ARQGA/1271

EFFECT OF ESOPHAGOGASTRIC DEVASCULARIZATION WITH SPLENECTOMY ON SCHISTOSSOMAL PORTAL HYPERTENSION PATIENTS' IMMUNITY

Fabio Gonçalves **FERREIRA**[1], Wilma Carvalho Neves **FORTE**[2], José Cesar **ASSEF**[1] and Armando **De CAPUA Jr.**[1]

ABSTRACT – ***Background -*** Surgical treatment of hemorrhagic complication in schistosomal portal hypertension in our hospital is an esophagogastric devascularization procedure with splenectomy. Infectious risks and immunological alterations imputed to splenectomy may have significant importance. To minimize the consequences of spleen absence, the use of subtotal splenectomy and spleen auto-transplantation were stimulated. ***Aim -*** To verify the immunologic alterations imposed by this procedure in our patients. ***Method -*** Twenty-eight patients with schistosomal portal hypertension and previous history of upper digestive bleeding due to esophagogastric varices rupture underwent elective esophagogastric devascularization and splenectomy. They were prospectively studied before esophagogastric devascularization procedure with splenectomy, 15 and 30 days, 3 and 6 months after the procedure. T and B-lymphocytes, CD4 and CD8 subpopulations were determinated by monoclonal antibodies. Immunoglobulins A, M, G and C3, C4 components of the complement were determinated by radial immunodiffusion. ***Results -*** We observed important reduction of all immune cells, increase of IgG and normal levels of IgM, IgA, C3 and C4 at preoperative. CD4/CD8 relation was normal. Six months after esophagogastric devascularization procedure with splenectomy, significant increase in T-lymphocytes, CD4, CD8 and B-lymphocytes were observed. CD4/CD8 relation remained normal. We noted significant increase in C3. IgA, IgM, IgG and C4 had increased, but without significant difference. ***Conclusion -*** Esophagogastric devascularization procedure with splenectomy determines an increase in T and B-lymphocytes, CD4 and CD8 subpopulations without compromising immunoglobulins and components of complement levels.

HEADINGS – Schistosomiasis mansoni. Hypertension, portal. Azygos vein, surgery. Splenectomy.

INTRODUCTION

Schistosomiasis is one of the ancient diseases of man: eggs have been recovered from Egyptian and Chinese mummies several thousand years old[26]. At the middle of the 19th century with the description of the Katayama syndrome (Fuji 1847) and by Theodor Bilharz (1852) who confirmed the presence of the worm known today as *Schistosoma hematobium* in mesenteric vessels of an autopsied Egyptian peasant, the disease called schistosomiasis started to be studied. In 1902, Manson found eggs with lateral spine, in patients from Antilles, admitting a new species of *Schistosoma*, which was classified as *S. mansoni*, by Sambon, in 1907[42].

According to the World Health Organization, schistosomiasis affects more than 200 million individuals distributed in 76 countries in Africa, Asia or America. Among these, 10% present the severe form of disease and 50% to 60% of infected people, that is more than 100 million people, present clinical manifestations of the disease, constituting a huge public health problem[44]. About 3% of the infected with the hepatosplenic form, over 100,000 patients, could be affected by schistosomal portal hypertension and may suffer rupture of esophagogastric varices[17].

Portal hypertension surgery has evolved widely in the last decades. Since the first surgical shunt was done in 1945 for the treatment of recurrent hemorrhage,

[1] Liver and Portal Hypertension Unit, Surgery Department and [2]Immunology Section, Santa Casa Medical School and Hospital, São Paulo, SP, Brasil. Correspondence: Dr. Fabio Gonçalves Ferreira - Rua Apinagés, 1060 – apt.93 - 05017-000 – São Paulo, SP, Brasil. E-mail: drfabioferreira@gmail.com

many surgical options have been developed including selective shunts, low diameter shunts and extensive devascularization procedures[28].

The authors only indicate surgical treatment in patients with hemorrhage antecedent in schistosomal portal hypertension. The preferred is an esophagogastric devascularization procedure with splenectomy (EGDS), based on Degni & Lemos-Torres procedure[10] standardized by De CAPUA Jr.[9].

In the past years, in low-risk (Child-Pugh classification A) schistosomal selected patients, our preference for EGDS is based in low rebleeding rate (11% to 15%), absence of postoperative encephalopathy and low operative mortality, 2.7% to 11.4% in rebleeding patients[1, 7, 12, 16, 27, 32, 33, 39, 43]. Rebleeding before EGDS has a benign course in most times, with some therapeutic aspects[2, 3, 38].

