Prevention of infection in patients with an absent or dysfunctional spleen

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Abstract

An impairment of all spleen functions is a matter of course in both congenital asplenia and asplenia caused by an injury to the spleen. There also exists a group of diseases which result in asplenia or functional hyposplenia. Absence or dysfunction of the spleen brings a higher risk of life-threatening infection. Preventive procedures for patients with congenital, acquired or functional asplenia involve three basic types of activity: vaccinations, chemoprophylaxis, and educating patients, their parents and medical personnel. In this paper we present recommendations for prevention of life-threatening infections in this group of patients.

Key words: *asplenia, immunization, prevention.*

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Introduction

The role of a healthy spleen is to filter blood and remove damaging elements from it. It also contains the largest set of immunocompetent cells that participate in antigen presentation, i.e. macrophages, reticular cells and plasmocytes. The free flow of blood through the spleen facilitates antigen presentation, antibody and cytokine production, as well as phagocytosis of opsonized bacteria [1]. Impairment of all spleen functions is a matter of course in both congenital asplenia and asplenia caused by an injury to the spleen. There also exists a group of diseases resulted in asplenia or functional hyposplenia (table 1) and the marker of this dysfunction is the presence of Howell-Jolly bodies in over 3.5% erythrocytes.

There are no exact data concerning splenectomies performed in Poland, but based on available literature it could be estimated that only one in three such surgeries at the most was necessitated by an injury [2]. The development of medical research into the role of the spleen in immunology has forced many centers to attempt saving surgeries, partial splenectomies and even autotransplantation of fragments of the removed spleen [3]. Absence or dysfunction of the spleen brings about a higher risk of life-threatening infection. The first report of septicemia involving a splenectomized patient was presented by O'Donell in 1929 [4]. The life-threatening infection in asplenic patients may have a mild course at the very beginning, resembling flu, but in several hours' time the patient's condition deteriorates dramatically and septicemia, cerebrospinal meningitis, and their complications develop [5]. It has been found that the risk of death from generalized infection is on average 50 times higher for asplenic individuals than for healthy individuals, but it also depends on the patient's age and the cause of spleen dysfunction. Children are more susceptible to infection than adults, and the risk of death is highest in the first two years after splenectomy [6]. Children with hemoglobinopathies and congenital spherocytosis are the most edangered by infection (their risk of infection is as much as 350 times greater than that of healthy individuals) [7]. Splenectomy forced by an injury carries a lower risk. According to the American Academy of Pediatrics (2000), 30% of registered generalized infections occurred during the first year after splenectomy, and 50% during the first two post-splenectomy years [8]. There are, however, reports on life-threatening infections occurring even as far as 20 years after splenectomy [6].

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Generalized infections can be caused by many microorganisms; however, for individuals with spleen dysfunctions, those induced by polysaccharide bacteria are especially dangerous. The most frequent pathogens for these patients are as follows: *Streptococcus pneumoniae*, *Haemophilus influenzae type b*, *Neisseria meningitidis* and *Escherichia coli* [2]. Infections caused by *Staphylococcus*, *Streptococcus*, *Salmonella* are also possible. Moreover, there have been reports of life-threatening infections in asplenic patients induced by a cat or a dog bite and consequent infection with *Capnocytophagus canimorsus* [9].

Preventive procedures for patients with congenital, acquired or functional asplenia involve three basic types of activity: vaccinations, chemoprophylaxis and educating patients, their parents and medical personnel. In clinical practice, preventive procedures for patients with spleen dysfunction depend on the mode of performed splenectomy. If splenectomy is performed as a matter of urgency, it should be accompanied by an antibiotic prophylaxis, and in case of infants, chemoprophylaxis ought to be given during the first year of life.

However, vaccinations still remain the basic element of prevention against polysaccharide bacterial infections. The first dosage of vaccine against *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria meningitidis* should be given, depending on the source, 7, 14 or 28 days after the surgery. We suggest that vaccinations should be administered 14 days after splenectomy [10].

If splenectomy is planned in advance, the optimal procedure would be to carry out the obligatory immunization schedule as well as vaccinations against polysaccharide bacteria and flu beforehand. When this is impossible, at least the first doses of vaccine against capsular pathogens should be given 14 days before the operation. Some authors report a positive, protective effect of these vaccinations even when administered 72 hours before the planned surgery [11].

Vaccinations

Whether the surgery was a planned one or performed in emergency, the essential role of protective vaccinations requires working out an individual program of vaccinations adapted to the patient's age and their history of previous inoculations.

Neither congenital asplenia nor having undergone splenectomy is a contraindication against vaccinations performed within the routine vaccination schedule [10]. A yearly flu vaccination is recommended to lower the risk of secondary bacterial infection [11]. The only vaccine that should not be given to this group of patients is the BCG vaccine, apart from the cases involving a high risk of tuberculosis. There are also few reports of chickenpox inoculations [12].

