equate mast-cell activation is known to occur in patients with malignant conditions, it has not, to our knowledge, been described in association with renal cancer. We do not know if the renal cancer (although radically excised) has anything to do with the patient's EIA. When creatinine clearance after nephrectomy diminishes, HIS kinetics might be altered. In renal failure, plasma HIS levels are elevated due to an increased number of mast cells in the skin and/or retention of HIS in renal insufficiency. This could be an explanation for why the patient became symptomatic only after nephrectomy; his creatinine clearance after nephrectomy was 42 ml/min (normal range, 80 to 120 ml/min), but before nephrectomy it was 98 ml/min. The severity of the HIS-release response is dependent on the plasma HIS level; life-threatening reactions can occur with HIS levels above 120 nmol/L. The patient's HIS concentration after the first bicycle test in the hospital was above 150 nmol/L. Subsequently, with antihistamine treatment, it was maximally 93.5 nmol/L.

As has been reported in the literature, antihistamine agents were not totally effective in preventing symptoms in EIA. As EIA shares many clinical features with systemic mastocytosis, in which prostaglandin (PG) D₂ overproduction is known to occur, we started carefully with aspirin treatment without measuring PGD₂. In our patient, aspirin did not have an additional effect.

In survivors of cardiac arrest without structural cardiac abnormalities, spasm-induced arrhythmias can be of importance. Ergonovine provocation of CAS can identify some of these patients. The simultaneous occurrence of a positive ergonovine test and HIS-induced CAS has been described. Ginsburg et al demonstrated HIS provocation of CAS in patients without CAS as a possible mechanism causing variant angina. In addition, HIS has positive chronotropic and inotropic effects via H₁- and/or H₂-receptors. It can mediate ischemic ventricular arrhythmias via a direct effect on an H₁-receptor, or it can cause reperfusion arrhythmias following a transient episode of HIS-induced CAS.

The 2 weeks of recurrent chest pain in our patient may have represented variant angina, followed by near-fatal cardiac arrest after ventricular fibrillation due to spasm of the right coronary artery. We believe this to be the first description of near-fatal arrhythmias in a patient with EIA, which can be another cause of CAS in patients with normal coronary arteries.

**References**


**Pleural Effusion in Multiple Myeloma***

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We report the first case of IgA-κ multiple myeloma presenting as a myelomatous and eosinophilic pleural effusion with increased adenosine deaminase activity. In a review of the literature, 80 percent of myelomatous pleural effusions are due to IgA multiple myeloma.

(Chest 1994; 105: 622-24)

| ADA = adenosine deaminase; MM = multiple myeloma; MPE = myelomatous pleural effusion; NV = normal value |

Multiple myeloma (MM) is a malignant proliferation of plasma cells that affects mainly bone marrow, but may involve other organs as well. The thorax may be invaded, producing thoracic skeletal abnormalities, plasmacytomas, pulmonary infiltrates, and pleural effusions (myelomatous and nonmyelomatous), among other manifestations. In the literature, 80 percent of myelomatous pleural effusions (MPE) are due to IgA MM.

Pleural fluid eosinophilia has occasionally been described in malignant diseases. Elevated adenosine deaminase (ADA) activity is usually employed in the differential diagnosis of tuberculous pleural effusion, but has, however, been reported elevated in some cases of malignancy too.

We present a patient with myelomatous and eosinophilic pleural effusion with elevated ADA activity as the first manifestation of MM, a circumstance which, to our knowledge, has never been described in the literature.