Including splenectomy, infectious risks and immunological alterations imputed to this procedure may have significant importance. So that, to minimize the consequences of spleen absence, the use of subtotal splenectomy and spleen auto-transplantation was stimulated[4, 5, 6, 15, 18, 22, 23, 25, 31, 34, 35, 41, 45].

Absence of the spleen predisposes individuals to risk of overwhelming infection of about 0.5% to 25%, with mortality rate from 50% to 80%. These infections are most often due to encapsulated organisms, especially *Pneumococcus*, *Haemophilus influenzae* type b, and *Meningococcus*, but any bacterial agent may cause the rapid onset of septicemia, meningitis, pneumonia, and shock characteristic of the asplenic condition. The risk is greatest in infants and young children, but asplenic adults also have an increased risk of infection. Prophylactic antibiotics and immunization with polyvalent *Pneumococcal*, *H. influenzae* type b, and *Meningococcal* vaccines have reduced the incidence of infections in asplenic individuals, but even these measures have not eliminated the risk. Therapies designed to interrupt the cascade of overwhelming sepsis have not yet been successful[13, 19, 23, 30, 37].

Since 1985, we had performed at minimum 250 EGDS in "Santa Casa" Medical School, Surgery Department, São Paulo, SP, Brazil. No cases of overwhelming postsplenectomy infection occurred, instead of the expressive number of patients treated and no routine immunization performed.

The aim of this study was to verify if there are significant immunologic alterations imposed by esophagogastric devascularization with splenectomy performed in the treatment of patients with hemorrhage antecedent in schistosomal portal hypertension.

METHOD

Twenty-eight patients with previous bleeding portal hypertension due to schistosomiasis were treated by elective esophagogastric devascularization procedure with splenectomy (EGDS) between June 2000 and March 2003 at "Santa Casa" Medical School, Surgery Department, Liver and Portal Hypertension Group.

Seventeen were male (60.7%) and 11 female (39.3%). They aged 39.6 years (17-57 years), and most where Caucasians (85.7%) with only four black patients.

They were examined and submitted to laboratorial examinations: three stool examinations (Kato-Katz method), and when negative, a rectal biopsy.

Abdominal ultrasonography, digestive endoscopy, functional hepatic tests, serology for viral detection (HCB and HCV) was done and, when clinical and laboratorial findings suggested another etiology, a transparietal hepatic biopsy was performed.

All patients had confirmed esophagogastric varices, normal liver function (Child-Pugh A), negative serology for viral hepatitis, absence of portal vein thrombosis and confirmed schistosomiasis diagnosis.

The main criteria used for surgical indication was digestive hemorrhage due to gastroesophageal varices rupture. Patients were submitted to the following surgical procedure: esophagogastric devascularization with splenectomy[10]. None of them received any routine immunization.

Blood samples were obtained, after patient's authorization and allowed by Committee of Ethics in Research in Human Beings of our Institution, at five moments: in the morning of the surgery, postoperative 15 days, 30 days, 3 months and 6 months.

The samples had been directed to our Laboratory of Immunology for accomplishment of the immunological examinations:

- counting of T and B-lymphocytes, $CD4^+$ and $CD8^+$ cells, using monoclonal antibodies anti-CD3, anti-CD19, anti-CD4 and anti-CD8 respectively. Separation of the lymphocytes obtained by gradient of Ficoll-Hypaque density. After the separation, incubation of the cells with the corresponding and conjugated monoclonal antibody. The fluorescent cells had been counted between two hundred cells, and absolute values had been obtained by analysis of the leucogram.
- Dosage of immunoglobulins IgG, IgA, IgM and C3 and C4 components of the complement by simple radial immunodiffusion[21].

Friedman's test was used to foresee significant statistical difference, and *t* Student's test to identify possible differences in the five moments of our study. When $P < 0.05$ we established significant statistical difference.

Patients were followed for 6 months and we had observed no major infectious complications.

RESULTS

Our data had shown important reduction of all immune cells at the preoperative, but the CD4/CD8 relation was normal.

Immunoglobulins A, M, complements C3 and C4 had normal values, only IgG had increased levels (Table 1).