The basic vaccination against *Haemophilus influenzae type b* is given to patients with spleen dysfunction according to the manufacturer's instructions, taking into consideration the patient's age. In case of adults and children over one year of age the basic inoculation includes a single dose of conjugate vaccine. There are no clear-cut recommendations as to administering booster vaccinations 3 (children under 10) or 5 years (over 10 years of age) after the last vaccination [12, 13]. The decision should be taken with regard to the patient's state of health and level of immunization.

Table 1. Medical conditions that may be associated with spleen dysfunction

congenital	– isolated congenital asplenia – congenital cyanotic heart disease
blood cancers	– chronic leukemia – acute leukemia – myeloproliferative syndrome – lymphoproliferative syndrome: lymphoma – other: histiocytosis
hematologic	– sickle cell disease – primary thrombocythemia – hemoglobinopathies (thalassemia) – Fanconi's syndrome – malignant histiocytosis
gastrointestinal	– celiac disease with or without dermatitis herpetiformis – inflammatory bowel disease (especially ulcerative colitis) – intestinal lymphangiectasia – chronic active hepatitis
autoimmune	– vasculitis – systemic lupus erythematosus – rheumatoid arthritis – Sjøgren's syndrome – Graves disease
miscellaneous	– HIV infection – graft-versus-host disease – bone marrow transplantation – total parenteral nutrition – high dose steroid therapy – Hodgkin's disease

Since introduction of *Haemophilus influenzae type b* conjugate immunization, pneumococci and meningococci have become the two most common causes of bacterial septicaemia in asplenic individuals. The number of doses of *Neisseria meningitidis* vaccine in infancy is determined by the manufacturers' recommendations. Asplenic patients travelling to areas with higher risk of meningococcal infections require special treatment; in their case an additional immunization with polysaccharide vaccines against A and C serotypes is necessary [12, 14]. Recommendations regarding immunization against *Haemophilus influenzae type b* and *Neisseria meningitidis* infections are presented in table 2.

The recommended schedule of vaccinations against *Streptococcus pneumoniae* for patients with asplenia or spleen dysfunction is more complex. Two types of vaccine

Table 2. Immunization against *Haemophilus influenzae type b* and *Neisseria meningitidis* in children with asplenia

Age at examination	Immunization against *Haemophilus influenzae type b*		Immunization against *Neisseria meningitidis* C	
	primary	booster	primary	booster
2-6 months	3 doses in 4-6 weeks interval (according to recommendations of manufacturer) 1 dose at age 16-18 months	1 dose 3-5 years after the most recent dose	2 or 3 doses in 8 weeks interval (according recommendations of manufacturer)	1 dose 3-5 years after the most recent dose
7-12 months	2 doses in 4-6 weeks interval (according to recommendations of manufacturer) 1 dose at age 16-18 months	1 dose 3-5 years after the most recent dose		
1-10 years	1 dose	1 dose 3-5 years after the first dose	1 dose	1 dose 3-5 years after the first dose
>10 years	1 dose	1 dose 5 years after the first dose	1 dose	1 dose 5 years after the first dose

are used for immunization: the 7-valent conjugate vaccine given since the second month of life, and the polysaccharide vaccine against 23 serotypes of *Streptococcus pneumoniae*, available to patients above 2 years of age. Detailed principles concerning the use of the conjugate vaccine in risk groups have been published as recommendations of the Polish Working Group for Invasive Pneumococcal Disease (table 3) [15]. Immunoprophylaxis of pneumococcal infections from the third to the fifth year of life depends on the history of previous vaccinations and the individual vaccination program for those children should be prepared in Immunization Advisory Clinics. The Polish Working Group for Invasive Pneumococcal Disease recommends that in case of adults and children over 5 years of age from the risk group, including those with spleen dysfunction, a single dose of pneumococcal conjugate vaccine should be administered, and 6-8 weeks after that, a single dose of polysaccharide vaccine [15]. A suggested schedule of inoculations against *Streptococcus pneumoniae* for asplenic children is presented in table 3.

A paper published in 2006 presented the effectiveness of conjugate vaccine immunization schedules that differed from schedules recommended by the manufacturer. In infancy, two or three doses ensured nearly 100% protection, and a single dose in children above 12 months of age – almost 95%. The authors did not find any impact of other coexisting illnesses on the effectiveness of vaccinations against *Streptococcus pneumoniae* [16].

Chemoprophylaxis

Canadian recommendations concerning chemoprophylaxis of bacterial infection for patients with asplenia/spleen dysfunction are based on one, well-planned research study among children under 3 years of age with sickle cell anemia [17]. Chemoprophylaxis is recommended until the fifth year of age, regardless of immunization level, and for older children and adults for a year after splenectomy [18]. American Academy of Pediatrics also recommends chemoprophylaxis until the age of 5 [8]. British sources present the need of a long-term use of antibiotics for all patients during the first two years after splenectomy, for all affected children under 16, as well as for patients with primary and secondary immune deficiencies [11].