**Case Report**

A 51-year-old man was an alcohol abuser (more than 100 g of alcohol per day) and heavy smoker (2 packs per day). One week before hospital admission, he presented with dyspnea and right-lower chest pain. From the Services of Internal Medicine (Drs. Pereira, Martínez, and Pujol), Hematology (Dr. Rodríguez), and Pathology (Dr. Conde), Hospital General de Huelva, Huelva, Spain. Reprint requests: Dr. Rodríguez-R, Via Faisajista Edif Hertzonte A7, 21003 Huelva, Spain.
pain aggravated by coughing and breathing. Physical examination showed only decreased breath sounds in the right base. Laboratory results revealed the following: urea 64 mg/dl (10.6 mmol/L); creatinine, 1.34 mg/dl (118 μmol/L); serum proteins, 8.9 g/dl (89 g/L); calcium, 12 mg/dl (3 mmol/L); and uric acid 9.42 mg/dl (560 μmol/L). Hemoglobin concentration was 10.2 g/dl (102 g/L); leukocytes count was 12.2 × 10⁹/L (64 percent neutrophils, 18 percent lymphocytes, 12 percent monocytes, 6 percent eosinophils); platelet count was 207 × 10⁹/L; and erythrocyte sedimentation rate was 130 mm in the first hour. Serum protein electrophoresis (Fig 1A, top) demonstrated a monoclonal component within the β-globulin band; quantification yielded raised IgA (5,270 mg/dl; normal value [NV], 90 to 450 mg/dl) and Ig light chain κ (670 mg/dl; NV, 200 to 440 mg/dl) and decreased IgG, IgM, and Ig light chain λ (329 mg/dl, 6 mg/dl, 27 mg/dl; NV, 800 to 1800 mg/dl, 60 to 250 mg/dl, 110 to 240 mg/dl, respectively); immunoelectrophoresis confirmed monoclonal IgA – κ. Bence-Jones proteinuria was negative.

Radiographic examination showed right pleural effusion (Fig 2) and osteolytic lesions in skull and pelvis. Thoracenteses were performed and revealed serofibrinous fluid with glucose level 11.7 mg/dl (6.5 mmol/L), protein level of 5.7 g/dl (57 g/L), lactate dehydrogenase level of 396 U/L, and ADA value of 61 U/L (NV < 45 U/L). Electrophoresis (Fig 1B, bottom) and immunofixation of pleural fluid showed the same serum paraprotein; quantification yielded raised IgA (5,900 mg/dl) and Ig light chain κ (85 mg/dl), and decreased IgG, IgM, and Ig light chain λ (253 mg/dl, 6 mg/dl, 33 mg/dl, respectively). Cytologic examination of pleural fluid revealed leukocytes of 2.5 × 10⁹/L (60 percent eosinophils, 30 percent lymphocytes, 10 percent neutrophils) and abnormal plasma cells (Fig 3). Pleural fluid cultures were negative. Specimens from a pleural biopsy (Abrams needle), which was performed twice, failed to demonstrate myelomatous involvement. Bone marrow aspiration showed 50 percent of atypical plasma cells and reduction of myeloid precursors. IgA-κ MM was diagnosed and chemotherapy with prednisone and melphalan was initiated, but no response was observed (serum IgA-κ and pleural effusion raised, this last circumstance required repeated thoracenteses for drainage). The patient died 11 months later due to evolution of MM.

**DISCUSSION**

Pleural effusions in MM occur in about 6 percent of patients and are due to several etiologies requiring different types of therapy. These etiologies are, most commonly, heart failure secondary to amyloidosis, followed by the following: pulmonary embolism; chronic renal failure; second neoplasm; and pleural myelomatous involvement (from adjacent skeletal or parenchymal tumors, direct implantation of tumor nodules on the pleura, and mediastinal lymph node infiltration with lymphatic obstruction). Pleural effusions secondary to pleural myelomatous involve have rarely been reported in the literature (in our review, 39 cases). Kintzer et al. in a review of 958 cases of MM, report only eight cases (0.8 percent) of MPE, but this condition as the first manifestation of MM is absolutely exceptional. Diagnostic criteria to confirm the
myelomatosal etiology are as follows: (1) demonstration of a monoclonal protein in pleural fluid electrophoresis; (2) detection of atypical plasma cells in pleural fluid; and (3) histologic confirmation using pleural biopsy specimen or autopsy. In our case, the first two criteria were fulfilled. Pleural biopsy specimen, however, failed to confirm the diagnosis probably due to a discontinuous myelomatosal affection of the pleura. In the literature, 80 percent of MPEs are due to IgA MM, perhaps as a result of a major tendency to invade extraosseous structures.2 This could be important in the differential diagnosis of pleural effusions in patients with IgA MM.