After EGDS, significant increase of all immune cells was noted at the first moment studied (PO 15). These counts decreased after 30 days, but at 6 months, they had normal values (Figure 1). The CD4/CD8 relation remained normal.

Statistical analysis show these significant increase in T-lymphocytes ($P = 0.006$), CD4 ($P = 0.007$), CD8 ($P = 0.001$) and B-lymphocytes ($P = 0.004$) observed after 6 months of EGDS, in comparison to preoperative levels.

TABLE 1. Distribution of immunity parameters' average, at five different moments, of 28 schistosomic portal hypertension patients submitted to EGDS

Immunity parameters	Preoperative	Postoperative 15 days	Postoperative 30 days	Postoperative 3 months	Postoperative 6 months
T-LYMPHOCYTES[a]	739.35±363,0	2145.35±909,1	2224.37±1571,9	1913.07±889,5	1758.41±1222.0
CD4+[a]	429.42±199.76	1269.81±586.10	1267.68±859.18	1099.53±536.43	1044.38±728.26
CD8+[a]	229.31±155.48	873.27± 384.83	909.16±595.70	785.13±418.82	746.00±547.21
CD4+/CD8+	1.47±0.26	1.46±0.23	1.45±0.38	1.45±0.28	1.44±0.31
B-LYMPHOCYTES[a]	174.46±89.89	495.42±243.22	506.53±280.85	406.80±206.66	403.69±263.83
IgA [b]	309.50±162.70	398.24±158.09	365.95±123.32	376.33±144.98	373.50±155.86
IgM [b]	160.98±76.14	160.77±62.14	190.29±70.21	176.91±75.33	178.02±76.23
IgG [b]	2023.58±851.90	2265.81±881.77	2238.42±882.02	2013.87±513.14	2197.06±751.40
C3 [b]	131.48±59.28	186.83±73.68	161.94±57.00	154.11± 45.10	166.98±52.58
C4 [b]	34.04±17.75	42.60±47.63	34.83±12.11	27.43±6.16	27.71±8.06

[a] absolute numbers/mL
[b] mg/dL

We noted that IgA, IgM, IgG and C4 had increased, but without significant difference. Only C3 (P = 0.042) had significantly increased after 6 months (Figures 2, 3).

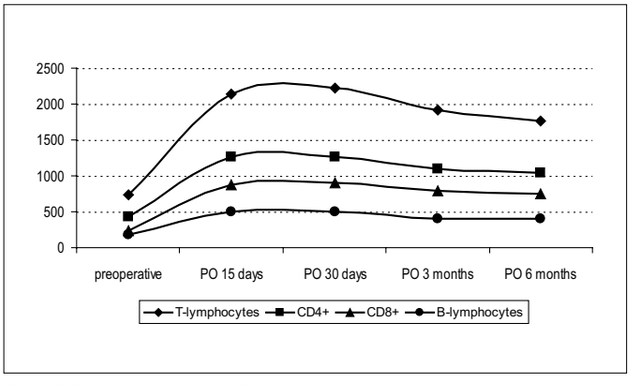

FIGURE 1. Lymphocytes/mL, at five different moments, of 28 schistosomic portal hypertension patients submitted to EGDS

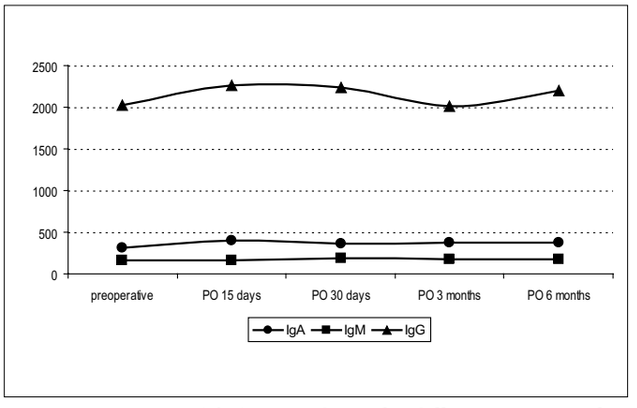

FIGURE 2. Immunoglobulins (mg/dL), at five different moments, of 28 schistosomic portal hypertension patients submitted to EGDS

