Risk factors of infection in neuroendovascular procedure

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ABSTRACT

Background: With the advent of neuroendovascular procedures, there has been a revolution in the management of neurovascular diseases. One of the major advantages for this minimally invasive procedure is low rate of infections, as compared to craniotomy for treatment of the diseases. However, the risk of infection in these procedures has not been reported widely in the literature. We studied the risk of infection in neuroendovascular procedures in our experience. **Materials and Methods:** We studied 256 procedures in 220 prospective patients who underwent neuroendovascular treatment from September 2006 to May 2008 at our institution. Sepsis was defined following the criteria of systemic inflammatory response syndrome plus a documented source of infection with blood cultures. **Results:** Sepsis occurred in 22 (8.6%) of the 256 procedures. Almost all of these cases were treated with antibiotics without complicating their intravascular devices infection. However, two sepsis cases of methicillin-resistant Staphylococcus aureus were intractable and took more than a month to resolve. **Conclusion:** This study emphasizes the risk of infections in endovascular procedures, and the importance of sterility in these procedures.

Key words: Infections, neuroendovascular, sepsis

INTRODUCTION

The advent of minimally invasive procedures using advanced equipment has prompted the recent popularity of neuroendovascular treatment. These procedures have an advantage due to the presumed low frequency of complicating infections. However, because neuroendovascular treatment is quite lengthy and involves the placement of foreign bodies in vessels, it may pose a heightened risk of infection. For example, we attach little importance to clean manipulations during neuroendovascular treatment compared with a craniotomy. Moreover, there are no detailed studies examining the rate of complications due to infection following neuroendovascular treatment. In this study, we examined the frequency of sepsis, the associated risk factors, and the sterility of the operating field in relation to this procedure.

Access this article online	
Quick Response Code:	Website: www.ijns.in
	DOI: 10.4103/2277-9167.110216

PATIENTS AND METHODS

Patients

We studied 256 procedures in 220 prospective patients (men: 129; women: 127; mean age: 60.2 years) who underwent neuroendovascular treatment from September 2006 to May 2008 at our facility. Repetitive procedures such as intra-arterial drug injections for vasospasm due to subarachnoid hemorrhage during short periods were regarded as one procedure. We did not distinguish transarterial approaches from transvenous approaches because an intra-arterial catheter for angiography was used in the latter. Antibiotic prophylaxis was used less frequently; however, we did use antibiotic prophylaxis for infectious patients (steroid administration, hemodialysis, cases involving cerebrospinal drainage tubes, and craniotomy).

Risk assessment

Sepsis was defined following the criteria of systemic inflammatory response syndrome plus a documented source of infection with blood cultures. Repetitive blood cultures were needed when patients developed a fever, an extreme increase of C-reactive protein, or other signs of infection within a month following neuroendovascular treatment. We excluded sepsis from other reasons such as pneumonia. For prediction of sepsis, blood cultures taken from the sheaths, catheter tip

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cultures, and palm-check cultures were examined during operation, and serodiagnoses (endotoxin, β-D glucan) were examined during postoperative days. Palm-check cultures – handprint cultures with a high detection rate of organisms – were prepared by pressing gloves onto media after operation. We regarded a surgeon and assistants in the same operating field as one sterility class, and examined one palm-check culture of the surgeon or assistant per procedure.

Although the same procedure was repeatedly performed, each procedure had subtle differences in the use of devices; therefore, we assessed associated risk factors: Patient history (diabetes mellitus, steroids, etc.,); operative particulars (operation, operation time, the location of the procedure, emergencies, and a hemorrhage or thrombus complication); device (sheath size and its retention time, the use of long guidewires, balloons, and hemostatic devices); and the sterility of the operating field (assessed by palm-check cultures) shown in Tables 1 and 2. The operation time was divided into less than 2 h, 2- −3 h, and more than 3 h. The length of time in the intensive care unit (ICU) and the intravenous drip period (<1 week, 1-2 weeks, and >2 weeks) were used to estimate the patients' condition. Surgical staff was classified by years of experience into six groups A-F (A-D; certified physicians of neuroendovascular treatment).

Statistics

Risk factors for neuroendovascular-related sepsis were evaluated by calculating the odds ratios (OR) with 95% confidence intervals (CI). Log regression analysis was performed with SAS version 3.0 PROC LOGISTIC using a stepwise procedure.

RESULTS

Sepsis occurred in 22 (8.6%) of the 256 procedures. Almost all of these cases were treated with antibiotics without complicating their intravascular devices infection. However, two sepsis cases of methicillin-resistant *Staphylococcus aureus* (MRSA) were intractable and took more than a month to resolve.