Polish patterns of using chemoprophylaxis for patients with congenital and acquired asplenia are often based on the experience of the Immunology Clinic and Department at the Children's Memorial Health Institute in Warsaw. The experience shows that regardless of the causes of asplenia all affected infants should undergo chemoprophylaxis during the first year of life. After the second year of life, the decision on long-term use of chemoprophylaxis ought

Table 3. Immunization against *Streptococcus pneumoniae* in asplenia or spleen dysfunction [15]

Age at examination	Immunization history	PCV7	PPV23	Booster immunizations
2-6 months	0 doses	3 doses in 4-8 weeks interval 1 dose at age 12-15 months	1 dose at age 24 months	1 dose PPV23 3-5 years after last dose of PPV
7-11 months	0 doses	2 doses in 6-8 weeks interval 1 dose at age 12-15 months	1 dose at age 24 months	
12-23 months	0 doses	2 doses in 6-8 weeks interval	1 dose at age 24 months 8 weeks after last dose of PCV7	
24-59 months	0 doses	2 doses in 6-8 weeks interval	1 dose at age 24 months 8 weeks after last dose of PCV7	
	4 doses PCV		1 dose at age 24 months 6-8 weeks after last dose of PCV7	
	1-3 doses PCV	1 dose	1 dose 6-8 weeks after last dose of PCV7	
	1 dose PPV	2 doses in 6-8 weeks interval 6-8 weeks after first dose of PPV		
5-18 years	0 doses	1 dose PCV	1 dose 6-8 weeks after PCV7 dose	
older then 18 years	0 doses	1 dose PCV	1 dose 6-8 weeks after PCV7 dose	

to be consulted with a specialist and based on individual recommendations that take the cause of asplenia, potential immune deficiency and the patient's medical history into account. Frequent infections are a clinical indication for long-term antibiotic therapy for asplenic patients; low antibody titer against polysaccharide antigens may be a serological indication.

The antibiotic recommended in prophylactic treatment is the orally administered penicillin or amoxicillin (table 4). In cases of hypersensitivity to antibiotics from this group, cotrimoxasol and macrolides can be used, but increasing resistance of pneumococci to these antibiotics poses a certain problem.

The available literature does not include descriptions of studies confirming the effectiveness of chemoprophylaxis for adult patients with asplenia. The decision to start such therapy ought to be carefully considered, as long-term antibiotic treatment is troublesome, and mistakes may lead to mycotic complications and selection of resistant strains.

Table 4. Suggested prophylaxis in splenectomized patients

Age	Antibiotic
birth to 5 years	– Amoxycillin 20 mg/kg/day – Ospen 2 × 250.000 j (1/2 tabl. a 500.000 j) – V-cylin 2 × 200.000 j (1/2 tabl. a 400.000 j) – Erythromycin 1 × 125 mg
children older than 5 years	– Amoxycillin 20 mg/kg/day – Ospen 2 × 500.000 j (1 tabl. a 500.000 j) – V-cylin 2 × 400.000 j (1 tabl. a 400.000 j) – Erythromycin 1 × 250 mg
adults	– Ospen 2 × 500.000 j (1 tabl. a 500.000 j) – V-cylin 2 × 400.000 j (1 tabl. a 400.000 j) – Amoxycillin 250-500 mg/day twice a day – Erythromycin 250-500 mg/day

Education

The parents of a child with asplenia/spleen dysfunction should be informed that despite chemoprophylaxis and active immunization, every elevation of body temperature may potentially be symptomatic of a rapidly developing generalized infection. All patients with asplenia or spleen dysfunction ought to have an antibiotic at hand – both at home and when travelling – and take it as soon as they notice any symptoms of infection, e.g. fever. Such patients should also wear a bracelet or carry a note with information about their disease and the need of urgent treatment of septicemia. It is a life-threatening condition, which requires immediate administration of an antibiotic effective against *S. pneumoniae*, *H. influenzae* and *N. meningitidis*. Initial antibiotic therapy should include a third-generation cephalosporin with or without vancomycin. Ceftriaxone in

doses of 100 mg/kg intravenously (IV), and in cases of hypersensitivity to beta-lactam antibiotics, clindamycin (10 mg/kg/day IV) have been recommended for use in empirical treatment [19].

The need for educational activity has been confirmed by a research project conducted in Switzerland, the results of which indicated that only 41% of asplenic patients were aware of the increased risk of infection. Only one in five patients in the study knew about the higher risk of developing an illness when travelling to tropical countries. There are no data that would confirm these observations for Poland; however, there is also no evidence that the awareness of these problems is any higher among Polish patients and their parents. The quoted study also found that only 59% of patients had undergone vaccinations before splenectomy. When asked about how to behave in case of fever, 22% of respondents answered that no special steps were necessary. Information about the dangers which asplenia involves should be disseminated among the patients and their families, not forgetting the need for continuing education of doctors.

The suggested schedule of prophylactic procedures, presented to general practicioners, pediatricians and surgeons, should help to reduce the risk of invasive diseases caused by polysaccharide bacteria in patients with congenital and acquired asplenia.

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