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Original Article

Septic Pulmonary Embolism Induced by Dental Infection

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Dental infection can be an important source for septic pulmonary embolism (SPE), but only a few cases of SPE accompanying dental infection have been reported. The aim of this study was to characterize the clinical features of SPE induced by dental infection. Patients who fulfilled the diagnostic criteria described in the text were recruited in a retrospective fashion. All 9 patients were men, with a median age of 59 years (range: 47 to 74 years). Eight patients had chest pain (88.9%), 5 had a preceding toothache (55.6%) and 3 had preceding gingival swelling (33.3%). Blood cultures obtained from 7 patients were negative. Periodontitis was found in all of the cases, periapical periodontitis in 5 cases, and gingival abscess in 3 cases. The median duration of hospitalization was 15 days, and symptoms were mild in some cases. In addition to antimicrobial therapy, tooth extraction was performed in 3 cases, tooth scaling in 6. SPE induced by dental infection has prominent clinical characteristics such as male preponderance, chest pain, preceding toothache, and mild clinical course.

Key words: bacteremia, chest pain, multiple nodular shadows, periodontitis, septic pulmonary embolism

Septic pulmonary embolism (SPE) is an uncommon disease associated with septicemia due to bacterial endocarditis of the right side of the heart, suppurative processes of the head or neck or pelvic thrombophlebitis [1–3]. Recently, it has been reported that indwelling catheters and prosthetic vascular devices are also important sources of bacteremia inducing SPE [4–6]. SPE induced by dental infection is thought to be rare, and only 8 cases have been reported to date [7–13]. Recently, we identified several cases of SPE induced by dental infection. We conducted a survey of SPE induced by dental infection at our hospitals to identify the clinical characteristics of this disease including symptoms, and laboratory and radiologic findings. The purpose of this study is to identify the characteristics of this disease.

Patients and Methods

A retrospective search was conducted to identify all adults (≥16 years old) seen at Kure Kyosai Hospital or Okayama Red Cross General Hospital during a 10-year period from 1997 to 2007, with septic pulmonary embolism induced by dental infection. The study was approved by the Kure Kyosai Hospital Ethics Committee and the Okayama Red Cross General Hospital Ethics Committee.

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Diagnostic criteria. To identity SPE induced by dental infection, we created criteria for SPE induced by dental infection, based on a modification of Cook's diagnostic criteria [1], as follows: 1. Multifocal lung lesions compatible with SPE on chest CT; 2. Presence of active dental infection as an embolic source, and absence of other infectious lesions; 3. Exclusion of other potential explanations for lung infiltrates; and 4. Resolution of lung infiltrates with or without antimicrobial therapy.

Inclusion and exclusion criteria. To ensure the absence of infectious lesions other than dental infection, we included only those patients who underwent echocardiography as well as CT or ultrasonography of the abdomen. Patients with lung cancer, metastatic lung cancer, pulmonary cryptococcosis, sarcoidosis, or tuberculosis were not included in this study. Patients with possible thrombophlebitis of the lower extremities also were not included.

Data abstraction. Chart review data included demographic findings, symptoms, physical examination findings, laboratory and microbiology data, and chest and dental radiographic reports. In the analysis of the CT images, attention was paid to the size, shape, and location of the lesion, and the presence of a cavity or a pleural effusion. Dental treatments and antibiotics therapy were also reviewed.

Results

We identified 9 cases of SPE induced by dental infection between 2002 to 2007 at Kure Kyosai Hospital and Okayama Red Cross General Hospital.

Clinical characteristics. Table 1 shows the clinical characteristics of the 9 patients with a diagnosis of SPE induced by dental infection. The age of the patients ranged from 47 to 74 years with a median age of 59 years. None of the patients were immunocompromised, or had any history of medical issues that would impair immunity.

Symptoms. The presenting symptoms included fever (77.8%), chest pain (88.9%), cough (55.6%), sputum production (22.2%), and wheezing (22.2%). Five patients had a preceding toothache (55.6%). Three patients (33.3%) had preceding gingival swelling. Chest pain developed in case 9, 2 days after dental caries were filled with a restoration material. The median interval between the preceding toothache, gingival swelling or pain and the pulmonary symptoms was 13 days, ranging from 2 to 60 days (Table 2).

