

Unexpected mesothelioma in a centenarian woman: an autopsy report

Mesotelioma inatteso in donna centenaria: un riscontro autoptico

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Summary

Malignant pleural mesothelioma, notoriously associated with asbestos exposure, mostly arises in male subjects, and generally shows an extremely long latency period (25-45 years). A centenarian woman was hospitalized with bronchopneumonia, chronic atrial fibrillation, dehydration, malnutrition and immobilization syndrome. X-ray examination showed a left pleural-pulmonary thickening. The autopsy revealed a diffuse, atypical pleural thickening in the left lung, multiple hyaline plaques in the bilateral parietal pleuras and diffuse adhesions between pleura and diaphragm; on the right side the pleura was discontinuously thickened with areas of fibromyxoid dystrophy. Histologically the pleura was extensively substituted by malignant cells of a biphasic malignant mesothelioma. The tumour was immunohistochemically positive for antibodies against cytokeratins, calretinin and vimentin. Accurate histological evaluation of lung specimens did not show the presence of asbestos bodies. Eur. J. Oncol., 14 (1), 33-36, 2009

Key words: pleural mesothelioma; centenarian; autoptic pathology

Riassunto

Il mesotelioma pleurico maligno è strettamente associato all'esposizione all'asbesto, insorge prevalentemente in soggetti di sesso maschile e può avere un periodo di latenza estremamente lungo (25-45 anni). Una donna centenaria fu ricoverata per broncopneumonia, fibrillazione atriale cronica, disidratazione, malnutrizione e sindrome da immobilizzazione. L'RX mostrò un addensamento pleuro-polmonare sinistro. All'autopsia si è riscontrato un diffuso, sospetto ispessimento pleurico a sinistra, multiple placche ialine pleuriche parietali bilaterali e diffuse aderenze pleuro-diaframmatiche; a destra la pleura si presentava irregolarmente ispessita, con distrofia fibromixoidale. All'esame microscopico sono state osservate cellule di mesotelioma maligno bifasico che sostituivano estesamente la pleura. La neoplasia si è rivelata immunoistochimicamente positiva per citocheratine, calretinina e vimentina. Un'accurata valutazione istologica dei campioni polmonari non ha evidenziato la presenza di corpi dell'asbesto. Eur. J. Oncol., 14 (1), 33-36, 2009

Parole chiave: mesotelioma pleurico; centenario; patologia autoptica

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Introduction

Exposure to asbestos (in particular to amphibole) is currently considered the most important aetiological factor for mesothelioma (over 90% of mesotheliomas has been observed in subjects employed in US and Canadian shipyards and they were related to asbestos). Moreover, the risk of developing pleural mesothelioma is directly linked to the amount, the kind of inhaled fibres (as well as their chemical stability) and the personal proneness to develop the disease, with a mean period of latency of 25-45 yrs. The sources of risk are mostly connected to the work environment and also to the living environment – flooring, insulation, machinery components or everyday tools containing asbestos, although the exposure to such items is in any case lower than in a professional context (1, 2). The pathogenetic role of the SV40 virus is still controversial: some studies have shown the presence of viral DNA sequences in 60-80% of malignant pleural mesotheliomas (3, 4). Other factors increasing the incidence of pleural mesothelioma are ionizing radiations, previous exposure to thorium dioxide (Thorotrast) with diagnostic purposes, chronic or tubercular inflammatory processes (5). Pleural mesothelioma morphologically consists in a wide thickening of the pleural serosa leading to the formation of a subtotal engulfing of lung parenchyma in homogeneous or multi-

nodular tissue with progressive invasion of the surrounding thoracic structures. Partial or total obliteration of the pleural cavity often occurs, even with concamerations filled with liquid which is mostly hemorrhagic, greyish, more or less dense, often viscous and stringy (6, 7).

Its histological patterns are the epithelial one (tubulus-papillary; epithelioid), sarcomatous (mesenchymal) form and biphasic or mixed form (component of epithelioid type mixed with a sarcomatoid part). Undifferentiated anaplastic shapes are worth to be mentioned, although their nosological autonomy is currently controversial.

