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Overwhelming Postsplenectomy Infection (OPSI): The Clinical Syndrome

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Summary

Critical examination of the infectious risk following splenectomy raises questions about several widely held notions. True hazard of OPSI is difficult to quantify and probably underestimated, susceptibility is life-long, questionably altered by splenosis, and persists despite penicillin prophylaxis and vaccination against common pneumococcal serotypes.

The insidious onset, fulminant course, high mortality, and lifelong hazard of overwhelming postsplenectomy infection (OPSI) is compelling evidence of the spleen's vital role in host defense. Elsewhere in this issue, pathogenesis of OPSI and prevention by spleen-sparing operations are carefully examined. Nevertheless, despite recent extensive reviews (1–3), misconceptions about this potentially lethal clinical syndrome abound, largely because incidence reports in patients are limited and incomplete. The purpose of this essay is to pinpoint the infectious hazards of splenectomy, focusing on the syndrome of OPSI and highlighting areas of current controversy and confusion.

OPSI in the "normal" asplenic host: Nature of the risk

Although a heightened risk of serious infection after splenectomy in young children and immunodeficient adults is generally well accepted, degree of susceptibility in the immunologically "non-compromised" asplenic host while crucially important remains vigorously debated (4–6). Among numerous indications for removing the spleen, traumatic rupture or iatrogenic injury during intraabdominal operations annually produces the largest asplenic patient population (4) with the most favorable life expectancy and thus the longest potential exposure to risk. By force of numbers alone, therefore, assessment of OPSI – presentation, treatment, and prevention – properly begins with the otherwise immunologically intact asplenic host.

Published experience with OPSI in previously healthy asplenic patients encompasses 34 reports of 55 episodes of infection in 52 individuals splenectomized for either external trauma or at operation and 2 with congenital asplenia (Table). These tabulations include 17 instances of OPSI in children between ages 7 and 15 years. Since the main features of host resistance (humoral, cell-mediated and monocytic-phagocytic) are fully developed by 5–6 years of age (7) these individuals may be considered immunologically "mature" at time of fulminant infection. Although this compilation undoubtedly represents only a fraction of the true incidence of OPSI, the information is sufficiently detailed and consistent to seriously question the following commonly held and often cited generalizations:

1. Most OPSI occurs within two years after removal of the spleen after which risk of infection is minimal (2): in this compiled series, fewer than 30% of infections occurred earlier than three years after splenectomy while more than 50% of fulminant infections, whether fatal or not, occurred later than five years after operation (Fig. 1). These data, highlighted by

Table Overwhelming postsplenectomy infection (OPSI) in patients without underlying disease*

