patient was treated with corticosteroids and bicalutamide therapy was discontinued; prompt resolution of symptoms and laboratory abnormalities followed. The patient refused a challenge study with this medication to see if the clinical picture would return.

This case strongly suggests a drug-induced eosinophilic lung disease as supported by the temporal relationship of events, the exclusion of all other causes, and the prompt clinical improvement following withdrawal of causative agent and institution of corticosteroid therapy.

Drug-induced lung injury is thought to be either a direct toxic effect of the drug or due to a hypersensitivity reaction. The clinical signs and symptoms usually are variable and nonspecific. Development of such an injury does not appear to be related to cumulative drug dose or duration of therapy. Chest roentgenographic findings are variable and nonspecific. The most common pattern is bilateral peripheral alveolar infiltrates with or without a migratory component and is often similar to other interstitial lung diseases. The usual pulmonary function deficit is a restrictive pattern with a reduction in diffusing capacity. Lung biopsy may reveal poorly defined granuloma formation, hyperplastic type II alveolar cells, and lymphocytic or eosinophilic infiltration affecting peribronchial, septal, and intra-alveolar spaces. Peripheral blood eosinophilia occasionally is noted. Therapy entails discontinuation of the offending agent. Clinical symptoms rapidly resolve, but clearing shown on a chest x-ray film usually lags behind the clinical improvement with less than 10% of patients having residual infiltrates. Corticosteroid therapy usually hastens recovery.

Conclusions

The data presented demonstrate that a new nonsteroidal antiandrogen agent, bicalutamide, is capable of causing drug-induced eosinophilic lung diseases. As more patients with advanced prostate cancers receive antiandrogen chemotherapy, more cases of drug-induced lung diseases may be encountered. Awareness of this entity is important since treatment entails simple withdrawal of the drug and institution of corticosteroid therapy in severe cases.

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ARDs Associated With Tumor Lysis Syndrome in a Patient With Non-Hodgkin’s Lymphoma*

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ARDS developed in association with tumor lysis syndrome (TLS) in a patient with non-Hodgkin’s lymphoma. Although a number of life-threatening complications have been noted to occur following TLS, this appears to be the first report of ARDS developing in association with TLS.

(CHEST 1998; 113:550-52)

Key words: acute respiratory distress syndrome; non-Hodgkin’s lymphoma; tumor lysis syndrome

Abbreviation: TLS = tumor lysis syndrome

Tumor lysis syndrome (TLS) is characterized by several metabolic derangements resulting from rapid lysis of tumor cells and is seen most frequently following chemotherapy for neoplasms with a high mitotic rate. Cardiac arrhythmias and renal failure are both well described fatal complications of the syndrome. A patient with high-grade lymphoma complicated by acute TLS developed ARDS. An extensive MEDLINE search (1966-1997) leads one to believe this is the first report of ARDS occurring in association with TLS.

Case Report

A previously healthy 26-year-old man presented with a 10-day history of abdominal pain, night sweats, and shortness of breath. A radiograph of the chest revealed bilateral pleural effusions, and cytologic analysis of the pleural fluid was consistent with lymphoma. CT scans of the chest, abdomen, and pelvis revealed massive pericardial, epicardial, and retroperitoneal lymphadenopathy. A staging laparotomy was performed and demonstrated ascites with multiple tumor nodules present throughout the abdominal cavity. Results of an omental biopsy confirmed the diagnosis of a high-grade lymphoma.

His immediate postoperative course was complicated by hypoxemia and failure to wean from the ventilator. Significant levels of positive end-expiratory pressure and a high fraction of inspired oxygen were needed to maintain adequate systemic oxygenation. A chest radiograph taken at this time revealed bilateral pulmonary infiltrates consistent with ARDS (Fig 1).

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Arterial blood gas value analysis, with fraction of inspired oxygen of 80%, revealed a pH value of 7.22; PCO<sub>2</sub>, 36 mm Hg; and PO<sub>2</sub>, 112 mm Hg. On postoperative day 1, the creatinine level had increased from 1.0 to 2.3 mg/dL (normal value, 0.6 to 1.2 mg/dL); phosphorus value, from 2.7 to 7.3 mg/dL (normal value, 2.5 to 4.5 mg/dL); and potassium level, from 4.1 to 5.2 mEq/L (normal value, 3.5 to 5.0 mEq/L). Calcium level had decreased from 9.8 to 7.2 mg/dL (normal value, 8.5 to 10.0 mg/dL) and uric acid value was markedly elevated at 28 mg/dL (normal value, 3.5 to 7.2 mg/dL). Amylase level was 130 U/L (upper limit of normal, 125 U/L). Pulmonary capillary wedge pressure was 15 mm Hg, pulmonary artery pressure was 40/24 mm Hg, cardiac output was 9.7 L/min, and calculated systemic vascular resistance was 574 dyne·s·cm<sup>-5</sup>.

The clinical diagnoses of TLS and ARDS were made. The TLS was treated aggressively with intravenous fluids, with alkalization of the urine, and with allopurinol therapy. Hemodialysis was necessary to control persistent hyperkalemia, which resolved as renal function slowly improved. ARDS was managed with continued mechanical ventilation, high levels of fraction of inspired oxygen, and positive end-expiratory pressure. The patient's alveolar-arterial oxygen pressure difference and pulmonary infiltrates gradually improved; he was weaned from mechanical ventilation over a period of 48 h and was successfully extubated 9 days after TLS developed.

