References


Splenic peliosis with spontaneous splenic rupture in a patient with immune thrombocytopenia treated with danazol

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We present a 79-year-old man diagnosed with immune thrombocytopenia (ITP), treated with danazol, who died as a result of a spontaneously ruptured spleen. The histopathological diagnosis was splenic peliosis. This patient presents a chronological association between the treatment with danazol and the development of peliosis, which suggests a clear cause-effect relationship. Facing an individual patient with ITP, clinicians should weigh the potential benefits of danazol with the possible development of serious complications, such as hepatic failure or splenic rupture due to peliosis.

Peliosis is an ectasial vascular process, characterized by the presence of blood-filled cavities in the parenchyma of the liver or spleen. Isolated splenic peliosis is rare. The liver is the most frequently affected organ, and most of the reported cases have been incidentally discovered in autopsies relating to tuberculosis and hematological malignancies. Recently, cases of patients treated with anabolic corticosteroids, with or without steroids, as well as Rickettsia-like organisms in HIV-infected patients have been reported. Peliosis may be asymptomatic, or may be responsible for hepatic failure or life-threatening intraperitoneal bleeding.

Danazol is a synthetic androgen used in the treatment of ITP. The response rate of ITP to danazol is variable. It may exhibit synergic action with steroids, which are considered standard initial treatment of ITP, reduces the need for steroids and may even replace them once remission has set in. Danazol is a well-tolerated drug. However, some unfavorable effects have been described. More significantly, danazol is regarded as a potential cause of hepatic injury, including cholestatic hepatitis, peliosis and neoplasia.

We present a 79-year-old male patient diagnosed with ITP in July of 1994 (8 × 10^10 platelets/L). Initially, he was treated with non-specific gammaglobulins (25 g/day, 5 days) with a favorable response (239 × 10^10 platelets/L). Later he developed a new episode of severe thrombocytopenia (19 × 10^10 platelets/L), and treatment with prednisone (1 mg/kg/day) was started, with response after three weeks of treatment (160 × 10^10 platelets/L). Steroid-related effects developed thereafter (diffuse osteoporosis, vertebral collapse, myopathy and behavior disorders) and the dose was therefore reduced (0.1 mg/kg/day). In January, 1995, danazol was added to the treatment (400 mg/day) with gradual normalization of platelet count. This allowed the gradual tapering of steroids, which were discontinued in July, 1995 (214 × 10^9 platelets/L). Two months later the patient was admitted to hospital with acute abdomen. Ultrasonography showed evidence of hemoperitoneum and spleen rupture. An emergency splenectomy was performed. The patient developed multi-organic failure, dying 11 days after surgery. The histopathologic findings showed a ruptured spleen with extensive splenic peliosis. No liver biopsies were obtained.

Peliosis appears to be the general histopathologic expression of a wide range of agents capable of damaging viscera, particularly the liver and spleen. How peliosis develops is unclear. One hypothesis relates its appearance to sinusoidal barrier damage. In HIV patients with peliosis, treatment of the rickettsial infection resolved both the hepatosplenomegaly and also liver function test abnormalities, which suggests the possible reversibility of the injury.

Danazol has been said to play an etiologic role in peliosis development. Nesher and Makdisi have published two cases of patients with hepatosplenomegaly who received danazol as treatment for ITP. Because the exposure to danazol in both patients was brief; these reports did not clearly demonstrate that danazol was the causal agent. However, it is probable that danazol could have had an additive or synergistic effect with other potential causes of peliosis like steroid therapy. The patient we present developed splenic rupture while being exposed to this drug, steroid treatment having been stopped three months before.

We feel that this report strongly suggests that danazol plays a main causal role in the development of splenic peliosis. It is tempting to speculate that the effects of steroids and danazol on endothelial function could converge not only in their therapeutic effect but also in the development of peliosis.

We think that the clinician must weigh the potential benefits of danazol with the possible development of serious complications, such as hepatic failure or
splenic rupture due to peliosis, specially in patients with myeloproliferative disorders and/or receiving glucocorticoids. In these patients, prompt detection of enlargement of the liver or spleen and careful monitoring of liver function tests may be rewarding, as peliosis can be reversible after stopping these drugs.

**Key words**
Peliosis, splenic, immune thrombopenia, danazol

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**Organization of an umbilical cord blood transplant program**

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The development of human umbilical cord blood transplants with hematopoietic repopulating cells has enabled some problems associated with bone marrow transplants to be solved. Frozen umbilical cord blood banks should facilitate the finding of suitable stem cell donors. However, further experience is necessary to define the optimal method for collection, separation, storage and cryopreservation of umbilical cord blood. We report our experience in the organization of a Cord Blood Bank.

Bone marrow transplants from related donors are the only alternative for some genetic, neoplastic, and non-neoplastic diseases, but they require an HLA identical donor, or with one mismatched antigen at most. Human umbilical cord blood (UCB) contains hematopoietic stem/progenitor cells and might be a clinically useful source of transplantaible hematopoietic repopulating cells.

In 1993 the New York Blood Center created the first cord blood bank for hematopoietic stem cell transplantation. In Spain there are two banks authorized by the National Transplant Organization, one in Barcelona and the other in Málaga. It is important to define the problems involved in organizing Cord Blood Banks. The different international centers should be associated in an International Cord Group, such as Eurocord. The legislation should be similar to that applied to the transplantation of other tissues.

We report our experience in the organization of a cord blood bank. UCB was collected from mothers of children who were candidates for a bone marrow transplant and from others for the constitution of an unrelated donor cord blood bank. Cord blood was not collected if there were obstetric complications. We had previously studied the organizational structure of the obstetrics unit which was co-ordinated with the cord blood bank. Subjects were recruited from the Materno-Infantil Hospital at the time of admission to labour and delivery. Human UCB samples were obtained from normal full-term vaginal deliveries. The mothers were from families with no known genetic disease and they gave written informed consent prior to delivery. Women with a history of a sexually transmitted disease, hepatitis, or other infectious disease were excluded from the study, even if an analysis was negative.

The method used by us for blood cord collection was the blood bag sterilized by betadine, to obtain the maximum volume for each collection in order to separate the cord blood mononuclear cell population. This is the method most commonly used. It may be important to reduce the cryopreserved cord blood volume from 100 mL (+50) to 50 mL or less. We used conventional 350 mL blood bags with CPD-A, reducing the anticoagulant volume to 25 mL in a sterile laminar flow hood. The modified bag and the samples for immunohematological controls, bacteriological and fungal cultures, flow cytometry and hematopoietic progenitor cell count were sterilized.