Ref	S/A at Spl	Indication	Interval before sepsis	Source of positive culture	Clinical outcome	Duration (hrs) from Onset	Duration (hrs) from Admission	Other features
8	M/7	T	1 Mo	B	D			
9	M/46	T	6 Mo	B (6)	D	12	4	+Smear, DIC
10	M/10	T	7 Mo	B, CSF (22)	S	–	–	+Smear, (CSF)
11	M/35	T	8 Mo	B	D	–	24	–
12	F/71	I	8 Mo	B	D	13	4	+Smear, DIC
13	M/8	T	9 Mo	CSF	D	24	–	BAH
14	M/8	T	10 Mo	B	D	10	6	–
10	M/19	T	1 Y	B	D	30	14	+Smear, DIC
15	F/72	T	1 Y	B	D	–	–	Streptococcus
16	M/6	T	1 Y $1\frac{1}{2}$	CSF (23 & 12)	S	–	–	–
17	F/10	T	2 Y	B	D	28	7	+Smear, BAH, splenic tissue
18	M/7	T	2 Y	B	D	8	0	BAH
19	M/19	T	2 Y	CSF	D	96	96	–
4	F/18	T	2 Y	B	S	–	–	Meningococcus
20	F/5	T	3 Y	B (22)	D	22	5	+Smear, DIC, splenic tissue, BAH
21	M/4	T	3 Y	B	D	–	–	–
22	M/16	T	3 Y	B, CSF	S	–	–	BSG
23	F/16	T	3 Y	Adrenal	D	<12	0	Splenic implants
23	M/17	T	4 Y	B	D	10	$\frac{1}{2}$	Splenic implants, BAH
8	M/10	T	4 Y	B	D	–	–	Meningococcus
8	M/13	T	4 Y	B	S	–	–	H. influenzae
24	M/46	T	4 Y	B, CSF	S	–	–	–
18	F/5	I	5 Y	B	D	15	0	BAH
25	M/6	T	5 Y	B	D	–	–	–
26	F/22	T	5 Y	B, CSF (23)	S	96	72	–
8	M/6	T	5 Y	B	D	–	–	–
27	M/17	T	6 Y	B, CSF	D	72	48	DIC
28	M/16	T	6 Y	B (4)	D	–	–	BAH
15	M/42	T	6 Y	B	D	–	–	–
15	M/52	T	6 Y	B	D	–	–	–
17	M/6	T	7 Y	B	D	14	5	BAH, splenic tissue
10	F/4	T	7 Y	B	D	36	0	Splenic tissue
29	M/24	T	7 Y	B	D	120	42	–
8	F/5	T	7 Y	B	D	–	–	–
30	F/4	T	8 Y	B, CSF	D	9	0	Splenic implants
8	F/8	T	8 Y	B	S	–	–	–
30	M/10	T	9 Y	B	D	26	14	Splenic implants, DIC
31	M/19	T	10 Y	B	S	–	–	Group B streptococcus
10	M/17	T	10 Y	B, CSF	D	12	1	DIC, BAH, accessory spleen
32	F/34	I	10 Y	B, CSF (12)	D	336	312	DIC, BAH
33	M/13	T	10 Y	CSF	D	72	2	+Smear, DIC
25	M/8	T	10 Y	B	S	–	–	SBE
34	F/20	T	12 Y	B	S	–	–	DIC, BSG
35	M/20	T	13 Y	B, CSF	D	24	"few"	+Smear, DIC, BAH
36	F/22	T	14 Y	B (4)	D	21	7	+Smear, DIC
37	M/21	T	15 Y	CSF	S	–	–	H. influenzae
10	M/	C	15 Y	B, CSF	S	–	–	DIC
38	M/12	T	17 Y	B	D	26	6	+Smear, splenic implants
39	M/22	T	25 Y	B	D	30	12	DIC
36	M/11	T	28 Y	B, CSF	D	19	2	+Smear, DIC
35	F/15	T	31 Y	B	S	–	–	BSG
40	M/	C	36 Y	B (12)	S	–	–	DIC
36	M/5	T	42 Y	B	S	18	–	+Smear
9	M/?	I	(? age 53 Y)	B (6)	D	72	2	+Smear, DIC

Abbreviations see next page

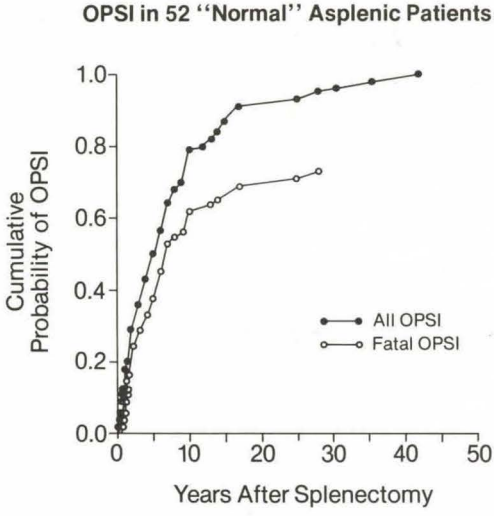

Fig. 1 Cumulative occurrence of overwhelming postsplenectomy infection (OPSI) in 52 asplenic patients without underlying disease. Contrary to common belief, risk of OPSI is by no means limited to the first five postoperative years (see Table and text for details)

an episode of OPSI 42 years after splenectomy, emphasize the lifelong nature of the infectious risk and cast serious doubt on projected risk estimates based on a mean follow-up period of only 5 years (see below).

2. The high incidence of splenosis or accessory spleens in splenectomized patients after traumatic rupture militates against OPSI (41): although autopsies were not performed in all cases, splenosis or accessory splenic tissue occurred in 10 (26%) of 39 fatal infections, roughly the same frequency at which scan-detectable splenic tissue occurs in the general population of patients splenectomized for injury (41).

3. Pneumococcal vaccination effectively protects against OPSI (42): nonpneumococcal organisms were responsible for 7 instances (13%) of OPSI, moreover, 2 of the 10 cases of pneumococcal OPSI in which the capsular serotype was determined included types absent from Pneumovax, the commercially availably polyvalent pneumococcal vaccine. Thus, even if Pneumovax affords complete protection against infection caused by pneumococci of the vaccine serotypes (probably an unwarranted assumption), protection against the full spectrum of agents responsible for OPSI falls far short of complete.

4. Penicillin prophylaxis effectively protects against OPSI (43): one patient in this series had received penicillin prophylaxis at time of infection; others sustained serious infection by organisms frequently resistant to penicillin; and in the majority, life-long penicillin prophylaxis (i.e. up to 42 years after splenectomy) would have been impractical.

