Negative effect of intravenous immunoglobulin administration on the scintiscans to identify accessory spleen in an idiopathic thrombocytopenic purpura patient

To the Editor: Idiopathic thrombocytopenic purpura (ITP) is a common autoimmune disease characterized by thrombocytopenia caused by autoantibodies that opsonize platelets, resulting in their destruction by phagocytes, principally in the spleen [1-2]. Life-threatening hemorrhages have been reported to occur in 1% to 5% of patients with severe thrombocytopenia [2]. In adult patients, splenectomy is the gold standard therapeutic option for those who fail to respond to 4-6 weeks of medical treatment with steroids or other pharmaceuticals. A subgroup of patients that initially responded to splenectomy will have residual accessory splenic tissue discoverable at relapse [3-4]. Intravenous immunoglobulin (IVIG) is currently used to treat ITP [5].

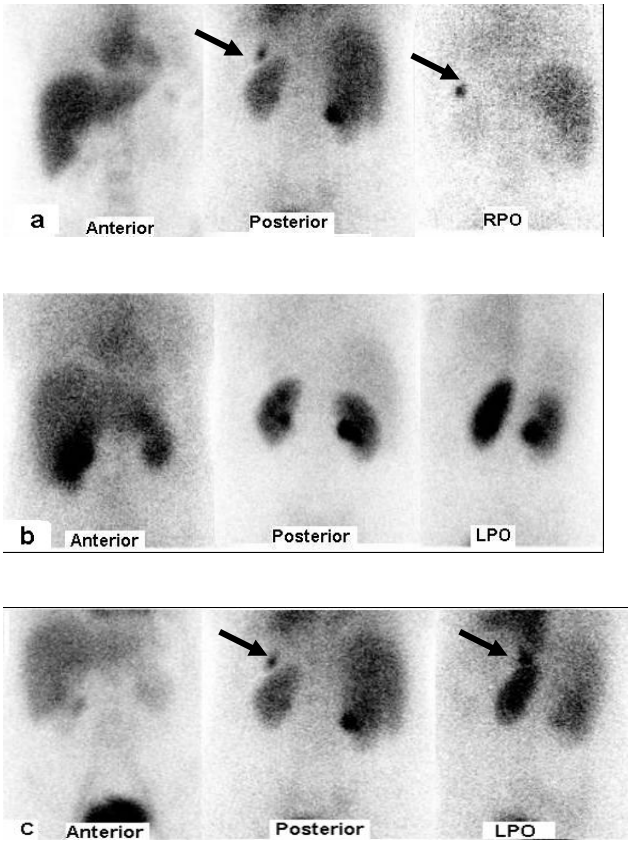

Figure 1. Accessory spleen was localized preoperatively (a). At the day of the operation control scintigraphy did not visualized any focus of uptake (b). After IVIG administration was stopped for 3 days, the accessory spleen was demonstrated again at the same area (c).

A 28 years old female patient with ITP was referred to our clinic with generalized ecchymosis, epistaxis and gingival bleeding and thrombocytopenia despite medical treatment. She had splenectomy 5 years ago. Abdominal magnetic resonance imaging revealed a 12mm in diameter accessory spleen in the upper left quadrant coherent, which was confirmed by technetium-99m labeled heat-denatured red blood cells (^{99m} Tc-HRBC) scintigraphy (Fig.1a). In our clinic we use the in vivo, in vitro technique. We administer intravenously the stannous pyrophosphate in a 3mL isotonic saline and 30min later we collect a blood sample of 3mL in a syringe containing an anticoagulant and the ^{99m}Tc-HRBC pertechnetate in a dose of 740MBq. This syringe is shielded and then is gently rotated to mix allowed to incubate at room temperature for 20min and is later incubated in a mixture water bath for 15min at 49.5±0.5°C degrees. The labeled sample was administered when cooled at room temperature [6-7]. Accessory splenectomy with the guidance of intraoperative gamma probe was planned. Thrombocytes were preoperatively $18x10^9$/L. After intravenously administering immunoglobulin (IVIG) in a dose of 400 mg/kg per day for 3 days thrombocytes increased to $295x10^9$ /L. At the day of the operation, control scintigraphy with ^{99m} Tc-HRBC did not visualize any focus of uptake due to IVIG (Fig.1b). After stopping the IVIG administration for 3 days, another ^{99m}Tc-HRBC scan which showed the accessory spleen (Fig.1c). With the guidance of a handheld gamma probe, the accessory spleen was identified and removed for months during the follow-up period thrombocytes remained normal.

