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Short reports

Pleural mesothelioma and the syndrome of inappropriate secretion of antidiuretic hormone

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The syndrome of inappropriate secretion of antidiuretic hormone has been described in association with a variety of diseases of the thorax, especially with intrathoracic neoplasms.[1–3] To our knowledge there is only one case report of mesothelioma associated with the syndrome of inappropriate secretion of antidiuretic hormone.[4] We describe another histologically proved case of the biphasic type of malignant pleura mesothelioma associated with the syndrome. Secretory granules were revealed by electron microscopy within the cytoplasm of tumour cells that could represent storage granules of antidiuretic hormone.

Case report

A 58 year old man was admitted to the hospital with a five month history of pain on the upper right hemithorax and right shoulder. A month before admission he had developed low grade fever (37·7°C) and a dry, unproductive cough. He had worked as a clerk in the city and had had no apparent exposure to asbestos. He had smoked 20 cigarettes a day for 10 years but had given up smoking five years earlier. On examination the temperature was 36·8°C, the pulse rate 68 beats/min, and the respirations 18/min. The blood pressure was 115/70 mm Hg. Breath sounds were slightly diminished over the upper right hemithorax. Liver and spleen were not palpable. Laboratory tests showed: red cells packed volume 0·42; haemoglobin 14·3 g/dl; white blood cells 8·5 × 10^9/l; (polymorphs 72%, lymphocytes 26%, monocytes 2%) and platelets 260 × 10^9/l; erythrocyte sedimentation rate (ESR) 68 mm in the first hour. The concentration of blood urea was 18 mg/100 ml (6·48 mmol/l); serum glucose 110 mg/100 ml (6·05 mmol/l); serum sodium 140 mmol(mEq)/l, potassium 4·9 mmol/l, and chloride 96 mmol/l; total serum proteins 71 g/l, albumin 41 g/l, globulin 30 g/l; serum aspartate transaminase 37 Karmen units/ml (0·30 μmol/s/l), serum alanine transaminase 39 Karmen units/mol (0·41/μmol/s/l), alkaline phosphatase 5 Bodansky units (0·45 nmol/s/l). Cytological examination of the sputum was negative for malignant cells. Culture of the sputum yielded no acid fast bacilli, fungi, or bacteria. A fluorescent antibody test for hydatid disease gave a negative result. Bone, liver, and brain radionuclide scans were normal. A chest radiograph and tomograms showed lobulated peripheral shadows typical of mesothelioma at the upper part of the right hemithorax with no signs of pleural effusion.

A right thoracotomy showed extensive diffuse thickening of the parietal pleura with plaque formation; multiple biopsy specimens were taken. Histological examination of the biopsy specimens showed a biphasic malignant mesothelioma with spindle cells and atypical epithelial cells. Electron microscopy of deparaffinized tissue from the area showing atypical epithelial cells revealed cytoplasmic "secretory" granules (fig) enveloped in a double cytoplasmic membrane, well developed granular endoplasmic reticulum, tonofilaments, and several mitochondria with lamellar cristae. The size of the granules was estimated at between 70 and 100 nm. The patient made a good recovery from the operation and was discharged from hospital a week later. No treatment was given.

He was readmitted a month later because of fever and confusion. On admission he was severely ill and lethargic, but there was no clinical evidence of fluid volume depletion. His temperature was 38·2°C, respirations 27/min, pulse 110 beats/min, and blood pressure 110/60 mm Hg. A chest radiograph showed extension of the lobulated peripheral shadowing on the right. Laboratory tests showed: haemoglobin 13·1 g/dl; packed cell volume 40%; ESR 85 mm in the first hour. The blood urea concentration was 21 mg/100 ml (7·56 mmol/l) and serum creatinine 0·9 mg/100 ml (80 μmol/l). The serum sodium concentrations ranged from 122 to 128 mmol/1, serum potassium from 4·1 to 4·5 mmol/l, and serum chloride from 95 to 99 mmol/l on repeated measurement. The blood glucose concentration was 95–110 mg/100 ml (5·3–6·05 mmol/l). Serum arginine vasopressin concentration measured by radioimmunoassay[5] was 15 pg/ml in plasma (normal range: 4–8 pg/ml). Plasma osmolality was 258 mmol(mosmol)/kg and urine osmolality 390 mosmol/kg. Urine had a specific gravity of 1·016 and urinary sodium excretion was 196 mEq(196 mmol)/24 h; the urine was otherwise normal. He was treated with fluid restriction but he failed to respond and died 27 days after admission. Permission for necropsy was not obtained.

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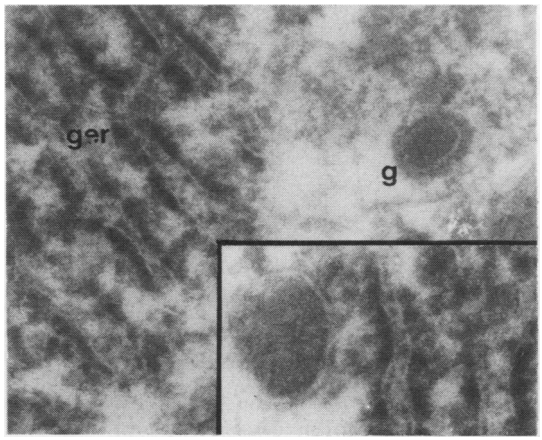

Electron micrograph of deparaffinised plastic embedded tumour tissue. Varying amounts of granular endoplasmic reticulum (ger) and secretory "endocrine type" granules (g) are seen within an atypical epithelial cell. The cytoplasmic secretory granules (g) are enveloped in a double cytoplasmic membrane. The size of the granules was estimated at between 70 and 100 nm. (Uranyl acetate, × 21 000; insert × 27 000).

Discussion

The diagnosis of malignant pleural mesothelioma of biphasic type was made on the basis of the histological and electron microscopic findings.[6-8] This case fulfils the criteria for diagnosis of inappropriate antidiuretic hormone secretion, as hyponatraemia, low serum osmolality relative to urine hypertonicity, continued renal excretion of sodium, and an increased concentration of arginine vasopressin in the serum were all present. The patient was not in pain or under severe emotional stress before his second admission. There were no signs of other intracerebral, endocrine or renal disease and he received no medication apart from acetylsalicylic acid. There were no clinical signs of fluid volume depletion during the second admission. The patient had normal skin turgor and there was no appreciable change in blood pressure. Our electron microscopic findings, which revealed cytoplasmic secretory granules in the cytoplasm of atypical epithelial type cell, suggest that antidiuretic hormone or an antidiuretic hormone like substance could be produced, stored, and released by the tumour cells. Similar secretory granules have been described in a patient with malignant pleural mesothelioma cells.[9] These granules were related to a hypoglycaemic syndrome. Our patient had no evidence of hypoglycaemia.

In the previous reported case[4] the authors could not detect antidiuretic hormone in various tissues, including tumour tissue, and therefore proposed that inappropriate production of arginine vasopressin from the hypothalamus might be stimulated by a vagal reflex stimulation. Neither their patient nor ours had evidence of disturbance of vagal reflexes, such as bradycardia or an abnormal breathing pattern. In view of the delay between death and necropsy they could not rule out the possibility of ectopic antidiuretic hormone production from the tumour cells.[4] In a retrospective study it was shown that hyponatraemia is a common finding in patients with mesothelioma, occurring in 62%; and it has been suggested that this tumour may often be accompanied by inappropriate secretion of antidiuretic hormone.[10] Our report offers support for this suggestion.

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