Original Article

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME AND POSTOPERATIVE COMPLICATIONS AFTER ORAL CANCER SURGERY

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Abstract

Systemic inflammatory response syndrome (SIRS) symptoms immediately after surgery have lately been regarded as potential warnings of impending postoperative complications and multiple organ failure. Reports discussing the relationship between operative stress and SIRS are found in the field of digestive surgery, but not in that of oral surgery. Forty oral cancer cases who had undergone neck dissection (Level III or higher) from January 1998 to June 1999 were involved in this study. We assigned 16 cases who met two of the several diagnostic criteria for SIRS and continued to meet them for at least 24 hours after surgery to the SIRS group. The other 24 patients were assigned to the non-SIRS group. Postoperative complications occurred in 56.3% of the SIRS group and 8.3% of the non-SIRS group ($p < 0.05$). In two cases, the postoperative fluctuation of IL-6 level was evaluated. These results suggest the importance of careful management of postoperative SIRS patients to prevent complications.

Key words: Systemic inflammatory response syndrome (SIRS) —
Postoperative complication — Oral cancer surgery —
Radical neck dissection — Interleukin 6

INTRODUCTION

The concept of “systemic inflammatory response syndrome” (or SIRS) was proposed at American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference⁷⁾. SIRS indicates a state of systemic inflammatory response induced by stress. More specifically, SIRS is defined as a range of symptoms that satisfies two or more conditions. In addition to infectious diseases, SIRS may be induced by various other factors,

such as injuries including surgery and burns.

Symptoms of SIRS recognized by simple criteria have lately been regarded as potential warnings of impending postoperative complications and multiple organ failure^{3,12)}. To prevent the occurrence of such conditions, Haga *et al.*³⁾ and Takasue *et al.*¹¹⁾ emphasize the clinical importance of the SIRS concept. Reports discussing the relationship between operative procedures and SIRS are found in the field of digestive surgery^{3,5,11-13)}, but not in that of oral surgery, because the incidence of multiple

Table 1 The types of neck dissection

Supraomohyoid neck dissection	21 cases (52.5%)
Modified radical neck dissection	10 cases (25.0%)
Radical neck dissection	8 cases (20.0%)
Bilateral supraomohyoid neck dissection	1 case (2.5%)
Total	40 cases (100.0%)

Table 2 SIRS diagnostic criteria

The response is manifested by two or more of following conditions:	
Temperature	<36°C or >38°C
Heart rate	>90 beats/min
Respiratory rate	>20 breaths/min or $Paco_2$ <32 torr
WBC	>12,000 cells/ μ l, <4,000 cells/ μ l or >10% immature (band) forms

Table 3 Surgical procedures and incidence of postoperative SIRS

			Rate of SIRS positive cases
Subject Neck dissection 40 cases	Neck dissection (N.D.) 12 cases	SIRS 3 cases	25.0%
		Non-SIRS 9 cases	
	N.D. and tumor resection with primary closure 7 cases	SIRS 2 cases	28.6%
		Non-SIRS 5 cases	
	N.D. and tumor resection with tongue flap or skin graft 4 cases	SIRS 2 cases	50.0%
		Non-SIRS 2 cases	
	N.D. and tumor resection with skin flap 17 cases	SIRS 9 cases	52.9%
		Non-SIRS 8 cases	

organ failure after oral surgery is believed to be low because it is less invasive than that of digestive surgery. After oral surgery, however, many complications such as pneumonia and infection occur, so we evaluated the relationship between SIRS and postoperative complications.

PATIENTS AND METHODS

From the oral cancer cases treated in our department from January 1998 to June 1999, 40 subjects (24 males, 16 females) who had undergone neck dissections (Level III or higher, Table 1) were involved to this study. Their ages ranged from 26 to 85, with an average of 61.0. The subjects' heart rates, body temperature, and white blood counts were

measured in a time series beginning immediately after surgery.

We assigned the patients who met two or more diagnostic criteria for SIRS (Table 2) within 1–7 POD, 10 POD, or 14 POD after surgery and continued for at least 24 hours to the SIRS group. The other patients were assigned to the non-SIRS group. Cases of pneumonia were defined as cases exhibiting obvious clinical signs and symptoms with clearly observable images of pneumonia in chest X-ray films and positive results in a sputum culture examination.