Pleural eosinophilia is defined as the presence of 10 percent or more eosinophils among the leukocytes in the pleural fluid, and it has been used as an indicator of good prognosis because it is a very rare finding in malignant pleural effusions. Several cases of tumors, however, have been reported as presenting pleural eosinophilia: lung carcinoma, mesothelioma, breast cancer, melanoma, sarcoma, and Hodgkin's disease.3,4 The association between pleural eosinophilia and MM has been reported in the literature only once before.5

Finally, the level of ADA activity is noteworthy. This has been found to be raised mainly in tuberculous pleural effusions, although high activity has been described in both benign and malignant conditions due to activation of lymphocytes in these processes. We have found only two other cases in the literature (one of them IgA-κ MM) reporting MPE and elevated ADA activity.2,5

In conclusion, we report the first case (to our knowledge) of IgA-κ MM presented as a MPE with eosinophilia and an increased ADA activity. In our case, no response was observed when treatment with chemotherapy was initiated.

REFERENCES


Myasthenia Gravis Associated With Small-Cell Carcinoma of the Lung*

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A 49-year-old man complained of a 3-month history of progressive generalized muscle weakness. He was diagnosed as having small-cell lung carcinoma at the same time. He received an intravenous injection of edrophonium chloride with remarkable improvement of muscle strength. Electromyographic studies revealed a compound muscle action potential that decreased after repetitive stimulation. These findings were considered representative of myasthenia gravis (MG), and inconsistent with Eaton-Lambert syndrome. The appearance of MG with small-cell lung carcinoma seems to be very rare, but possible. (Chest 1994; 105: 624-25)

MG = myasthenia gravis; nAChRs = nicotinic acetylcholine receptors

Myasthenia gravis (MG) results from autoantibodies against nicotinic acetylcholine receptors (nAChRs) in the motor end plate. The disorder is characterized clinically by intermittent muscle weakness that improves after anticholinesterase medication and by decremental neuromuscular transmission during the repetitive nerve stimulation test at frequencies of 1 to 50 Hz. Although there seems to be an association between MG and thymic hyperplasia, as well as thymic tumors, such a relationship with bronchogenic carcinoma is not well established. In this report, we describe a patient who simultaneously developed MG and small-cell lung carcinoma.

CASE REPORT

A 49-year-old male cigarette smoker complained of a 3-month history of progressive generalized muscle weakness, dyspnea, and cough. He had difficulties in walking, chewing, and swallowing. He also noted an 8-kg weight loss within 3 months. On physical examination, a right supraclavicular lymph node swelling and a reduction of respiratory sound at the left lung field were noted. Neurologic examination showed evidence of ptosis and proximal muscle weakness. Results of routine laboratory examinations were all within normal ranges. Arterial blood gases showed hypoxemia (PaO₂, 61.2 mm Hg). Autoantibody against acetylcholine receptors was negative. Chest radiograph showed a dextrocardia, left hilar soft-tissue mass, and mediastinal lymph node swelling (Fig 1). Biopsy specimen of the left upper lobe lesion obtained with fiberoptic bronchoscope demonstrated an anaplastic small-cell carcinoma. Muscle biopsy specimens (stereoneuromastoides muscle and intercostal muscle) showed no remarkable change.

Because of the patient's muscle weakness, he received an intravenous injection of edrophonium chloride with remarkable though transient improvement of muscle strength. Electromyographic studies revealed normal motor and sensory nerve conduction velocities. Repeti-

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