5. The relative risk of OPSI may be determined by comparing rates of infection in splenectomized patients with those in an age-matched general population (44): the characteristic features of OPSI (extraordinarily fulminant course, frequent absence of a septic focus, high level of bacteremia manifested by microorganisms readily visible on peripheral blood smear, common association with Waterhouse-Friderichsen syndrome of shock, con-

Abbreviations from the Table:

B	=	Blood	M	=	Male
BAH	=	Bilateral Adrenal Hemorrhage	Mo	=	Month
BSG	=	Bilateral Symmetrical Gangrene	Ref	=	Reference
C	=	Congenital asplenia	S	=	Survived
CSF	=	Cerebrospinal Fluid	S/A	=	Sex/Age
D	=	Died	SBE	=	Subacute Bacterial Endocarditis
DIC	=	Disseminated Intravascular Coagulation	Spl	=	Splenectomy
F	=	Female	T	=	Trauma
I	=	Incidental	Y	=	Year

+Smear = Bacteria present in peripheral blood smear

Numbers in parentheses refer to pneumococcal serotype

*Adapted and expanded from Oakes, D.D., reference 3

sumption coagulopathy, adrenal hemorrhage, and high mortality), are rarely if ever encountered in immunologically normal eusplenic patients. On the other hand, figures commonly cited for comparable incidence of bloodborne infection in the general population fail to distinguish between those with and without serious associated disease – in other words, though age-matched, individuals are not disease-matched.

Accordingly, since neither the type of infections nor the status of patients are comparable, current information on the relative risk of OPSI is misleading.

These case reports further point out that infections incurred after splenectomy include not only the fulminant bacteremia characteristic of OPSI but also an unusual, lingering and resurgent bacteremia often in conjunction with meningitis (26). Although seldom fatal, resurgent infection raises the possibility that splenectomy produces not only an early blood clearance defect but also a lasting inability to eradicate bloodborne organisms.

In conclusion, the hazard of OPSI in the asplenic host who is otherwise in good health is neither easily calculated nor reliably prevented by penicillin, vaccination, or so-called "born again" spleens; moreover, infections after splenectomy may be either fulminant and rapidly fatal or fluctuating and resurgent. Finally, the risk is lifelong.

OPSI in children

Information on infection in asplenic children is both more extensive and more reliable than in splenectomized adults. Three major series include respectively all 413 Swedish children age 0–14 years splenectomized for trauma during 1968–1977 (8); 821 children representing 85% of English and Welsh children age 0–16 splenectomized for any indication during 1960–1964 (13); and a composite total of 2,795 children representing those splenectomized at Texas Children's Hospital during 1954–1970 together with reports from 23 additional series (44). Because splenectomy for trauma is uncommon in children under 5 years of age, these reports unfortunately provide little additional information on OPSI in the young but otherwise immunologically competent asplenic host.

As in adults, OPSI in young children is potentially lethal, often precipitated by encapsulated bacteria, and may develop long after splenectomy. Incidence of infection varies with age and reason for splenectomy: in general, the younger the child and more severe the underlying disease, the greater the risk of OPSI. As many as 1/5–1/2 of infants under 12 months incur serious infection after splenectomy compared with less than 1% of children over 5 years. With respect to indications for splenectomy, the risk of OPSI among children splenectomized for hereditary spherocytosis is nearly 3%, for underlying reticuloendothelial disease such as cirrhosis and portal hypertension or Gaucher's disease 10%, and for hypersplenism in thalassemia major as great as 25%.

Infection after splenectomy for Hodgkin's disease

Splenectomy has been increasingly advocated in Hodgkin's disease and selected non-Hodgkin's malignant lymphomas to assess (stage) more accurately extent of dissemination before or after treatment (45), to correct life-threatening or therapy limiting cytopenias from hypersplenism (46), and on occasion to raise peripheral blood counts and tolerance to radiotherapy (47). In these individuals, splenectomy compounds immune suppression produced by chemotherapy or irradiation. Adults (48), adolescents and children (49, 50) splenectomized for Hodgkin's disease demonstrate increased risk of sepsis and meningitis usually from S. pneumoniae or H. influenzae, and fatal infection may occur long after curative remission (51). As expected, where therapy is aggressive with combined chemotherapy and irradiation, immune impairment is greatest (52) and risk of OPSI particularly high (48–51).