RESULTS

1. Surgical procedures and SIRS

Table 3 lists the surgical procedures and the

Table 4 Characteristics of SIRS group

Case number	Age	Sex	Operation procedures	Operation time (min)	Amount of bleeding (g)	Duration of SIRS (day)	Postoperative complications
1	71	F	Modified RND + hemiglossectomy (free flap)	625	954	3	pneumonia
2	62	M	SOND + marginal glossectomy, marginal mandibulectomy (tongue flap)	312	473	4	flap necrosis
3	67	F	SOND + excision of buccal mucosa (free flap)	272	604	2	
4	57	M	RND	252	224	1	
5	53	F	SOND + marginal mandibulectomy (free flap)	369	891	1	
6	60	M	RND	303	657	2	
7	37	F	Modified RND + hemiglossectomy (free flap)	530	1,205	1	
8	69	M	SOND + marginal glossectomy	212	389	3	
9	41	M	SOND + partial maxillectomy, hemimandibulectomy, hemiglossectomy (A – O plate and free flap)	920	5,967	3	pneumonia
10	58	M	Modified RND + marginal mandibulectomy (A – O plate and free flap)	690	852	1	pneumonia
11	52	F	Modified RND + hemiglossectomy (free flap)	492	722	6	wound infection
12	48	M	RND + marginal mandibulectomy (tongue flap)	330	865	3	pneumonia
13	54	F	Modified RND + marginal glossectomy (free flap)	408	1,105	1	pneumonia
14	70	F	SOND + marginal glossectomy (free flap)	320	321	1	flap necrosis
15	59	F	SOND + marginal glossectomy	240	118	1	
16	80	F	Bilateral SOND	165	88	1	wound infection

SOND : Supraomohyoid neck dissection

RND : Radical neck dissection

Modified RND : Modified radical neck dissection

incidence of SIRS. The incidence varied from 25.0% in the cases with simple neck dissection to over 50% in the cases with skin grafts; the incidence tended to rise as the scale of surgery increased.

2. Characteristics of the SIRS and non-SIRS groups

Table 4 lists the SIRS group cases, while Table 5 lists the non-SIRS group cases. The

SIRS group consisted of 16 cases (16/40 = 40.0%: 7 males, 9 females) with ages ranging from 37 to 80, averaging 59.0. The time required for surgery ranged from 2 hours 45 minutes to 15 hours 20 minutes, averaging 6 hours 42 minutes. The amount of bleeding ranged from 88 g to 5,967 g, averaging 969 g. The case highest in terms of duration of surgery and amount of bleeding was that of central adenoid cystic carcinoma (Case 9). In

Table 5 Characteristics of Non-SIRS group

Case number	Age	Sex	Operation procedures	Operation time (min)	Amount of bleeding (g)	Postoperative complications
17	59	M	SOND + hemiglossectomy	215	213	
18	62	M	SOND	120	212	
19	55	M	Modified RND + marginal glossectomy (free flap)	470	1,106	
20	57	F	SOND	255	189	
21	26	F	SOND + marginal glossectomy	300	251	
22	49	M	SOND + marginal glossectomy	240	509	
23	62	M	Modified RND + marginal glossectomy (free flap)	255	698	
24	56	M	RND	235	757	
25	67	M	SOND + excision of buccal mucosa (skin graft)	320	1,113	
26	68	M	SOND	278	525	
27	62	M	Modified RND + excision of buccal mucosa (free flap)	432	558	
28	70	M	Modified RND + segmental mandiblectomy (free flap)	520	1,802	
29	68	M	SOND	277	502	
30	83	M	RND	173	689	pneumonia
31	75	F	SOND + segmental mandiblectomy (A – O plate and free flap)	272	466	
32	68	M	RND + segmental mandiblectomy (D – P flap)	585	1,952	
33	49	F	Modified RND	210	849	
34	85	F	UND + excision of oral floor	252	242	
35	68	F	SOND + excision of buccal mucosa, marginal mandiblectomy (free flap)	242	849	
36	57	F	SOND + excision of buccal mucosa (free flap)	236	187	
37	62	M	SOND + marginal mandiblectomy	229	159	
38	67	M	RND	230	393	
39	64	M	RND	200	510	<i>Herpes zoster</i>
40	62	M	SOND + partial maxillectomy (skin graft)	333	1,210	

UND : Submandibular or submental neck dissection

SOND : Supraomohyoid neck dissection

RND : Radical neck dissection

Modified RND : Modified radical neck dissection

this case, we could not confirm the margin of tumor infiltration by diagnostic imaging, necessitating more than ten additional resections using frozen sections. This advanced case eventually required supraomohyoid neck

dissection, hemimandibulectomy, partial maxillectomy, hemiglossectomy, and reconstruction with a forearm skin flap. The duration of SIRS episodes was 1 day after operation in 8 cases (50.0%), 2 days in 2 cases (12.5%), 3

