Acutely promyelocytic leukemia (APL) is a distinct subtype of acute myeloid leukemia (AML) distinguished from all other AMLs by characteristic blast morphology, life-threatening coagulopathy, and specific rearrangement of the chimeric PML/RARα gene resulting from the balanced translocation t(15;17), which confers a special sensitivity to all-trans retinoic acid (ATRA). Since the discovery of the differentiating activity of all-trans retinoic acid (ATRA) in acute promyelocytic leukemia (APL), the treatment of this disease has greatly improved. Currently, the combination of ATRA and chemotherapy is considered the best treatment for patients with APL. This approach has consistently extended the remission rate and disease-free survival of APL patients with low mortality. Among ATRA’s adverse effects, the retinoic acid syndrome is the most important. It consists of fever, dyspnea, weight gain, pulmonary infiltrates and pleural and cardiac effusions. Other findings occasionally described are lower extremities edema and leukocytosis. We report a case of an retinoic acid syndrome associated with cardiac tamponade due to massive pericardial effusion. This adverse effect, not previously reported, was successfully treated by performing pericardiocentesis followed by the administration of dexamethasone.

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pnea and progressive hypoxemia (pO2, 59 mmHg) associated with precordial pain, silenced cardiac tones, tachycardia, hypotension and a low urinary output. Pulmonary arterial pressure was 35/24 mmHg, pulmonary capillary wedge pressure 22 mmHg and central venous pressure 18 mmHg. Radiographs of the chest showed bibasal infiltrates. Echocardiography detected a large pericardial effusion causing cardiac tamponade. The patient was admitted to the critical care unit 20 hours after the onset of symptoms, and pericardiocentesis was then performed. Macroscopically, the pleural fluid obtained was clear. At cytological examination no cells were detected, and the biochemical analysis showed the following results: glucose 117 mg/dL, proteins 6 g/dL and LDH 824 U/L (protein and LDH levels in plasma were 6.6 g/dL and 325 U/L respectively).

At this time, ATRA was discontinued and therapy with dexamethasone was started (10 mg/12h intravenously over three days). The clinical status of the patient improved progressively and he was discharged in complete remission two weeks later. Currently, fourteen months after diagnosis, the patient maintains normal cardiac function and is in continuous complete remission.

Discussion

Nowadays, the combination of ATRA and chemotherapy is considered the best treatment for patients with APL. This approach has consistently improved the remission rate and disease-free survival of APL patients with low mortality. Among ATRA’s adverse effects, retinoic acid syndrome is the one most frequently reported, with an estimated incidence of 26%. Though not well defined, the physiopathology of this syndrome seems to be related to ATRA-induced cytokine secretion by APL blasts. These cytokines may increase the number of circulating blasts, their adherence and activation, which, in turn, would lead to the distress symptoms and the pericardial and pleural effusions seen in individuals with this complication. To prevent the development of this syndrome, simultaneous treatment with ATRA and chemotherapy is generally recommended when the leukocyte count at diagnosis exceeds 6×10^9/L. However, this approach is not always effective and, as occurred in our patient, the retinoic acid syndrome may develop. In those patients with low leukocyte numbers it is mandatory to perform complete blood counts daily once ATRA has been started. Additional chemotherapy could be administered if an increase in leukocytes is observed. Once established, this syndrome is difficult to manage, though early administration of dexamethasone (10 mg/12 hours) has achieved the best results.

Although the appearance of a pericardial effusion in patients treated with ATRA is a known and common feature of retinoic acid syndrome, we wish to draw attention of the development of cardiac tamponade with secondary cardiogenic shock as a severe and not previously reported manifestation of this syndrome.

References