Littoral cell angioma of the spleen in a patient with severe aplastic anemia

Littoral cell angioma (LCA) is a rare benign tumor of the spleen. We describe a patient with aplastic anemia who, following multiple treatments with rabbit and horse anti-thymocyte globulin and anabolic steroids developed marked splenomegaly and hypersplenism. LCA was diagnosed post-splenectomy. This is the first case of LCA associated with aplastic anemia and its treatment.

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Introduction. The most common primary tumors of the spleen are benign and originate from the vascular endothelium. Rarely they develop from the lining cells of the red-pulp sinuses, so called littoral cells, giving rise to littoral cell angiomas (LCA), first described by Falk *et al* in 1991.[1] LCA is symptomatic in half of the cases, the remainder being discovered incidentally. An association with malignancies has been reported but its etiology remains unclear.[2,3] We describe a case of splenic LCA in a patient with longstanding severe aplastic anemia treated with multiple courses of rabbit and horse anti-thymocyte globulin (ATG) and anabolic steroids, and suggest that immunosuppression may have been related to its development.

Case. A 48-year old lady presented in June 1996 with pancytopenia. Bone marrow examination confirmed aplastic anemia. Biochemistry, PNH screen and cytogenetics were normal. The patient received supportive treatment. Over the initial 6-month period she received a course of rabbit ATG followed by horse ATG but failed to respond. Because of undesirable side effects, cyclosporin A (CsA) was only given for 2 months. In February 1997 high dose oxymethalone was commenced, resulting in reduction of transfusion requirements. Due to clinical deterioration in June 1998 a further course of horse ATG was given while oxymethalone was continued. In June 2000 the patient's condition deteriorated again. Liver function tests showed elevated transaminases, ferritin was 3,410μg/L. Auto-antibodies and hepatitis screen were negative. Abdominal ultrasound (US) showed mild splenomegaly. Bone marrow examination revealed continuing aplasia. Oxymethalone was discontinued and a fourth course of horse ATG followed by low dose CsA was given, to which she failed to respond. In June 2002 she remained severely transfusion-dependent a blood and platelets. Examination now revealed marked hepatosplenomegaly. She denied any B-symptoms and there was no palpable lymphadenopathy. Computed tomography (CT) showed an enlarged liver but no focal abnormalities whilst the spleen was enlarged with several low attenuation lesions of variable size. Hepatic wedge pressures and a ^{99}Technetium (^{99}Tc) scan of the liver and spleen were normal. For diagnostic and therapeutic purposes she underwent splenectomy. The spleen measured 26x14x6cm, weighed 1,434g and contained prominent nodules composed of angiomatous tissue with areas of sinus formation and papillary changes (Figure 1). The endothelial lining cells were positive for CD31 and FVIIIrAg but negative for CD34 consistent with a sinusoidal endothelial origin, though CD8 was negative. The features were those of LCA. The patient recovered well from surgery and her blood and platelet requirements improved significantly following splenectomy.

Discussion. LCA represents a distinct new clinicopathological entity of a very rare benign tumor of the spleen.[1] We report the first case in association with aplastic anemia and its treatments. Most patients are diagnosed in their 50s They present with anemia, pyrexia of unknown origin and a variable degree of splenomegaly leading to hypersplenism. However, a significant number of cases are asymptomatic and discovered incidentally post-splenectomy.[1,2] Radiological diagnosis is difficult as the findings on US, CT and ^{99}Tc- scanning are non-specific. On magnetic resonance imaging (MRI) changes of siderosis are commonly observed due to the hemophagocytic capacity of littoral cells.[4,5] Histologically the lesions are always situated within the red-pulp of the spleen, are of variable size and commonly multi-nodular but can also be solitary. They are composed of anastomosing vascular channels with irregular lumina featuring cyst-like spaces. They are lined by tall endothelial cells (littoral cells), which exhibit both endothelial and histiocytic/macrophage differentiation (CD31^{+}, FVIIIrAg^{+}, CD34$^{+/-}$, CD21$^{+/-}$, CD8^{-}, CD68$^{+/-}$). Atypical cells or mitosis are absent.[1,6] LCA has also been associated with synchronous malignancies. Fourteen cases reported to date describe coincidental findings with lymphoma, colonic cancer, renal cancer, ovarian cancer, pancreatic cancer, seminoma and gastric leiomyosarcoma.[3,7] The natural history of LCA is that of a benign tumor of the spleen, which does not recur post-splenectomy. However, it needs to be differentiated from its malignant form, the littoral cell angiosarcoma. This has the same histological and immunohistochemical pattern but reveals a high degree of cell atypia and mitosis.

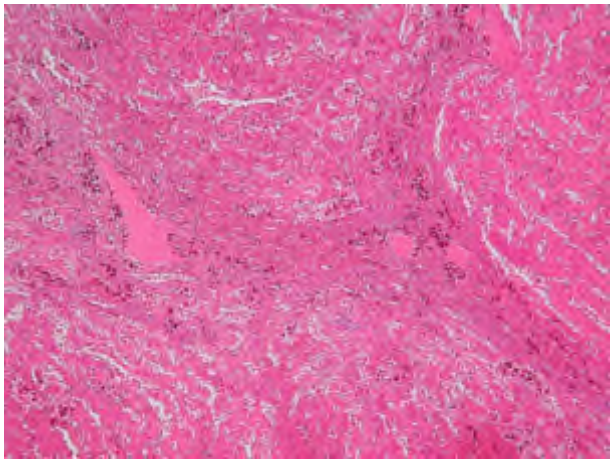

Figure 1.

Clinically the patients may show metastatic disease (liver, abdominal masses, brain) at time of diagnosis or relapse.[1,2,8] The etiology of LCA remains unclear and an immune mechanism has been hypothesized.[1,3] In our case the patient was heavily pre-treated with immunosuppressive agents (ATG, CsA) and anabolic steroids for severe aplastic anemia. We suggest that the development of LCA may be related to treatment with ATG, CsA and anabolic steroids, although the association might be coincidental.

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