Table 6 SIRS duration and postoperative complication

SIRS duration	Incidence of complication	Mann-Whitney U test
1 day (n=8)	4/8 cases (50.0%)	n.s.
2 days or longer (n=8)	5/8 cases (62.5%)	
2 days or less (n=10)	4/10 cases (40.0%)	n.s.
3 days or longer (n=6)	5/6 cases (83.3%)	

n.s.: not significant

Table 7 Comparison between the SIRS group and non-SIRS group about age, operation time and bleeding
(M±SE)

	SIRS	Non-SIRS	Mann-Whitney U test
Age	58.63±11.32	62.54±11.74	n.s.
Operation time (min)	402.54±202.37	291.54±110.96	p<0.05
Amount of bleeding (g)	964.69±1,376.81	660.08±483.76	n.s.

n.s.: not significant

Fig. 1 Details of postoperative complications (11 cases)

days in 3 cases (18.7%), 4 days in 2 cases (12.5%), and 6 days in 1 case (6.3%). In the SIRS group, we found no differences in the duration of SIRS and the incidence of complications between patients whose SIRS duration was 1 day and patients whose SIRS duration was 2 days or longer, or between patients with a 2-day or less duration and those with a 3-day or longer duration (Table 6).

The non-SIRS group consisted of 24 cases (24/40=60.0%: 17 males, 7 females) with

ages ranging from 26 to 85, averaging 63. The duration of surgery ranged from 2 hours to 9 hours 45 minutes, averaging 4 hours 54 minutes. The amount of bleeding ranged from 159 g to 1,952 g, averaging 660 g. Based on this data, we conducted a significance test for age, duration of surgery, and amount of bleeding in both the SIRS and non-SIRS groups (Table 7). We found no significant differences between the groups in age and amount of bleeding, but the duration of sur-

Fig. 2 Levels of interleukin 6 (IL-6) in cases numbered 14 and 15

gery was significantly longer in the SIRS group than in the non-SIRS group ($p < 0.05$, Mann-Whitney U test).

3. SIRS immediately after surgery and postoperative complications

Postoperative complications arose in 11 of the 40 cases (Fig. 1); in the SIRS group, they arose in 9 of 16 cases (56.3%), and in the non-SIRS group, in 2 of 24 cases (8.3%). The incidence of complications was significantly higher in the SIRS group than in the non-SIRS group ($p < 0.05$ Mann-Whitney U test).

4. Fluctuation of IL-6 level in two SIRS patients with and without complications

Levels of interleukin 6 (IL-6) were measured in a time series in Cases 14 and 15 (Fig. 2). In Case 14, the preoperative IL-6 level was 3.2 pg/ml, increasing more than 10 times to 33.3 pg/ml on the first day after surgery. This case was diagnosed as SIRS on that day, and the next day the patient became SIRS negative. IL-6 fell to 17.3 pg/ml on POD 3, but rose again to 21.2 pg/ml on POD 5. This patient began to show skin flap necrosis on POD 5 followed by infection. In Case 15, the preoperative IL-6 level was 2.7 pg/ml, resulting in a SIRS diagnosis on the first day after surgery. The patient became SIRS negative on POD 2, with IL-6 levels at 19.7 pg/ml, which declined to 8.7 pg/ml on the next day and to 5.6 pg/ml on POD 6. This patient had no

postoperative complications.

DISCUSSION

In this paper, we evaluated the relationship between SIRS immediately after surgery and postoperative complications in oral surgery in order to prevent such postoperative complications.

The incidence of SIRS was 40.0% in our experience with oral cancer surgery. The incidence in digestive surgery is reported to be 73.0% for gastrectomy cases, 54.1% for colorectal resection cases, 37.5% for cholelithiasis surgery cases, and 67.0% for esophagectomy cases^{12,13)}. These data suggest that oral cancer surgery is not necessarily less invasive than other digestive organ surgery. The SIRS duration in patients undergoing oral cancer surgery averaged 2.2 days; an average SIRS duration of 6.9 days is reported for esophageal carcinoma surgery, and of 6.1 days for digestive organ surgery in general^{4,5)}. We found significantly a longer duration in the SIRS group, but found no significant differences between the two groups with respect to age or amount of bleeding. With respect to reconstruction techniques for local resection, the incidence of SIRS-positive cases was generally higher in cases that took longer, such as reconstruction with a free flap. Hagiwara *et al.*⁴⁾ reported significantly longer

surgical durations for esophageal carcinoma surgery cases in a SIRS group than in those who remained SIRS-free but found no significant differences between groups with respect to age, amount of bleeding, or nutritive condition.