**Discussion**

Acute TLS usually is seen as a complication of chemotherapy for several hematologic and nonhematologic malignant neoplasms. It also has been reported to occur after steroid therapy and spontaneously in a patient with lymphoma and a large tumor burden. Cell lysis with subsequent release of potassium, nucleic acids, and phosphates into the extracellular environment is believed to be responsible for the hyperkalemia, hyperuricemia, hyperphosphatemia, hypocalcemia, and azotemia characteristic of this syndrome. Complications of TLS that have been reported in the medical literature include life-threatening arrhythmias from hyperkalemia, acute renal failure from uric acid and xanthine nephropathy, and seizue resulting from electrolyte abnormalities. Preexisting renal failure and low urine output appear to increase the risk of complications developing with TLS. Effective treatment strategies that have been reported to be useful in TLS include vigorous hydration to increase urine flow and administration of allopurinol to decrease uric acid levels. Alkalizing the urine decreases the solubility of uric acid but also has been shown to increase the risk of calcium phosphate precipitation; therefore, its use in the presence of hyperphosphatemia remains controversial. Hemodialysis occasionally is needed to control life-threatening hyperkalemia, as illustrated in the case described herein.

The evolution of this patient's clinical course fulfills the clinical criteria for TLS based on the presence of hyperkalemia, hyperphosphatemia, hyperuricemia, hypocalcemia, and azotemia in the setting of a high-grade lymphoma. It is likely that surgery and manipulation of the tumor mass precipitated tumor lysis. From the review of the medical literature, the natural history and mortality of TLS are not clearly defined. However, there is a consensus that early recognition and aggressive therapy can minimize mortality. The case reported here demonstrates these aspects of TLS.

Although in this case it appears that ARDS was a direct result of TLS, the possibility that ARDS was secondary to mild pancreatitis cannot be completely excluded. However, the trivial elevation in serum amylase and the normal-appearing pancreas shown on the CT scan of the abdomen and at exploratory laparotomy make this unlikely.

The pathogenesis of ARDS in the setting of tumor lysis is unclear. It is unlikely to be related to the serum electrolyte abnormalities since these occur in other disease processes and do not result in ARDS. In this case, ARDS and hyperpyrexia occurred rapidly following the onset of tumor lysis, suggesting that they could have been due to the result of the release of cytokines or other active mediators. The use of high-dose cytokines as treatment for certain malignant neoplasms has been associated with an increase in pulmonary capillary pressure leading to the development of noncardiogenic pulmonary edema and would support such a mechanism for ARDS occurring in the setting of TLS. The risk of ARDS developing in the setting of TLS may depend on the degree of cell lysis, the speed of release of mediators into the pulmonary circulation, and the susceptibility of the alveolar-capillary membrane to injury.

**Conclusion**

This case would indicate that ARDS can occur due to tumor lysis alone. For this reason, ARDS should be added to the differential diagnosis of respiratory failure occurring in patients with aggressive lymphoma undergoing tumor lysis.
REFERENCES


Key words: hypertrophic cardiomyopathy; right ventricular aneurysm

Abbreviations: HCM= hypertrophic cardiomyopathy; LV= left ventricular; RV= right ventricular; RVA= right ventricular aneurysm

Right Ventricular Aneurysm Associated With Advanced Hypertrophic Cardiomyopathy*

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A previously undescribed case of right ventricular aneurysm (RVA) associated with hypertrophic cardiomyopathy in an advanced stage is reported. The diagnosis was established by noninvasive (cardiac two-dimensional echocardiogram and nuclear MRI) and invasive (cardiac catheterization, angiography, and biventricular endomyocardial biopsy) cardiac examinations, which documented hypertrophied, dilated and hypokinetic biventricular chambers associated with typical histologic findings (histologic hypertrophic cardiomyopathy index of 66%). A prominent narrowing of myocardial arterioles, extended to the right ventricular myocardium, has been identified and has been hypothesized as being responsible for RVA formation.

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Case Report

A 63-year-old man was admitted to the hospital because of chest discomfort associated with dyspnea on moderate effort (New York Heart Association II). These symptoms had started 6 months earlier. A family history was negative for sudden death or hypertrophic cardiomyopathy. At the time of admission, results of a physical examination were normal. In particular, during heart auscultation no murmurs or abnormal sounds were heard. BP was 130/80 mm Hg. Results of routine laboratory tests (hematologic and biochemical studies and urine analysis) were within normal limits. A chest x-ray film showed a moderate prominence of the third left arch of the cardiac silhouette. The ECG showed sinus rhythm with left ventricular hypertrophy and diffuse nonspecific abnormalities of the ST-T wave.

The two-dimensional echocardiogram showed a moderate degree of concentric left ventricular (LV) hypertrophy (interventricular septum, 15 mm; LV free wall, 13 mm). The left ventricle was moderately dilated (LV end diastolic, 60 mm) with mild diffuse reduction of LV contractility (LV ejection fraction, 0.45). The right ventricle was mildly dilated, and the anteropapical wall was thin and showed an aneurysm with a maximum diameter of 40 mm. Inside the aneurysm a stratified thrombus was present. These data were confirmed by a transesophageal echocardiogram (Fig 1). No abnormalities of a valvular pattern were found. Cardiac magnetic resonance scanning was performed at 0.5 T (Vector; GEMS, Milwaukee) in vertical and horizontal long and short axis, with a multislice spin echo sequence (TR/TE=R-R/40 ms; 3 NEX; matrix, 160X256; slice thickness, 10 mm, slice gap, 1 mm) and cine-MRI, both ECG-triggered. The study confirmed the presence of an apical RV aneurysm (Fig 2), with a subtle mural thrombus, and demonstrated the presence of myocardial segmental hypertrophy, particularly in the right ventricle where thickened segments (end-diastolic [ED] thickness, 7 mm) alternated with thinned segments (ED thickness, 2.5 mm).

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552

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