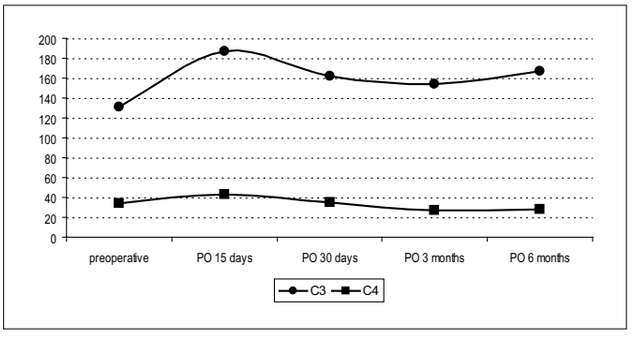

FIGURE 3. Complement (mg/dL), at five different moments, of 28 schistosomic portal hypertension patients submitted to EGDS

DISCUSSION

The immunology of schistosomiasis is largely dependent on the biological characteristics of the parasite itself. After skin penetration, schistosomula undergo a complex migratory life cycle in the vertebrate host before they settle, in the case of *S. mansoni*, in the blood vessels of the portal and mesenteric system. This continuous release of soluble antigens has important implications in the regulation of the immune response, both in terms of antigenic competition and as direct factors of immunodepression or tolerance.

The persistence of the trematodes in an immunological hostile environment has been attributed to their ability to acquire or synthesize, during their maturation, surface antigenic determinants (host antigens) to which the animal is unresponsive. The worm tegument, which undergoes a continuous and rapid turnover, acquires numerous host molecules ranging from various serum proteins or glycolipid to major histocompatibility antigens. This phenomenon has been considered as an essential escape mechanism "to be deceptive" to the immunologic system of the host allowing its survival until occurs reproduction[8, 36].

In the beginning of the infection for *S. mansoni* all the individuals have the capacity to develop and to express strong immunological reaction against antigens of the parasite, in all the phases of its life cycle. Later,

the majority of the sick people modulate this reply through a variety of immunological down regulating mechanisms[5, 24, 29]. It is controversy whether the spleen of the patient with portal hypertension should be preserved: some authors are favorable and others had created methods to preserve de spleen tissue, such as subtotal splenectomy and splenic auto transplantation.

The favorable indications for total splenectomy include the partial reduction of portal pressure, improving the indices of rebleeding, when associated to azigoportal disconnection, laboratorial correction of the hypersplenism, removal of the great spleen mass, and the correction of the values of the hormone of the growth in reply to the stimulations of hipoglicemia, promoting the somatic growth in children and adolescents[3, 9, 10, 40]. On the other hand, adverse arguments to the total splenectomy in schistosomiasis are those imputed to the splenectomy in general, where if its indication mix all, mainly hematological and trauma. In these cases the risk of development of complications infectious, between them the development of overwhelming postsplenectomy infection is increased and well registered in literature.

DREW et al.[11] observed after splenectomy for trauma decrease in serical IgM and complement pathway levels.

CAMUS et al.[8] had shown that the splenectomy does not modify the high levels of IgG in the hepatosplenic form, and observed improvement of the immunodepression after splenectomy. HOOD and BOROS[14] had demonstrated that the removal of the spleen and for consequence, the majority of T-suppressors lymphocytes, increases the granulomatous reply to eggs of the parasite in rats.

MA et al.[20] observed in advanced form of schistosomiasis that splenectomy, besides reducing the pressure of system, improves the functions of cellular immunity, what can increase the resistance against pathogens.

Concordant results had been found in this study. We have show the positive correction in cells of the immunity caused by splenectomy in our patients and we can say that after 6 months of EGDS, the values of cellular immunity are significant greater that in preoperative.

On the other hand, IgM is pointed in literature as factor of immunodepression due to its diminution after splenectomy. We show that the average of its value remains normal after 6 months. IgG remained steady, practically without variation and IgA, important in mucosal defense increase in the end of the study, however without significant results. The components of the complement had revealed equal or higher in the postoperative, levels of C3 significantly higher after 6 months and C4 discrete diminished, but without statistics significance. Thus, we can say that after EGDS was not observed damage detected in humoral immunity and complement.

Therefore, the schistosomal patients in hepatosplenic form do not seem to be more susceptible to infection in the postoperative, as the splenectomized for other indications. The techniques of

Ferreira FG, Forte WCN, Assef JC, De Capua Jr. A. Efeito da cirurgia de desconexão ázigo-portal com esplenectomia na imunidade de doentes com hipertensão portal esquistossomótica. Arq Gastroenterol. 2007;44(1):44-8.

