

Absent Splenic Uptake of Indium-111-Oxine-Labeled Autologous Leukocytes in Functional Asplenia

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An incidental finding of absent splenic uptake of autologous, indium-111-oxine-labeled leukocytes in an immunosuppressed renal transplant recipient was documented to be associated with functional asplenia based on absence of technetium-99m-sulfur colloid clearance by a morphologically normal spleen. The patient had recently suffered an episode of disseminated varicella infection that might have led to the development of functional asplenia.

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Functional asplenia is characterized by failure of a morphologically normal spleen to remove colloidal material from the blood and the presence of Howell-Jolly bodies in red blood cells indicating splenic dysfunction (1,2). This condition is typically associated with sickle cell anemia (1) but has been described in other conditions including graft-versus-host disease (3-5), systemic lupus erythematosus (6,7), sarcoidosis (8), various immunologic malignancies (9-11), and amyloidosis (12). We report a case of apparent functional asplenia which was identified as an incidental finding on an indium-111-leukocyte scan.

CASE REPORT

A 39-yr-old white male with a history of renal transplantation 5 yr earlier presented for investigation of low-grade fevers. The renal transplantation had been performed for end-stage renal failure associated with chronic glomerulonephritis and complicated by secondary hyperparathyroidism. He had been chronically immunosuppressed with prednisone and cyclosporine. At the time of admission, the prednisone dose was 10 mg per day and the cyclosporine dose was 120 mg per day. The patient had not received anti-lymphocyte globulin for over 3 mo. Two months before the current admission he had developed fulminant hepatitis secondary to documented dis-

seminated varicella zoster infection. Although initially considered for liver transplantation, he showed excellent recovery in hepatic function following treatment with acyclovir.

The patient had been discharged ten days before he presented with a five-day history of intermittent fevers of 100-102°F. There were no localizing symptoms or signs to suggest a source. He was no longer jaundiced. Biochemical analysis of serum electrolytes showed evidence of mild renal impairment with a urea of 31 mg/dl (normal 7-21) and a creatinine of 1.9 mg/dl (normal 0.8-1.4). There was ongoing evidence of hepatocellular damage with markedly elevated gamma glutamyl-transferase levels at 427 IU/l (normal 10-70 IU/l) and serum transaminase levels which were more than twice normal (AST 102 IU/l and ALT 105 IU/l with normal ranges up to 35 and 45 IU/l, respectively). Urine microscopy and culture were normal. Examination of the peripheral blood revealed a reduced red blood cell count at 2.66 million per cubic millimeter (normal 4.6-6.2), a normal leukocyte count at 8.7 thousand per cubic millimeter (normal 4.0-10.0), and the presence of Howell-Jolly bodies. No sickle cells were identified.

Computed tomography scanning of the pelvis showed a fluid collection in the pelvic portion of the right psoas muscle adjacent to the renal transplant, which was believed likely to represent either an abscess or a lymphocele. CT-guided aspiration of this collection yielded clear, straw colored fluid which was sterile on bacterial and fungal culture. Despite drainage of the collection, the patient continued to spike fevers and an ¹¹¹In-oxine leukocyte scan was ordered to assess alternative septic foci.

Autologous leukocytes were labeled with 500 μCi of ¹¹¹In-oxine using a method similar to that originally described by Thakur et al. (13). Whole-body imaging was performed 24 hr later (Fig. 1). A linear area of increased uptake in the right thigh corresponding in position to the superficial femoral vein and a serpiginous focus in the right calf were felt to be compatible with visualization of a deep venous thrombosis, possibly reflecting the inflammatory response to acute thrombosis or direct incorporation of inadvertently radiolabeled platelets in the clot. On direct questioning, the patient recalled having intermittent aching discomfort in the right leg for the preceding 10-14 days. In view of the history of renal transplantation and mildly impaired renal function, ultrasound examination of the lower extremity venous system was recommended. This procedure confirmed deep venous thrombosis which was subsequently shown, on ventilation-perfusion

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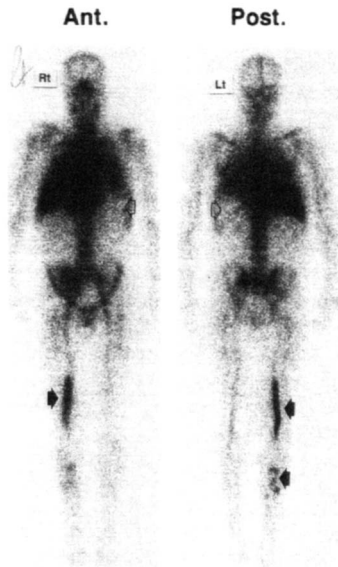


FIGURE 1
Absent splenic accumulation was noted (open arrow) in anterior and posterior whole-body scintigraphy performed 24 hr after i.v. administration of 500 μ Ci of ^{111}In -labeled autologous leukocytes. There was also focally increased accumulation of activity in the right thigh and calf (solid arrows) in a distribution suggestive of deep venous thrombosis. This diagnosis was subsequently confirmed on ultrasound.

lung scanning and pulmonary angiography, to be complicated by pulmonary embolism.