After being repeatedly hospitalized for bronchopneumonia, diverticulitis and chronic atrial fibrillation, a centenarian woman was admitted to hospital for problems connected to a severe immobilization syndrome, as well as for a serious arterial hypotension, with dehydration and protein-energetic malnutrition. Laboratory analyses show high phlogosis indexes (VES 28 mm/1h; PCR 97.4 mg/L), alteration of electrolytes (K 4.21 mEq/L; Ca 7.30 mg/dL) and of liver functionality (SGOT 77 U/I; SGPT 52 U/I; bilirubin 4.57 mg/dL), as well as sideropenic anaemia (haemoglobin 0.1 g/dL; iron 10 mg/dL) and severe hypoalbuminaemia (41.8%). Chest X-ray examination showed a multifocal thickening, partly pleural and partly parenchymal, in the left lung, which was clinically suggestive of a rehegthened



Fig. 1. a) The left lung is imprisoned by a massive pleural neoplastic thickening; the right lung has pleural and parenchymal metastases. b) The longitudinal section of the left lung shows how the neoplasia involves the whole pleura

chronic bronchopneumonic inflammatory process. The patient died 18 days after she was hospitalized and a post-mortem investigation was requested. The clinical diagnosis was bronchopneumonia, dehydration and cachexy of unknown cause.

Materials and methods

A post-mortem autopsy was performed. The pathologist was informed about the patient's chest X-ray examination, clinical and laboratory diagnosis. The autoptical specimens were fixed in 10% formalin, embedded in paraffin, sectioned and stained with hematoxylin and eosin.

Immunohistochemical studies were performed on paraffin-embedded tissues. Representative section

were immunostained with the following antibodies: cytokeratins (CK 5 and CK 8), calretinin, vimentin, epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA), b72.3 and TTF1.

Results

The autopsy showed that the left lung was almost globally confined into a showy and irregular pleural thickening, which had adhesions also with the tunica adventitia of the thoracic aorta (fig. 1). The parietal pleura and the homolateral hemidiaphragm had hyaline plaques. The visceral pleura had adhesions both with the pericardium and with the diaphragm. The right lung had multiple pleural-parenchymal metastases, foci of lung fibromixoid dystrophy, wide