RESUMO – *Racional* - A cirurgia de desconexão ázigo-portal com esplenectomia é utilizada no tratamento da complicação hemorrágica varicosa dos esquistossomóticos hepatoesplênicos com hipertensão do sistema portal, no Serviço de Fígado e Hipertensão Portal da Santa Casa de São Paulo. Envolvendo a esplenectomia, os riscos infecciosos e alterações imunológicas imputados a ela têm importância significativa. A esplenectomia subtotal e o auto-implante esplênico foram alternativas descritas para minimizar as conseqüências da esplenectomia nesses doentes. ***Objetivo*** - Avaliar o estado imunológico dos esquistossomóticos hepatoesplênicos e qual a alteração imunológica imposta pelo procedimento nesses doentes. **Método** - Vinte e oito esquistossomóticos com hipertensão portal e episódio hemorrágico varicoso foram estudados prospectivamente antes, 15 e 30 dias e 3 e 6 meses após a desconexão ázigo-portal com esplenectomia. Realizou-se contagem de linfócitos T, B, células $CD4^+$ e $CD8^+$ através de anticorpos monoclonais e dosagem das imunoglobulinas A, M, G e frações C3 e C4 do sistema complemento por imunodifusão radial. ***Resultados*** - Obteve-se diminuição importante de todas as células, aumento de IgG e níveis normais de IgM, IgA, C3 e C4 no pré-operatório. A relação $CD4^+/CD8^+$ foi normal. Seis meses após a cirurgia, houve aumento significativo do número de linfócitos T, $CD4^+$, $CD8^+$ e linfócitos B. A relação $CD4^+/CD8^+$ manteve-se normal, sem variação. Houve aumento significativo nos níveis de C3. IgA, IgM, IgG e C4 também aumentaram, mas sem diferença significativa. ***Conclusão*** - Os linfócitos T, suas subpopulações $CD4^+$ e $CD8^+$, e os linfócitos B estão diminuídos no pré-operatório. Decorridos 6 meses da desconexão ázigo-portal com esplenectomia houve aumento do número de linfócitos T, das subpopulações $CD4^+$ e $CD8^+$, e dos linfócitos B. Após a desconexão ázigo-portal com esplenectomia não houve alteração das dosagens de imunoglobulinas nem diminuição do sistema complemento.

DESCRITORES – Esquistossomose mansoni. Hipertensão portal. Veia ázigos, cirurgia. Esplenectomia.