Laboratory data. Eight of the 9 patients demonstrated an increased white blood cell count (> 8, 000). The mean (±SD) leukocyte count was 9,569 ± 4,329/μL. The mean (±SD) serum C-reactive protein was 7.0 ± 6.4 mg/dL. Arterial blood gas analysis was performed in 5 patients. The mean (± SD) PaO_2 was 75.9 ± 7.3 mm Hg, and 3 of 5 patients showed a decreased PaO_2 (< 75 mm Hg; Table 3). Microscopic studies yielded a likely responsible pathogen in one of the cases. The pathogen was *Streptococcus intermedius*, isolated from a pleural effusion. In 7 patients studied, all had sterile blood cultures.

Chest CT. All pulmonary lesions were analyzed in the 9 cases. (Table 4) The 44 peripheral lung lesions detected by CT were classified into 3 types: peripheral nodular shadows; wedge-shaped lesions; and parenchymal infiltrates, and these types comprised 25 lesions (56.8%), 11 lesions (25.0%), and 8 lesions (18.2%), respectively. Thirty-eight lesions (86.4%) abutted the pleura. All cases in this

Table 1 Demographic Data of the 9 Patients with SPE Induced by Dental Infection

Case	Age	Sex	Smoking	Complications	Hospital stay (days)
1	52	M	S	Hypertension	7
2	74	M	NS	None	19
3	55	M	S	None	15
4	59	M	S	Hypertension, Emphysema	54
5	70	M	S	Aortic aneurysm, Bladder stone	15
6	65	M	S	Cerebral infarction	0
7	59	M	S	Hyperlipidemia	21
8	47	M	S	None	0
9	56	M	S	None	7

*NS, non smoker; S, smoker; M, male.

Table 2 Dental and pulmonary symptoms and the interval between them

Case No.	Preceding dental symptoms			Pulmonary symptoms			Interval between the 2 symptoms (days)
	Toothache	Gingival pain	Gingival swelling	Chest pain	Cough	Sputum	
1	+			+			60
2			+	+	+		Unknown
3			+	+	+		Unknown
4	+				+	+	50
5		+		+			7
6	+			+			13
7	+			+	+		50
8			+	+	+	+	5
9	+			+			2

Table 3 Blood count, serum CRP concentration, arterial blood gas and blood culture data in 9 patients

Case No.	Leukocyte (/mm^3)	Neutophil (%)	CRP (mg/dl)	PaO_2 (mmHg)	$PaCO_2$ (mmHg)	$Pa(A\text{-}a)O_2$ (mmHg)	Blood culture
1	8,000	79.8	5.5	ND	ND	ND	ND
2	9,740	84.8	6.7	ND	ND	ND	ND
3	12,220	73.2	6.5	82.4	37.0	21.3	Negative
4	15,970	78.0	22.4	68.0	36.2	36.7	Negative
5	8,590	71.2	4.9	72.9	36.3	31.7	Negative
6	8,320	77.2	4.5	ND	ND	ND	Negative
7	8,050	82.3	9.7	84.7	25.8	33.0	Negative
8	11,030	77.0	1.0	ND	ND	ND	Negative
9	4,200	46.1	1.4	71.4	41.7	21.5	Negative

*ND = not determined

Table 4 CT Findings of 44 periopheral lung lesions in 9 patients

Peripheral lesions (44)	
Shape	
Nodule	25 (56.8%)
Wedge shaped lesion	11 (25.0%)
Parenchymal infiltration	8 (18.2%)
Cavitation	7 (15.9%)
Subpleural lesion	38 (86.4%)

study had at least one pulmonary lesion abutting the pleura, a characteristic finding of SPE as reported by Iwasaki [14]. In case 6, the chest CT showed multiple nodular shadows abutting the pleura. (Fig. 1) Pleural effusion was detected in 6 cases out of 9.