Non-pneumococcal postsplenectomy infections

In most series, S. pneumoniae (pneumococcus) accounts for 50–90% of postsplenectomy in-

fections and H. influenzae the bulk of the remainder, in keeping with the spleen's known importance in clearing encapsulated organisms from the bloodstream. Less commonly, OPSI is produced by N. meningitidis, Staph. aureus, E. coli, Klebsiella, Pseudomonas, or Salmonella species. Scattered reports refer to bacterial, viral, parasitic and yet-to-be classified agents causing unusually severe infections in asplenic hosts. For example, β-hemolytic Streptococcus Group B sepsis, most commonly associated with perinatal infections, has been documented recently in two splenectomized adults (31, 53). High-grade bacteremia typical of OPSI was present in both patients, one of whom died. Similarly, though death from disseminated gonorrhaea is extremely rare, fulminant and rapidly fatal gonococcemia with adrenal hemorrhage occurred in a previously splenectomized 19-year-old (54). A gram-negative organism operationally referred to as DF-2, apparently acquired through dog bites, has also been responsible for bacteremia in adults, four of whom were splenectomized (55), raising the possibility of an association between dog bites, bacteremia, and splenectomy.

Absence of the spleen's unique pitting function may pose serious consequences for splenectomized patients contracting parasites which infect host erythrocytes. A reservoir of Babesia microti on New England coastal islands makes these destinations unsafe for vacationers lacking spleens, because human babesiosis, ordinarily a self-limited illness in the normal host, is potentially lethal in splenectomized patients (56). Transfusion-acquired quartan malaria or brucellosis may produce severe manifestations in asplenic recipients, and longstanding asymptomatic infection with quartan malaria may suddenly become activated after removal of the spleen (see Splenic Functions in Malaria).

Though experimental studies have provided no consistent evidence that splenectomy affects resistance to virus, unusually severe infections with cytomegalovirus (CMV) (57), herpes zoster (58), and influenza virus (59) have been sporadically attributed to lack of splenic tissue. Others, however, have been unable to substantiate a relation between splenectomy and frequency or severity of viral infection (60, 61).

In summary, reports of postsplenectomy sepsis caused by microbes other than encapsulated bacteria are isolated and few, and claimed association with asplenia is thus far unsupported by experimental evidence. Nonetheless, these reports serve as admonition that when the function of an organ is incompletely understood, unnecessary extirpation is unwise. As a corollary, claims that pneumococcal vaccination now permits splenectomy with impunity are equally misguided.

Preventing OPSI

Nonoperative methods to avert postsplenectomy infection include penicillin prophylaxis and polyvalent pneumococcal capsular polysaccharide vaccination. Each approach offers partial protection but carries serious drawbacks. If, as available data suggest, the hazard of OPSI is indeed lifelcng and 50% of infections develop more than 5 years after splenectomy, then penicillin prophylaxis for only two years is inappropriate and if prescribed indefinitely expensive and probably unenforceable. For these reasons and because its efficacy in preventing OPSI has not been documented in patients splenectomized for trauma, we recommend penicillin prophylaxis only for patients with greatly heightened risk of OPSI (e.g. children with thalassemia or Wiskott-Aldrich syndrome). The remainder should be advised that any acute febrile illness requires immediate medical consultation and prompt initiation of penicillin in therapeutic doses.

The proposed value of polyvalent pneumococcal vaccines in preventing OPSI is based on data in young adults (62, 63) that vaccination is highly effective in preventing pneumonia caused by pneumococci bearing vaccine-contained serotypes. Since, it is argued, the 14 vaccine serotypes are responsible for the bulk of pneumococcal infections, vaccine administration should prevent 1/2–3/4 of pneumococci-induced OPSI. Because nonpneumococcal organisms account for 10–50% of OPSI, the vaccine has theoretically been prepared to offer 25 to 65% protection against the post-

splenectomy infection syndrome. However, the accuracy of this optimistic estimate hinges on two as yet unproven assumptions: first, the vaccine boosts resistance to pneumococcus as readily in asplenic as in eusplenic hosts and second, vaccine-contained serotypes cause as great a proportion of pneumococcal infections in the asplenic as in the eusplenic host. Unfortunately, available evidence suggests that asplenic patients after capsular polysaccharide vaccination produce much less type-specific IgM and IgG antibody than do intact controls (64), and in the presence of underlying disease, especially immunosuppression, chemotherapy or radiotherapy, antibody response is further impaired (65). Similarly, underlying disease and age each lower the likelihood of vaccine-contained serotypes causing bacteremia (66) probably because impaired host resistance enhances susceptibility to relatively non-pathogenic serotypes not included in the vaccine. Discouragingly, as the risk of infection increases, the potential for vaccine-acquired protection decreases.

In summary, penicillin prophylaxis and pneumococcal vaccine offer limited protection to the asplenic host. Permanent protection resides with operative and non-operative measures that preserve or boost splenic function (see Preservation of the Spleen).

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