REFERENCES

1. Assef JC. Recidiva hemorrágica após operações não descompressivas para tratamento de hemorragia digestiva alta em esquistossomóticos [dissertação]. São Paulo. Faculdade de Ciências Médicas da Santa Casa de São Paulo; 1992.
2. Assef JC. Tratamento da recidiva hemorrágica por varizes de esôfago, após operações não descompressivas, em doentes com hipertensão portal esquistossomótica [tese]. São Paulo: Faculdade de Ciências Médicas da Santa Casa de São Paulo; 1999.
3. Assef JC, De Capua Jr A, Szutan LA. Treatment of recurrent hemorrhagic esophageal varices in schistosomotic patients after surgery. Rev Assoc Med Bras. 2003;49:406-12.
4. Bader-Meunier B, Gauthier F, Archambaud F, Cynober T, Mielot F, Dommergues JP, Warszawski J, Mohandas N, Tchernia G. Long-term evaluation of the beneficial effect of subtotal splenectomy for management of hereditary spherocytosis. Blood. 2001;97:399-403.
5. Brandt CT, Araújo LB, Barbosa CM. Auto transplantation of spleen tissue in children with mansonic schistosomiasis who underwent splenectomy: evaluation of splenic residual functions. Acta Cir Bras. 1998;13:212-6.
6. Brandt CT, Leite CRC, Caneca OAF, Castro CMMB, Araújo LB. Auto transplant of spleen tissue in children with schistosomiasis: evaluation of splenic function after splenosis. Mem Inst Oswaldo Cruz. 2001;96:117-22.
7. Carneiro JLA, Mies S, Raia S. A circulação colateral gastroesofágica após desconexão ázigo-portal: portografia trans-hepática na esquistossomose mansônica. Rev Col Bras Cir. 1983;10:191-202.
8. Camus D, Zalis MG, Vannier-Santos MA, Banic DM. The art of parasite survival. Braz J Med Biol Res. 1995;28:399-413.
9. De Capua Jr. A Desconexões ázigo-portais. In: Colégio Brasileiro de Cirurgiões. Aspectos técnicos na cirurgia do aparelho digestivo. São Paulo: Robe; 1991. p.185-8.
10. Degni M. Rational basis of a new technique for the treatment of portal hypertension: Lemos Torres-Degni technique. Bull Soc Int Chir. 1963;22:3-8.
11. Drew PA, Kiroff GK, Ferrante A, Cohen RC. Alterations in immunoglobulin synthesis by peripheral blood mononuclear cells from splenectomized patients with and without splenic regrowth. J Immunol. 1984;132:191-6.
12. Ferraz AA, Lopes EP, Barros FM, Sette MJ, Arruda SM, Ferraz EM. Splenectomy plus left gastric vein ligature and devascularization of the great curvature of the stomach in the treatment of hepatosplenic schistosomiasis. Postoperative endoscopic sclerosis is necessary? Arq Gastroenterol. 2001;38:84-8.
13. Hansen K, Singer DB. Asplenic-hyposplenic overwhelming sepsis: postsplenectomy sepsis revisited. Pediatr Dev Pathol. 2001;4:105-21.
14. Hood AT, Boros DL. The effect of splenectomy on the pathophysiology and egg-specific immune response of *Schistosoma mansoni*-infected mice. Am J Trop Med Hyg. 1980;29:586-91.
15. Jiang HC, Sun B, Qiao HQ, Xu J, Piao DX, Yin H. Clinical application of serial operations with preserving spleen. World J Gastroenterol. 2001;7:876-9.
16. Kelner S. Critical evaluation of schistosomiasis portal hypertension surgery. Mem Inst Oswaldo Cruz. 1992;87:357-68.
17. Kelner S, Ferreira PR, Dantas A, Lima Filho JFC, Souza AP, Carreiro Jr JCP, Ferraz EM, Silveira M, Coelho ARB, Câmara Neto, RD, Domingues LAW. Ligadura de varizes esôfago-gástricas na hipertensão porta esquistossomótica: avaliação de 25 anos. Rev Col Bras Cir. 1982;9:140-6.
18. Kamel R, Abbas MM, Metwally DM, Ezzat AG, El-Azzazi H, Saleh WA. Assessment of splenic functions in patients with hepatosplenic schistosomiasis using non-invasive techniques. J Egypt Soc Parasitol. 1999;29:203-13.
19. Krivit W, Giebink GS, Leonard A. Overwhelming postsplenectomy infection. Surg Clin North Am. 1979;59:223-33.
20. Ma BY, Gui X, Yang ZC, Xiong Y, Wang HC, Wang ZB. Effect of splenectomy on disorder of cellular immunoregulation in patients with advanced schistosomiasis. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi. 1993;11:288-90.
21. Mancini G, Carbonara AO, Heremans JF. Immunochemical quantization of antigens by single radial immunodiffusion. Immunochemistry. 1965;2:235-54.
22. Marques RG, Petroianu A, Coelho JM, Portela MC. Regeneration of splenic auto transplants. Ann Hematol. 2002;81:622-6.
23. Marques RG, Petroianu A. Overwhelming postsplenectomy infection. Arq Gastroenterol. 2003;40:47-54.
