systemic or localized. Systemic amyloidosis in non-haematological malignancy is uncommon and renal carcinoma accounts for about half of such associations.¹ In some cases nephrotic syndrome due to renal amyloidosis in association with renal carcinoma has remitted following surgical extirpation of the tumour.^{3,4} The pathogenetic factors in systemic amyloidosis with carcinoma are unknown. However, hereditary factors, hyperglobulinemia, tissue breakdown with subsequent inflammation and immune factors causing regression of tumour growth have been invoked to explain the association.¹

Localized amyloidosis is often found in tumours of endocrine origin, especially medullary carcinoma of the thyroid, islet cell tumour of the pancreas, pituitary adenoma and pheochromocytoma, whereas other hormone-secreting tumours produce amyloid only rarely.^{5,6} The amyloid fibril proteins found in endocrine tumours are related to hormones produced by the endocrine cells.⁵ Amyloidosis associated with non-endocrine tumours is a distinctive subgroup of amyloidosis occurring mostly in squamous or squamous-related tumours and is usually composed of cytokeratins.⁷

The association of ovarian carcinoma with systemic amyloidosis has not to our knowledge been reported previously (Medline bibliographic search 1966–October 1993). The absence of evidence of a chronic pre-existing disease of a relevant family history in this patient supports the view that the association is real rather than coincidental.

References

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