Risk factors for sepsis

We evaluated the frequency and risk factors for sepsis in 193 procedures (men: 104; women: 89) without a central venous catheter or hemodialysis, which were suspected sources of infection, using multiple regression analysis [Table 1]. Sepsis occurred in 11 (5.7%) of the 193 procedures [Table 3], and although it was most frequently observed with carotid artery stenting (CAS), the procedure was not significant to sepsis. Meningioma embolization (OR=13.25; *P*=0.04; 95% CI 1.07-163.56) without antibiotic prophylaxis was a significant source of risk [Table 4]. A large sheath size (>7 F; OR=5.03; *P*=0.01; 95% CI 1.29-19.47) was also significant. The most experienced staff A (OR= 0.09; *P*=0.05; 95% CI 0.09-0.97) was less significant to sepsis.

Risk factors for sterility of the operating field

One hundred twenty-nine (50.2%) procedures

Table 1: Risk factor for sepsis

Variables	Sepsis (*n*=22/256)		OR	*P*
	Cases (%)	Controls (%)		
Palm check positive	59.1	49.8	1.46	0.41
Sex (male)	54.5	49.4	1.23	0.64
Age (10s age classes)			1.01	0.45
Diabetes mellitus	9.1	9.8	0.92	0.92
Steroid	13.6	10.6	1.33	0.67
Central venous catheter	45.5	22.6	2.86	0.02
Preoperative antibiotic	31.8	17	2.28	0.09
Operating room				
Old interventional radiology suite	27.3	27.2	1.32	0.62
New interventional radiology suite	36.4	24.7	1.95	0.20
Clean room	36.4	48.1	1.00	
Duration of procedure				
<2 h	31.8	28.5	1.00	
2-3 h	50	41.7	0.55	0.35
>3 h	18.2	29.8	1.07	0.89
Emergency	45.5	26.8	2.28	0.07
Operation				
Carotid artery stenting	27.3	17	1.83	0.24
Embolization of cerebral aneurysm	36.4	44.7	0.71	0.45
Embolization of AVM	4.5	13.6	0.30	0.25
Percutaneous transluminal angioplasty	9.1	4.7	2.04	0.38
Embolization of cerebral tumor	9.1	5.1	1.86	0.44
Embolization of subdural hematoma	0	3	-	
Intra-arterial drug injection	13.6	11.5	1.22	0.76
Sheath size, ≧7F	45.5	23	2.79	0.02
Number of sheath, ≧2	31.8	34	0.90	0.83
Sheath retention time>1 day	45.5	25.1	2.49	0.04
Balloon	50	34.5	1.90	0.15
Long guidewire	31.8	25.1	1.39	0.49
Complication (bleeding, infarction)	13.6	5.1	2.93	0.12
Hemostatic device	50	46	1.18	0.72
Surgical staff				
A	45.5	63.4	0.48	0.10
B	40.91	45.53	0.83	0.68
C	59.09	52.34	1.32	0.55
D	31.82	46.81	0.53	0.18
E	45.45	47.66	0.92	0.84
F	31.82	20.85	1.77	0.24

AVM – Arteriovenous malformation; OR – Odds ratios

Table 2: Risk factors for unclean operating field

Palm check positive (*n*=129/256)

Variables	Cases (%)	Controls (%)	Odds ratio	*P*
Operating room				
Old interventional radiology suite	22.3	32.3	0.67	0.19
New interventional radiology suite	30	21.3	1.38	0.30
Sterile operating room	47.7	46.5	1.00	
Duration of procedure				
<2 h	27.7	29.9	1.00	
2–3 h	41.5	43.3	1.04	0.91
>3 h	30.8	26.8	1.24	0.51
Emergency	30.8	26	1.27	0.40
Operation				
Carotid artery stenting	18.5	17.3	1.08	0.81
Embolization of cerebral aneurysm	43.8	44.1	0.99	0.97
Embolization of AVM	13.1	12.6	1.04	0.91
Percutaneous transluminal angioplasty	7.7	2.4	3.44	0.07
Embolization of cerebral tumor	5.4	5.5	0.98	0.96
Embolization of subdural hematoma	0.8	4.7	0.16	0.09
Intra-arterial drug injection	9.2	14.2	0.62	0.22
Sheath size, ≧7F	28.5	21.3	1.47	0.18
Number of sheath, ≧2	34.6	33.1	1.07	0.79
Sheath retention time >1 day	30.8	22.8	1.50	0.15
Balloon	41.5	29.9	1.66	0.05
Long guidewire	26.9	24.4	1.14	0.65
Complication (bleeding, infarction)	5.4	6.3	0.85	0.76
Surgical staff				
A	66.9	56.7	1.55	0.09
B	47.7	42.5	1.23	0.41
C	48.5	57.5	0.70	0.15
D	43.8	47.2	0.87	0.58
E	46.9	48	0.96	0.86
F	27.7	15.7	2.05	0.02