24. Martins-Filho AO, Cunha-Melo JR, Lambertucci JR, Silveira MAS, Colley DG, Gazzinelli G, Correa-Oliveira R. Clinical forms of human *Schistosoma mansoni* infection are associated with differential activation of T-cell subsets and co stimulatory molecules. Dig Dis Sci. 1999;44:570-7.
25. Miko I, Brath E, Nemeth N, Toth FF, Sipka S, Kovacs J, Sipka Jr.S, Fachet J, Furka A, Furka I, Zhong R. Hematological, hemorheological, immunological, and morphological studies of spleen auto transplantation in mice: preliminary results. Microsurgery .2003;23:483-8.
26. Nunn JF, Tapp E. Tropical diseases in ancient Egypt. Trans R Soc Trop Med Hyg. 2000;94:147-53.
27. Orozco H, Mercado MA. The evolution of portal hypertension surgery: lessons from 1000 operations and 50 years' experience. Arch Surg. 2000;135:1389-93.
28. Orozco H, Mercado MA, Chan C, Ramos-Gallard G, Galvez-Trevino R, Salgado-Nesme N, Cisneros De-ajuria R, Anthon FJ. Current role of surgery for the treatment of portal hypertension. Ann Hepatol. 2002;1:175-8.
29. Pancre V, Delacre M, Herno J, Auriault C. Schistosomal egg antigen-responsive CD8 T-cell population in *Schistosoma mansoni*-infected BALB/c mice. Immunology. 1999;98:525-34.
30. Peitzman AB, Ford HR, Harbrecht BG, Potoka DA, Townsend RN. Injury to the spleen. Curr Probl Surg. 2001;38:925-1008.
31. Petroianu A, Silva RG, Simal CJR, Carvalho DG, Silva RAP. Late postoperative follow-up of patients submitted to subtotal splenectomy. Am Surg. 1997;63:735-40.
32. Pugliese V. Desconexão ázigo-portal e esplenectomia associadas à escleroterapia endoscópica no tratamento das varizes do esôfago na esquistossomose hepatoesplênica: avaliação de parâmetros clínicos, laboratoriais e hemodinâmicos portais [tese]. São Paulo: Faculdade de Medicina da Universidade de São Paulo; 1996.
33. Raia S, Mies S, Macedo AL. Surgical treatment of portal hypertension in schistosomiasis. World J Surg. 1984;8:738-52.
34. Resende V, Petroianu A. Functions of the splenic remnant after subtotal splenectomy for treatment of severe splenic injuries. Rev Assoc Med Bras. 2002;48:26-31.
35. Resende V, Petroianu A. Functions of the splenic remnant after subtotal splenectomy for treatment of severe splenic injuries. Am J Surg. 2003;185:311-5.
36. Riffkin M, Seow H, Jackson D, Brown L, Wood P. Defense against the immune barrage: helminth survival strategies. Immunol Cell Biol. 1996;74:564-74.
37. Rose AT, Newman MI, Debelak J, Pinson CW, Morris Jr. JA, Harley DD, Chapman WC. The incidence of splenectomy is decreasing: lessons learned from trauma experience. Am Surgeon. 2000;66:481-6.
38. Sakai P, Boaventura S, Ishioka S, Mies S, Sette H Jr, Pinotti HW. Sclerotherapy of bleeding esophageal varices in schistosomiasis. Comparative study in patients with and without previous surgery for portal hypertension. Endoscopy. 1990;22:5-7.
39. Silva LC, Strauss E, Gayotto LCC, Mies S, Macedo AL, Silva AT, Silva EF, Lacet CMC, Antonelli RH, Fermanian J, Fosters S, Raia A, Raia S. A randomized trial for the study of the elective surgical treatment of portal hypertension in mansonic schistosomiasis. Ann Surg. 1986;204:148-53.
40. Silveira M, Kelner S, Silveira RK. Tratamento cirúrgico emergencial em varizes esofagogástricas sangrantes por esquistossomose: esplenectomia com ligadura da veia gástrica esquerda. In: Rocha JW, editor. Hemorragia digestiva alta: diagnóstico e tratamento. São Paulo: Atheneu; 2003. p.225-45. (Clínica Brasileira de Cirurgia. Colégio Brasileiro de Cirurgiões, ano 8, volume 1).
41. Smith E, De Young NJ, Drew PA. Decreased phagocytic capacity of auto transplanted splenic tissue. Aust N Z J Surg. 2003;73:894-6.
42. Sturrock RF. Schistosomiasis epidemiology and control: how did we get here and where should we go? Mem Inst Oswaldo Cruz. 2001;96 Suppl:17-27.
43. Szutan LA. Resultados imediatos e tardios da esplenectomia e desvascularização esofagogástrica no tratamento da hemorragia digestiva alta em esquistossomóticos [tese]. São Paulo: Faculdade de Ciências Médicas da Santa Casa de São Paulo; 1993.
44. World Health Organization. The control of schistosomiasis. Report of the WHO expert committee. Geneva: WHO; 1993. (Technical report series 830). 86p.
45. Zhang H, Chen J, Kaiser GM, Mapudengo O, Zhang J, Exton MS, Song E. The value of partial splenic auto transplantation in patients with portal hypertension: a prospective randomized study. Arch Surg. 2002;137:89-93.

Recebido em 17/2/2006.
Aprovado em 18/7/2006.