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LETTER TO THE EDITOR

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Transient severe symptomatic pulmonary hypertension as onset symptom in multiple myeloma

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Dear Editor,
Pulmonary hypertension (PH) has been reported as a rare complication of multiple myeloma (MM). It was particularly described at the time of diagnosis in some patients with POEMS syndrome [1]. Abnormal release of vasoactive cytokines has been implicated in the pathogenesis of the disease [2]. Pulmonary arterial hypertension secondary to vascular deposition of amyloid in the lungs is exceptional [3]. As far as we know, the present study is the first described case in which transient severe PH has been the symptom of onset of MM. A 31-year-old man, in November 2002, began to complain of dyspepsia, abdominal tenderness, and distension. He came to our observation at the end of March 2003. At physical examination, the patient was pale, tachypnoic (24 breaths/minute), and tachycardiac with presystolic gallop rhythm (104 beats/minute). Distension of jugular vein, right pleural effusion, and hepatosplenomegaly with ascites were appreciable. The echocardiogram showed a normal-sized left ventricle with paradoxical motion of the interventricular septum. The right ventricle was dilated (34 mm). High velocity tricuspid regurgitation allowed the estimation of systolic pulmonary pressure of 80 mmHg (Fig. 1). Transesophageal echocardiography, cardiac MRI and lung perfusion scintigraphy, and spiral TC did not disclose etiology of PH.

Laboratory examination showed a normochromic anemia, thrombocytopenia, and increased plasma protein (9.6 g/dl) with hypergammaglobulinemia (40.2%), IgGλ monoclonal peak (IgG 3290 mg/dl) with Bence Jones λ proteinuria (1,694 mg/24 h) X-ray showed multiple advanced lytic bone lesions. Bone marrow biopsy revealed 80% clonal plasma cells ($CD20^+$, $CD38^+$, k^-, λ^+, $clgG^+$). A diagnosis of MM stage III was made [4]. Biopsy of periumbilical fat was diagnostic for amyloidosis, but neurophysiological studies were negative. After a vincristine, adriamycin, and dexamethasone (VAD) chemotherapy cycle, echocardiographic examination showed a significant decrease in the size of the right ventricular, trivial tricuspid regurgitation, and disappearance of paradoxical motion of interventricular septum. Calculated pulmonary artery pressure was in the normal range. At the end of August 2003, after the fourth VAD cycle, two additional cycles of melphalan 30 mg/m^2 were administered. However, clinical response was only partial [5] so that a double autologous peripheral blood stem cells transplant (PBSCT) with melphalan 200 mg/m^2 was scheduled. The first PBSCT was performed at the end of December 2003 and the second one on April 2004. Upon discharge, the patient achieved complete remission and was in good clinical condition; physical examination and laboratory tests were normal except for a drug-induced cytopenia.

At 18 months follow-up he was still in clinical remission and had resumed his work and physical activities. Serial echocardiographic examinations confirmed a normal-sized left ventricle (EF >60%), no more than trivial tricuspid regurgitation, and normal-sized right heart chambers.

The dramatic response to the treatment with steroids and chemotherapeutic agents inducing a substantial decrease of bone marrow plasma cells, associated with a sudden decrease of pulmonary artery pressure (about 40 mmHg in systolic pulmonary artery pressure in 10 days), suggests that vasoactive mediators released by neoplastic cells such as proinflammatory cytokines, other than increase plasma viscosity, may have played a role in the pathogenesis of transient pulmonary hypertension. We cannot rule out that abnormalities of diastolic function due to cardiac amyloid deposition may have contributed to increased pulmonary artery pressure. The patient had amyloid in periumbilical fat; however, at right heart catheterization, pulmonary

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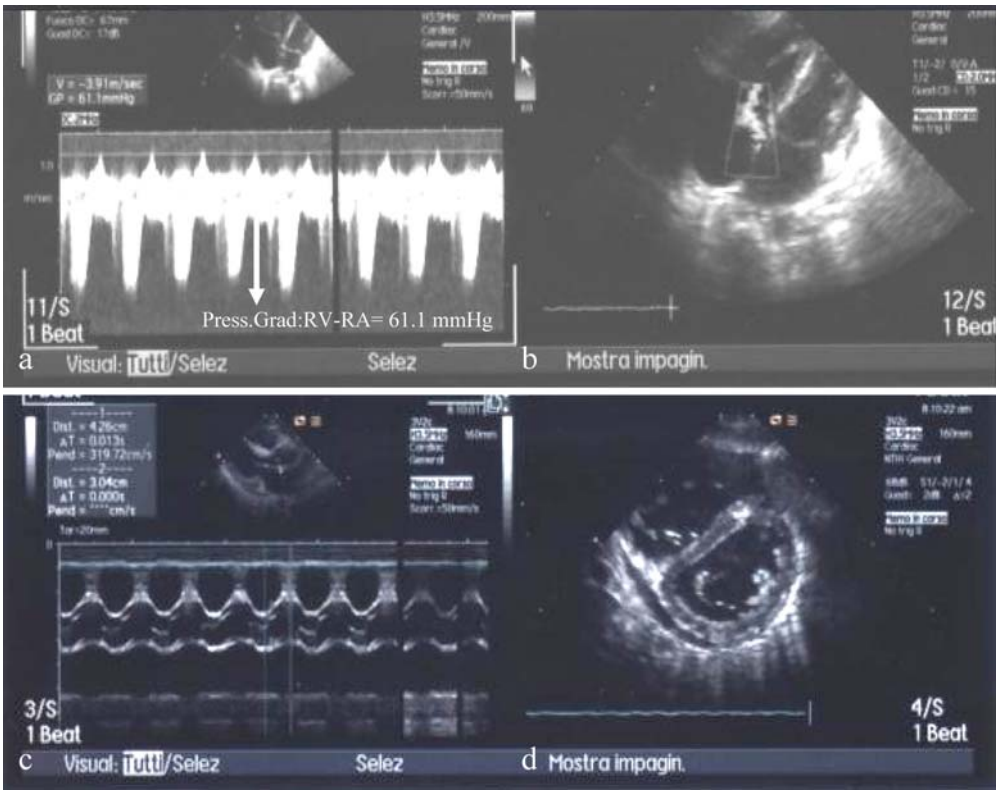

Fig. 1 The exam shows **a** high velocity tricuspid regurgitant flow (right ventricle–right atrium pressure gradient= 81.1 mmHg), **b** subcostal image of eccentric tricuspid regurgitant flow, **c** M_mode echo of LA and aorta; **d** short axis echocardiogram demonstrates paradoxical motion of interventricular septum and dilated right ventricle

wedge pressure was normal. Thereafter, Doppler examination of left ventricular diastolic function has always been within normal limits.

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