Echocardiography, abdominal ultrasonography, abdominal CT, and perfusion lung scan. All 9 patients underwent echocardiography. Case 5 had thickening of th noncoronary cusp of the aortic valve. Case 6 had mild aortic and mitral valve regurgitation. Neither had valvular vegetation. No patients had findings of infective endocarditis or right ven-

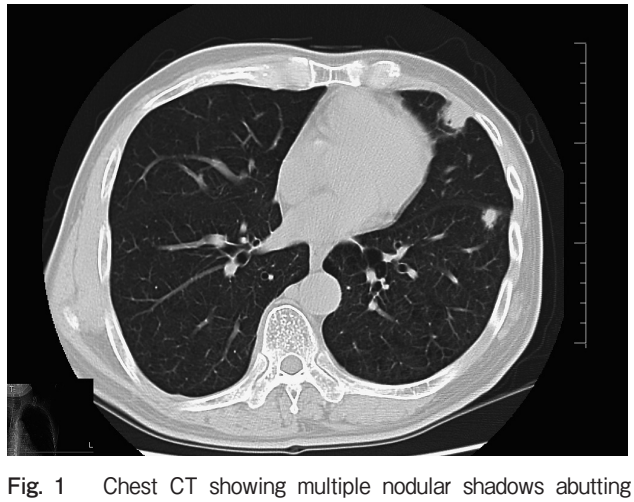

Fig. 1 Chest CT showing multiple nodular shadows abutting pleura in case 6. Scale divisions represent 1 cm each.

Table 5 Dental findings in 9 patients

Case	Present status				Dental history	
	Marginal periodontitis	Priapical periodontitis	Gingival abscess	Bone resorption	Treated tooth No.	Lost tooth No.
1	+	+		+	ND	10
2	+	+		+	6	7
3	+		+	+	20	5
4	+			+	16	5
5	+	+		+	11	20
6	+	+	+	+	1	3
7	+	+	+	+	4	20
8	+			+	ND	ND
9	+			+	7	10

ND: not determined

tricular overload. Perfusion lung scans with technetium 99m macroaggregated albumin showed areas of decreased perfusion in all 4 cases studied.

Dental findings. A panoramic radiograph of the teeth was examined in all 9 cases. Moderate to severe periodontitis was found in all cases, periapical periodontitis in 5 cases, and gingival abscess in 3 cases. The number of decayed teeth that had been already treated and the number of lost teeth at the initial presentation are shown in Table 5. Poor dental hygiene in the past for most of the patients was also found.

Treatment. Six of the 9 patients received parenteral antimicrobial therapy. Five patients were treated with imipenem/cilastatin. Clindamycin, vancomycin, or ciprofloxacin were also administered intravenously. Two of the 9 patients were treated only with oral antimicrobial therapy including clarithromycin, levofloxacin, or amoxicillin. Case 5 underwent tube thoracostomy for drainage of a large infected massive pleural effusion. All patients recovered from their illness. Seven patients required hospitalization. The median duration of hospitalization was 15 days (range, 7 to 54 days). Follow-up CT scans demonstrated improvement in all of the patients. Tooth extraction was recommended in 7 cases. Six patients underwent scaling of the teeth.

Discussion

To diagnose SPE induced by dental infection properly, we made vigorous attempts to exclude other possible infectious sources. All 9 cases underwent either abdominal ultrasonography or CT to rule out a possible infectious lesion in the abdomen. There were no symptomatic, radiographic, echographic, or laboratory findings suggestive of infectious lesions other than dental lesions, in all the cases included in this study. Therefore, we could conclude that all 9 of our cases had SPE induced by dental infection.

Several studies have shown an association between gender and periodontitis, with men having higher prevalence and severity of periodontal destruction than women [15–17]. In has been reported that infective endocarditis is associated with dental infections, and men are more often affected with infective endocarditis than women (mean male-to-female ratio, 1.7 : 1) [18]. In this study, a male preponderance of SPE induced by dental infection was also shown. Periodontitis is rare in children, but common in the middle-aged population. Advancing age is associated with diminished immune function. Abdellatif *et al.* reported that the prevalence of periodontitis increases with age up to through age group 55–59, then shows a reduction which could be explained by the greater loss of affected teeth in the older-age groups [19]. This could be the reason why SPE induced by dental infection tended to occur in a middle-aged population in this study.