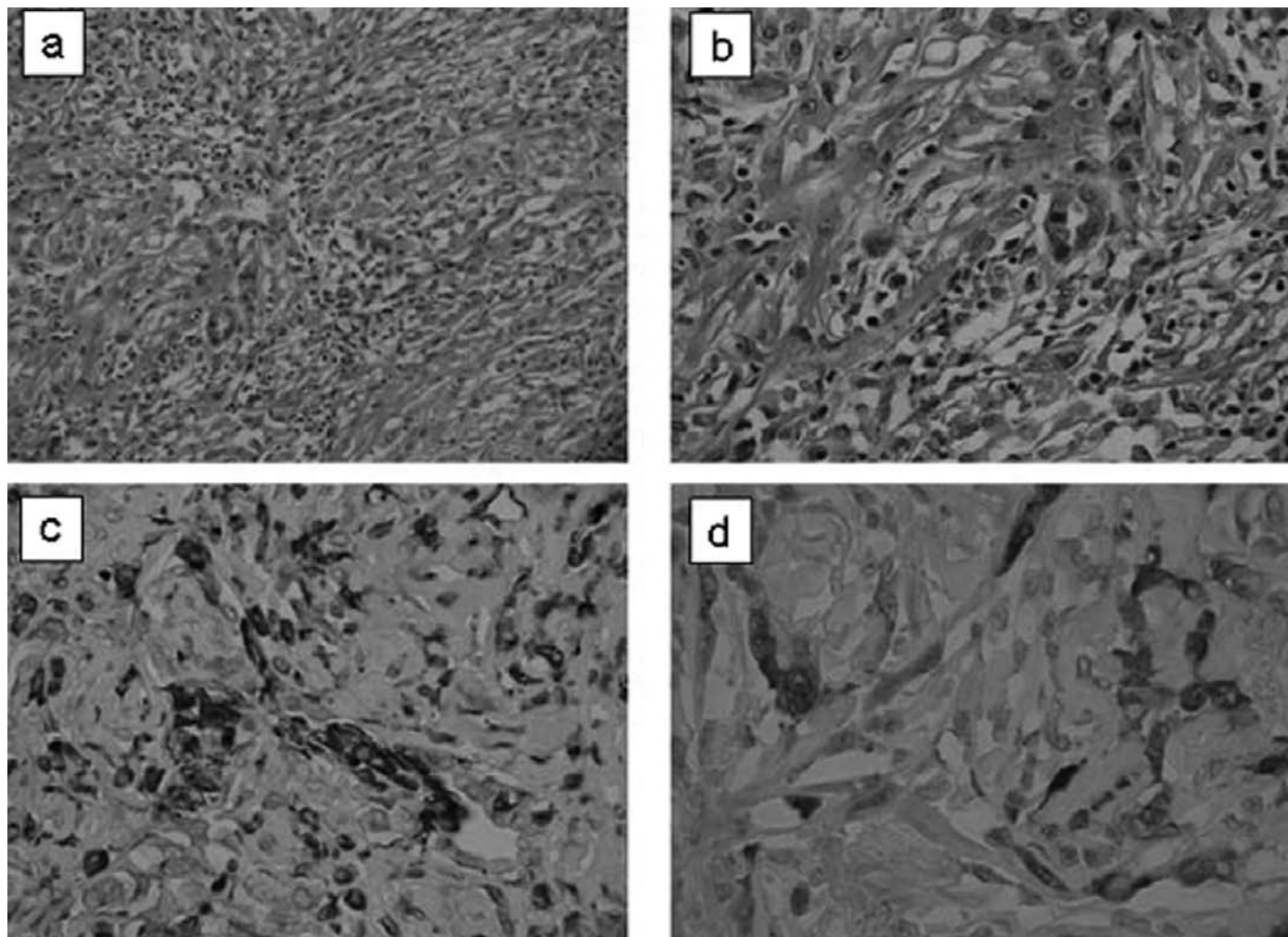


Fig. 2. a) Bifasic malignant mesothelioma: thick proliferation of small tubular epithelial structures mixed with fascicular and fused cells, H&E at 40X and b) 100X. c) Tumour strong expression of calretinin (80X). d) Positivity of tumour cells to vimentin (100X)

anthracoses and fibroses associated with a bronchopneumonic process at basal level. The lymph nodes of the lung hilum were metastasized. The macroscopic anatomopathological picture was suggestive of a pleural mesothelioma. A severe arteriosclerosis of the aorta, with arteriosclerotic kidneys and an ischemic cardiopathy were also present.

Histologically the pleural specimens showed mixed microtubular and micropapillary structures with fibrovascular axis, intermingled with fasciculated proliferation of fusate cells with oval nucleus, scarce cytoplasm and prominent nucleoli (fig. 2a and 2b). Accurate histological evaluation of multiple lung specimens collected during the autopsy did not show the presence of asbestos traces. The immunohistochemical investigation revealed that the neoplastic cells strongly expressed cytokeratins 5 and 8, calretinin (fig. 2c) and vimentin (fig. 2d), while the tumour cells did not express EMA, CEA, b 72.3 and TTF1. All these data confirmed the diagnosis of a biphasic mesothelioma.

Discussion

In the US, pleural mesothelioma shows a 2.2/1000000 incidence and affects in particular male subjects (men/women ratio: 3/1) (8-10). In 2006 in Trieste, mesothelioma cases found in male subjects represented 87.5% of the total of mesothelioma cases (the mean age of male subjects was 69 yrs., while the mean age of female subjects was 72 yrs.). The discovery of this lesion in a female subject, in particular a centenarian one, is considered extremely rare and currently, to our knowledge, no other similar reports in literature are present. Other characteristics which make this case peculiar are negative anamnesis for exposure to asbestos (this woman was not self-sufficient, not oriented in time and space and she had been living in a rest home for

years) and absence of metastasis in other internal organs. This condition is certainly connected with the age of the patient; in fact, in our autoptic experience, most old people with malignant neoplasms do not show any metastatic diffusion.

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