AVM – Arteriovenous malformation

Table 3: Specific procedures and sepsis

Procedures		Sepsis
Embolization of cerebral aneurysm	61	2
Ruptured cases	[7]	[1]
Unruptured cases	[54]	[1]
Carotid artery stenting	45	5
Embolization of arteriovenous malformation	31	
Intra-arterial drug injection	25	1
Malignant lymphoma	[22]	[1]
Maxillary carcinoma	[3]	
Embolization of cerebral tumors	14	2
Meningioma	[12]	[2]
Maxillary carcinoma	[1]	
Hemangioblastoma	[1]	
Percutaneous transluminal angioplasty	10	1
Vasospasm due to subarachnoid hemorrhage	[1]	[1]
Chronic stenosis	[8]	
Embolization of the middle meningeal artery for subdural hematoma	7	
	Total [193]	11

tested positive in palm-check cultures [Table 2]. Less experienced staff F (OR=1.98; *P*=0.03; 95% CI 1.07-3.67) was a significant risk factor for sterility of the operating field according to simple and multiple regression analyses [Tables 2 and 4]. However, the sterility of the operating field was not associated with sepsis.

Study of organisms

The organisms for sepsis in procedures without central venous catheters or hemodialysis and the operating fields were individually analyzed [Table 5]. Coagulase-negative *Staphylococcus* (CNS) was primarily responsible for sepsis. Normal physiological floras, including CNS, were mainly found in the operating field.

Importance of antibiotic prophylaxis

Of the 19 cases receiving antibiotic prophylaxis without central venous catheters and hemodialysis, only one case of arterial injection for malignant lymphoma suffered from sepsis. On the other hand, of the 28 cases receiving antibiotic prophylaxis with central venous catheters and hemodialysis, 11 suffered from sepsis. Changing the antibiotic prescription from broad spectrum (piperacillin, cefazolin) to one (ceftriaxon, meropenem, vancomycin) that specifically targets bacteria cured most cases of sepsis. No differences between the organisms, the severity of symptoms, and the time of recovery were observed with or without antibiotic prophylaxis.

Sensitivity of the cultures and serodiagnoses

We also investigated the detection tests for sepsis. Only a few positive reactions were observed with endotoxin and β-D glucan tests. Sensitivity was low in the blood and catheter tip cultures examined during the operations. The palm-check cultures were quite sensitive (59%) but their specificity was low (<50%) [Table 6].

DISCUSSION

Endovascular treatments are minimally invasive and thus less prone to cause infection. Despite these findings, the occurrence of infection following endovascular treatments is increasing. Some reports suggest that sepsis occurs 4% of the time after angiography, whereas 32% of the time after endovascular treatments.[1,2] Endovascular treatments are typically performed in aged patients or in patients with serious conditions in an interventional radiology suite not equipped with air cleaners. Many hospitals are now performing emergent intervention procedures for acute stroke cases as well as ruptures aneurysms. In addition, surgeons seldom wash their hands although with clean gloves. Under these types of circumstances, endovascular treatments seem to pose a great risk of infection. We investigated the frequency of

Table 4: Multivariate logistic regression for sepsis

Risk factors	OR	95%CI	*P* 値
Sheath size, ≧7F	5.03	1.29-19.47	0.02
Embolization of meningioma	13.25	1.07-163.56	0.04
Surgical staff A	0.09	0.09-0.97	0.05
Multivariate logistic regression for unclean operating field			
Risk Factors	OR	95%CI	*P* 値
Surgical staff F	1.98	1.07-3.67	0.03

CI – Confidence interval; OR – Odds ratio

Table 5: Organisms

Organisms	Sepsis (*n*=11/193)	Operating field (*n*=129/256)
CNS	5	96
Micrococcus	-	42
Bacillus	-	28
Corynebacterium	1	7
Gram negative rods	-	4
MRSA	-	1
MSSA	3	-
Propionebacterium	-	-
Enterococcus faecalis	2	-
Neisseria spp	-	1
Candida albicans	-	1
Total organism	11	180

CNS – Coagulase negative *staphylococcus*; MRSA – Methicillin registant *staphylococcus aureus*; MSSA – Methicillin sensitive *staphylococcus aureus*

Table 6: The accuracy of the inspections

Type of inspection	Sensibility	Specificity
Palm check cultures	0.59	0.5
β-D glucan	0.09	1
Endotoxin	0.05	1
Blood cultures	0.14	0.97
Catheter tip cultures	0.32	0.93

sepsis following neuroendovascular treatment, the risk factors, and tests to detect sepsis early. We observed that the occurrence rate of sepsis was 8.6% in all procedures with central venous catheters and hemodialysis, which were suspected sources of infection, and 5.7% in 193 procedures without them. Our infection rate 5.7% seems to be high because of many patients in serious conditions, however we may frequently prescribe antibiotic for postoperative feverish patients in actual clinical scene.