The presence of a toothache prior to pulmonary symptoms was found in 5 cases (55.6%) and seems to be a characteristic feature of this disease. Although almost all patients had fever (77.8%) or chest pain (88.9%); some patients had cough (55.6%) or sputum production (22.2%). Histopathologic confirmation of the diagnosis is uncommon in clinical practice, and the

recognition of SPE relies on the presence of typical radiographic features and the exclusion of other disease processes that can mimic pulmonary embolism [1]. Therefore, we paid a great deal of attention to CT findings of SPE. The CT findings in our cases were similar to previously published findings [14, 20, 21]. Recent guidelines for infective endocarditis suggest that transthoracic echocardiography should be used in the evaluation of naive valves because it has excellent specificity for identifying vegetation (98%) [22]. Considering symptoms and laboratory findings in addition to the absence of valvular vegetation, it is unlikely that our 9 patients had infectious endocarditis causing SPE.

In a previous report, blood cultures were obtained in 4 patients with SPE induced by dental infection, and a causative organism was detected in one case [7, 8, 12, 13]. In our study, all the blood cultures were negative in the 7 cases in which blood cultures were obtained. Although negative cultures might have been associated with the administration of antimicrobial agents before blood was drawn for culture or due to an intermittent and low-load bacteremia, it seems reasonable to conclude that blood cultures tend to be negative in SPE induced by dental infection. This is in contrast to continuous bacteremia and the high frequency of positive blood cultures seen with infectious endocarditis [23]. In odontogenic infection, treatment combines mechanical debridement and/or surgery, and systemic antibiotic therapy. Debridement should be the first step in therapy because draining the infection and eliminating necrotic tissue is essential in controlling the infection. Tooth extraction also provides a drainage route and eliminates the entrance route for infection [24]. In this study, extraction of the teeth was strongly recommended in 7 cases. Without appropriate mechanical dental treatment, SPE might recur.

Odontogenic infections are polymicrobial. In the course of dental caries, the bacteria that penetrate the dental tubules are mainly facultative anaerobes, and when the pulp tissue suffers necrosis, the bacteria that advance through the pulp canal are mainly anaerobes [25]. The most common aerobic species are *Streptococci*. If the causative organism of SPE is *Streptococcus*, the antibiotic of choice is penicillin. Salinas *et al.* reported that the common use antibiotic with the greatest sensitivity and lowest resistance in odontogenic infection is amoxicillin/clavulate [26]. In this study, imipenem/cilastatin was given intravenously in most cases, and clarithromycin or levofloxacin were given orally in some cases. Penicillin was given in one case. As both aerobic and anaerobic bacteria are present in odontogenic infection, carbapenems might be better than penicillin in controlling odontogenic infection. Almost all the patients in the present study recovered quickly with antibiotic therapy.

As described before, infective endocarditis has been reported to be associated with dental disease and treatment [27-29]. Although the infectious lesions in bacterial endocarditis and septic pulmonary embolism differ, the mechanisms responsible for how the disease develops seem to be similar. Several reports indicate that bacteremia is more frequently inducible in patients with severe periodontitis than in those who have healthy periodontal tissue after dental procedures [30]. It is reasonable to speculate that dental infection could be an important source of infection in SPE as in infective endocarditis. In this series of patients, some had very mild symptoms and showed prompt recovery, which is an unusual feature of SPE.

In conclusion, SPE induced by dental infection occurs mostly in middle-aged men with acute onset of chest pain and usually is preceded by dental symptoms such as toothache or gingival swelling. Blood cultures are usually negative, and prompt recovery is common. We should pay more attention to the existence of SPE induced by dental infection, which has prominent clinical characteristics, and requires dental treatment in addition to systemic antibiotic therapy.

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