SIRS is generally regarded as a warning sign, and some SIRS cases may eventually develop organ failure complications at a later date. One report states that 62.3% of patients placed in the ICU are SIRS patients⁵⁾. Another report argues that the diagnostic criteria for SIRS are so broad that the majority of cases will meet them¹⁾. It is important to distinguish SIRS cases, observe them carefully, obtain a good understanding of the condition, and determine which high-risk SIRS cases are likely to progress to multiple organ failure. High-risk SIRS cases may feature extended SIRS duration, many SIRS-positive criteria⁹⁾, and severity of individual aspects. Our postoperative complications included pneumonia, infection resulting from incomplete suture of incised wounds, infection resulting from necrosis of grafted tissue, and viral infectious disease probably caused by lowered immunity. The SIRS group had nine cases of complications (56.3%), while the non-SIRS group had two (8.3%). Clearly, the SIRS group showed a significantly higher incidence. For esophageal carcinoma, the incidence of complications was reported to be 31.0% in the non-SIRS group but significantly higher at 83.0% in the SIRS group⁴⁾. Despite the lower incidence of complications with oral cancer surgery than esophageal carcinoma surgery, we need to remain vigilant concerning the occurrence of complications in the SIRS group.

Organ dysfunction and multiple organ failure are reportedly likely to occur in proportion to the duration of SIRS²⁾. We found, however, no significant relationship between SIRS duration and complications. Kitamura *et al.*⁶⁾ reported that the duration of SIRS in patients recovering without complications following digestive organ surgery was 3.3 days on average, but 8.5 days in patients with multiple organ failure. The discrepancy is probably

because 50.0% of our SIRS cases involved SIRS duration of only 1 day; the longest duration was 6 days. In our experience with oral cancer surgery, we encountered no cases involving multiple organ failure. Hirasawa *et al.*⁵⁾ reported that multiple organ failure occurred in 11 (4.8%) of 231 postoperative SIRS patients among digestive organ surgery cases and that it occurred in 4 (12.9%) of 31 SIRS patients among emergency surgery cases. These data suggest that oral cancer surgery led to few severe complications because the SIRS duration following oral surgery was short, although the SIRS incidence was relatively high.

It is well known that operative stress affects endocrine function and metabolism in various ways. In addition to reactions from these nerve endocrine systems, reactions induced by cytokines following stress have recently drawn significant attention. Cytokines are now believed to play a principal role. SIRS is considered to primarily involve hypercytokine production^{5,10)}. If the body is subjected to a major operative stress, levels of inflammatory cytokines—i.e., TNF- α , IL-1 β , IL-6, and IL-8—will increase, along with near-simultaneous increases in noninflammatory cytokine such as IL-4, IL-1ra, and IL-10. Blood IL-6 is particularly easy to detect, enabling its use as an SIRS marker in many cases^{5,6,10)}. Reports have revealed that IL-6 levels are significantly elevated in the postoperative SIRS group^{5,8)}, remain high in deaths within the SIRS group^{5,8)}, and accurately reflect the scale of the surgical stress. We studied pre- and postoperative IL-6 fluctuations in two of our SIRS group cases. In the one case followed by postoperative complications, IL-6 values tended to rise more steeply than in the other case without complications, supporting the close relationship among IL-6, SIRS, and postoperative complications.

CONCLUSION

After studying SIRS immediately after surgery and postoperative complications in 40

cases subjected to oral cancer surgery with level III or higher neck dissection, we arrived at the following conclusions.

1. SIRS was observed in 40.0% of our subjects. There were no significant differences between the SIRS group and non-SIRS group with respect to age or amount of bleeding, but the duration of surgery was significantly longer in the SIRS group.

2. The number of days of SIRS duration following surgery was 1 day for 50.0% of SIRS patients, 2 days for 12.5%, 3 days for 18.7%, 4 days for 12.5%, and 6 days for 6.3%.

3. Complications occurred in 56.3% of the SIRS group and 8.3% of the non-SIRS group ($p < 0.05$).

4. Complications in the SIRS group included 5 cases of pneumonia, 2 cases of incision infection, and 2 cases of grafted tissue necrosis. Complications in the non-SIRS group included 1 case of mild pneumonia and 1 case of herpes zoster.

5. There were no significant correlations between SIRS duration and complications.

6. Pre- and postoperative fluctuation of blood IL-6 level was studied in two SIRS cases with and without postoperative complications.

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