The ^{99m} Tc-HRBC scintigraphy has been demonstrated to be an accurate method for identifying accessory spleens [6-7]. Intravenous immunoglobulin is currently used to treat a multitude of autoimmune disorders including ITP. Although the exact mechanism of action of IVIG in ITP remains unknown it is suggested that increases the expression of an inhibitory receptor; Fc receptor IIB thus blocking the clearance of opsonized platelets [5-9]. Cells of the reticuloendothelial system of the spleen possess large numbers of Fc receptor (FccR)-bearing phagocytic cells which can bind and destroy opsonized platelets.

The non-visualization of the accessory spleen in the ^{99m} Tc-HRBC scintigraphy after IVIG administration is possibly due to prolonged in vivo clearance of radiolabeled, antibody-sensitized RBC [9, 11].

In conclusion, it is important to intermit administration of IVIG for 3 days in order to prevent non-visualization of accessory spleen in the ^{99m} Tc-HRBC scintigraphy.

Bibliography

1. Martin Stangel M, Pul R. Basic principles of intravenous immunoglobulin (IVIg) treatment *J Neurol* 2006; 253 [Suppl 5]: V/18–V/24.
2. Bierling P, Godeau B. Intravenous Immunoglobulin for Autoimmune Thrombocytopenic Purpura. *Human Immunology* 2005; 66: 387-94.
3. Choi YU, Dominguez EP, Sherman V et al. Laparoscopic Accessory Splenectomy for Recurrent Idiopathic Thrombocytopenic Purpura *JSLS* 2008; 12: 314-7.
4. Stanek A, Stefaniak T, Makarewicz W et al. Accessory spleens: preoperative diagnostics limitations and operational strategy in laparoscopic approach to splenectomy in idiopathic thrombocytopenic purpura patients. Langenbecks *Arch Surg* 2005; 390: 47-51.
5. Crow AR, Song S, Siragam V et al. Mechanisms of action of intravenous immunoglobulin in the treatment of

immune thrombocytopenia. *Pediatr Blood Cancer* 2006; 15: 47(5 Suppl): 710-3.
6. Pohlson EC, Wilkinson RW, Witzum KF et al. Heat-damaged red cell scan for intraoperative localization of the accessory spleen. *J Pediatr Surg* 1994; 29: 604-8.
7. Phom H, Kumar A, Tripathi M et al. Comparative evaluation of Tc-99m-heat-denatured RBC and Tc-99m-anti-D IgG opsonized RBC spleen planar and SPECT scintigraphy in the detection of accessory spleen in postsplenectomy patients with chronic idiopathic thrombocytopenic purpura. *Clin Nucl Med* 2004; 29: 403-9.
8. Crow AR, Lazarus AH. The mechanisms of action of intravenous immunoglobulin and polyclonal anti-d immunoglobulin in the amelioration of immune thrombocytopenic purpura: what do we really know? *Transfus Med Rev* 2008; 22: 103-16.
9. Fehr J, Hofmann V, Kappeler U. Transient reversal of thrombocytopenia in idiopathic thrombocytopenic purpura by high-dose intravenous gamma globulin. *N Engl J Med* 1982; 306: 1254-8.
10. Lazarus AH, Crow AR. Mechanism of action of IVIG and anti-D in ITP. *Transfus Apher Sci*. 2003; 28: 249-55.
11. Cooper N. Intravenous immunoglobulin and anti-RhD therapy in the management of immune thrombocytopenia. Hematol Oncol Clin North Am 2009; 23: 1317-27.

Muge Oner Tamam MD, Mehmet Mülazimoğlu MD, Hatice Sumeyye Yavuz MD, Nurcan Edis Med Phys, Serafettin Hacimahmutoglu MD, Tevfik Ozpacaci MD.

Department of Nuclear Medicine, Okmeydani Training and Research Hospital, Istanbul, Turkey

Muge Oner Tamam MD
Okmeydani Training and Research Hospital, Kagithane, Istanbul, 34400 Turkey,
Tel:+90 212 2217777
E-Mail: mugetamam@yahoo.com

Hell J Nucl Med 2010; 13(2): 175-176