The duration of operation, a long sheath retention time, multiple stents, local hematoma, restenting procedures, the use of multiple punctures, as well as long guidewires and hemostatic devices were all mentioned as risk factors during endovascular treatments of coronary and peripheral vessels (2-4, 9). However, in our study, the risk factors for sepsis included a large sheath size (>7 F; OR=5.03; *P* = 0.01; 95% CI 1.29-19.47) and preoperative meningioma embolization (OR=13.25; *P*=0.04; 95% CI 1.07-163.56). The degree to which experienced staff A (OR=0.09; *P*=0.05; 95% CI 0.09-0.97) affected the incidence of sepsis was less significant. We concluded that the organisms tend to invade through the large-size sheaths; although we could not prove the correlation of the complex procedures with balloons or long guidewires. Skilled staff can reduce the risk of sepsis in these types of complex procedures. As to the preoperative meningioma embolization, we expected the concern of steroid administration to reduce edema around lesion and patients' general condition which were evaluated by duration of time in the ICU and intravenous drip period; however, we could not find those factors' significances.

Because approximately half of the cultures analyzed in the operating field were positive, we believe that the operating field was not sterile. Less experienced staff F (OR=1.98; *P*=0.03; 95% CI 1.07-3.67) was a significant risk factor affecting the sterility of the operating field. Inexperienced staffs may contaminate devices. However, we could not find a correlation between the sterility of the operating field and sepsis when a strict definition is applied. It is necessary to maintain a clean operating field because the incidence of *S. aureus* is known to occur in acute infections, while CNS plays a major role in chronic infections during endovascular treatment of coronary and peripheral vessels.[3-5] Similar organisms were isolated in our study. Although we used an antibiotic prophylaxis only in several cases, we presumed it was useful especially for patients in poor general condition because most cases receiving antibiotic prophylaxis did not suffer from sepsis. However, patients with other infectious factors, such as a central venous catheter, hemodialysis, or ventricular drainage tube, tended to suffer from sepsis despite the use of antibiotic prophylaxis. Therefore, we suggest preselecting the appropriate type and course of antibiotics for these patients because they seemed to be affected by extraordinary organisms.

It may be unusual to mention other infective factors such as central venous catheters. We emphasize that sepsis cases caused intravascular device infection have poor prognoses, regardless of whether sepsis was caused by endovascular treatment or other infective factors. The reported occurrence rate of device infection is approximately 1% following the placement of coronary stents, and similarly, the occurrence rate following aortic and peripheral vessel procedures is 0.04-6%.[3,5,6] Reviewing the neurovascular treatment literature, we found five reports of complicating abscesses following coil embolization of cerebral aneurysms[7,8] and reports of stent infection following CAS.[9] However, we could not find a correlation between the placement of devices and sepsis, we presume that there are certain conditions

for device infections, such as the type of devices and a certain extent injury of vascular inner membrane which organisms can adhere to, because stent infection cases are often reported. Not only devices for lesion but also one for hemostasis such as angioseal should be taken to our consideration as another risk factor for infection nowadays. We in our institution frequently use the hemostasis device when we puncture a femoral artery to insert sheath over 7 French with systemic heparinization. Subcutaneous or wound infection has sometimes seen especially in the case of multiple punctures, in poor general condition and in pseudoaneurysm formation at puncture site. The hemostasis device contains collagen type of tissue to plug the hole of artery to stop bleeding. This collagen could be the source of infection if it is contaminated. We should pay most attention to the manipulation of hemostatic device not to be infectious.

To avoid device infection, we must diagnose sepsis early and proceed with appropriate treatment. The various cultures and serodiagnoses examined during operations were not useful as early predictors of sepsis due to their inherently low sensitivity. Palm-check cultures may support the early detection of sepsis caused by normal physiological flora because the sensitivity of these cultures was higher than those of other types of cultures examined in our study. However, it takes a few days to obtain results from palm-check cultures, so we concluded that those tests are not as useful in early detection of sepsis.

CONCLUSION

We found that the rate of sepsis following neuroendovascular treatment was quite high (5.7%) at our facility. Even majority of our septic cases turned out be clinically silent, this risk may occasionally complicate pseudoaneurysms or thrombosis with device infection, resulting in a poor prognosis. Therefore, we should maintain clean sanitary conditions and diligent manipulations in the operating field for endovascular treatment as minimally invasive modality.

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How to cite this article: Ishihara S, Ishihara H. Risk factors of infection in neuroendovascular procedure. Indian J Neurosurg 2013;2:41-5.

Source of Support: Nil, Conflict of Interest: None declared.