The absence of splenic uptake of radiolabeled leukocytes and a relative increase in pulmonary uptake compared with that normally seen at 24 hr were thought likely to represent impaired leukocyte or splenic function. To evaluate splenic function further, 5 mCi of $^{99\text{m}}\text{Tc}$ -sulfur colloid were administered intravenously and absent splenic uptake was demonstrated (Fig. 2). An abdominal CT scan performed 3 days earlier had documented the presence of the spleen (Fig. 3). The presence of the spleen was also confirmed by ultrasound 5 days after the autologous leukocyte and liver-spleen scan.

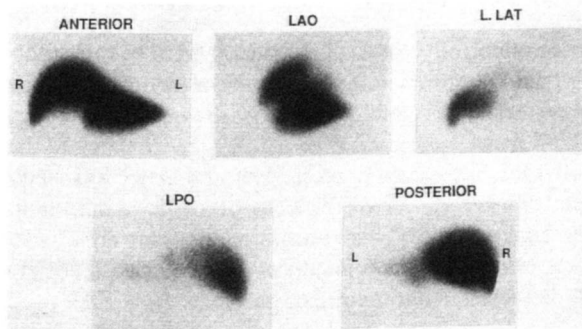


FIGURE 2
Absent splenic extraction of tracer was demonstrated after i.v. administration of 5 mCi of $^{99\text{m}}\text{Tc}$ -sulfur colloid. Abdominal scintigraphy was performed in the anterior, left anterior oblique (LAO), left lateral (L. LAT), left posterior oblique (LPO), and posterior projections.

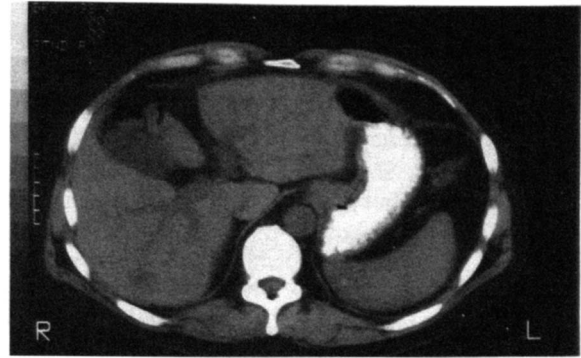


FIGURE 3
Computed tomography performed 3 days before the leukocyte scan revealed a spleen of normal size and attenuation. There were no stigmata of splenic infarction. Intravenous contrast was withheld secondary to the history of renal transplantation and mildly impaired renal function.

Neither CT or ultrasound demonstrated any structural abnormality in the spleen.

DISCUSSION

The combination of Howell-Jolly bodies in peripheral red blood cells, a normal spleen on CT and ultrasound (Fig. 3), and absent clearance of $^{99\text{m}}\text{Tc}$ -sulfur colloid by the spleen (Fig. 2) strongly support the diagnosis of functional asplenia in this patient. Absent splenic accumulation of autologous, ^{111}In -oxine labeled leukocytes in association with functional asplenia was documented.

The functional asplenia in this patient might have been a sequel to his recent disseminated varicella infection. There have been two previous reports of functional asplenia developing in association with this infection, although both were described in children (14,15). The postulated mechanism for the development of functional asplenia in these cases was splenic infarction secondary to disseminated intravascular coagulation (15). However, there was no clinical evidence of splenic infarction in our patient in that he gave no history of recent abdominal pain and the spleen was not tender. The concomitant liver disease in this patient may be relevant since reversible, functional asplenia has also been described in chronic aggressive hepatitis (16). Other cases of functional asplenia in association with transplantation and immunosuppression have been related to graft-versus-host disease in patients with hematologic malignancies and do not appear to be directly related to the use of steroids or cyclosporine (3-5). Consequently, it seems unlikely that the functional asplenia observed in our patient was related to medications that the patient was receiving. An additional possible cause of decreased or absent splenic sequestration of leukocytes, idiopathic persistent leukocytosis, also appears unlikely in view of the normal white cell count in this patient (17).

The spleen has diverse physiologic functions that may be pathologically impaired (18). These differing types of dysfunction may be uniquely characterized by a combination of radioisotopic tracer techniques. For example, a previous report of functional asplenia in association with Sezary syndrome documented absent ^{99m}Tc -tin colloid but preserved ^{99m}Tc -sulfur colloid and ^{111}In -radiolabeled leukocyte uptake in the spleen (19). Similarly, Wagman and Dworkin recently described preserved sequestration of ^{99m}Tc -radiolabeled, heat-damaged red blood cells in a patient with functional asplenia diagnosed on the basis of Howell-Jolly bodies on peripheral smear and absent splenic sulfur colloid uptake (20). A significant proportion of the total leukocyte pool is normally resident in the spleen, representing sequestration of circulating leukocytes by capillaries and adherence to endothelial surfaces (21). Our case suggests that this important splenic function may be impaired in patients with peripheral blood smear features indicative of splenic dysfunction and that this impairment can be identified by the use of ^{111}In -oxine-labeled autologous leukocytes.

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