Case Report

Pericardial Effusion in Association With Periodontitis: Case Report and Review of 8 Patients in Literature

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Abstract

Periodontal diseases are well-known background for infective endocarditis. Here, we show that pericardial effusion or pericarditis might have origin also in periodontal diseases. An 86-year-old man with well-controlled hypertension and diabetes mellitus developed asymptomatic increase in pericardial effusion. Two weeks previously, he took oral new quinolone antibiotics for a week because he had painful periodontitis along a dental bridge in the mandibular teeth on the right side and presented cheek swelling. The sputum was positive for *Streptococcus* species. He was healthy and had a small volume of pericardial effusion for the previous 5 years after drug-eluting coronary stents were inserted at the left anterior descending branch 10 years previously. The differential diagnoses listed for pericardial effusion were infection including tuberculosis, autoimmune diseases, and metastatic malignancy. Thoracic to pelvic computed tomographic scan demonstrated no mass lesions, except for pericardial effusion and a small volume of pleural effusion on the left side. Fluorodeoxyglucose positron emission tomography disclosed many spotty uptakes in the pericardial effusion. The patient denied pericardiocentesis, based on his evaluation of the risk of the procedure. He was thus discharged in several days and followed at outpatient clinic. He underwent dental treatment and pericardial effusion resolved completely in a month. He was healthy in 6 years until the last follow-up at the age of 92 years. We also reviewed 8 patients with pericarditis in association with periodontal diseases in the literature to reveal that periodontal diseases would be the background for developing infective pericarditis and also mediastinitis on some occasions.

Keywords

pericardial effusion, pericarditis, periodontitis (periodontal disease), positron emission tomography, *Streptococcus*

Background

Periodontal diseases are infectious and inflammatory conditions in periodontal tissues which include gingival mucosa, periodontal ligaments, teeth, and alveolar bone. Gingivitis is used as a diagnostic term when inflammation is limited to gingival mucosa while periodontitis indicates the destruction of alveolar bone which is evident on x-ray imaging. Periodontal diseases have been recognized as associating factors and underlying factors for the development and exacerbation of systemic diseases such as cardiovascular diseases and diabetes mellitus.[1-9] Oral hygiene to control periodontal diseases is also important to reduce postoperative complications of pulmonary, cardiovascular, and gastrointestinal surgeries.[10,11] Oral health would also play a role for treatment outcome in patients with cancers and leukemia.[12]

In particular, infective endocarditis is well known as sequelae to bloodstream infection from periodontitis.[13-15] Dental treatment and periodontal procedures, indeed, lead to bacteremia.[16] In this study, we present a patient with pericardial effusion, which might be related with periodontitis. We

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also review 8 patients in the literature who developed pericarditis in association with periodontal diseases.[17-24]

Case Report

An 86-year-old man was referred to a University Hospital from a cardiologist because he showed asymptomatic increase in pericardial effusion. He was healthy and pointed out to have a small volume of pericardial effusion for the previous 5 years. He was working as an ophthalmologist 3 days a week in a local hospital. He had been taking oral medications toward essential hypertension and diabetes mellitus from his fifties. He did not smoke or drink alcohol. In the past history, he had cataract surgeries with intraocular lens implantation in both eyes at the age of 72 years. At the age of 76 years, he underwent the insertion of drug (sirolimus)-eluting coronary stents (Cypher 3.5 x 13 mm, Cordis, Cardinal Health, Dublin, Ohio) at 2 locations of the left anterior descending branch. The left ventricular ejection fraction was 69% within the normal limit at that time. At 78 years, he had 2 successive episodes of tonic clonic generalized seizure, suspected of acute disseminated encephalomyelitis, 5 days after influenza vaccination, and had no aftereffects ever since. At 82 years, he had antibiotics to eradicate gastric *Helicobacter pylori*. Two weeks before the referral visit at 86 years, he took oral new quinolone antibiotics for a week because he had painful periodontitis along a dental bridge in the mandibular premolar teeth on the right side (Figure 1A) and presented cheek swelling. He had been experiencing mild periodontitis for several years. Serum C-reactive protein (CRP) was elevated to 2.9 mg/dL 10 days before the referral. Just before the referral visit, he had fecal occult blood and underwent gastroscopic and colonoscopic examinations to detect no abnormalities except for colonic polyp at another hospital. Sputum tests detected *Streptococcus* species at 3+ level and *Candida albicans* at 1+ level, but showed no acid-fast bacilli. Serological tests for syphilis, including rapid plasma reagin test and treponemal pallidum latex agglutination, were both negative. Interferon-γ-releasing assay with T-SPOT (Oxford Immunotec, Ltd., Oxfordshire, UK) was negative as well.

On the referral visit, physical and neurological examinations detected no particular findings. The height was 158 cm and the body weight 54 kg. The blood pressure was 108/65 mm Hg and the pulse rate 65 beats per minute. He said that his best pulse rate was around 48 beats per minute. He was healthy and did not have fever, but still had mild periodontal pain on the right side. The current medications were sitagliptin 50 mg and glimepiride 0.5 mg daily for diabetes mellitus, clopidogrel 75 mg daily for the coronary stents, eplerenone 25 mg and a combined tablet of olmesartan medoxomil 10 mg and azelnidipine 8 mg daily for hypertension, and lansoprazole 15 mg as a proton pump inhibitor. A week later on admission for detailed examinations of pericardial effusion, red blood cell count was $4.54 \times 10^6/\mu L$, hemoglobin 11.6 g/dL, platelet count $331 \times 10^3/\mu L$, white blood cell count $4.56 \times 10^3/\mu L$ with differentials of 9.4% lymphocytes, 84.1% neutrophils, 5.9% monocytes, and 0.7% eosinophils. C-reactive protein which was elevated to 6.7 mg/dL a week before the admission was decreased to 1.17 mg/dL. Brain natriuretic peptide (BNP) was mildly elevated to 47.7 pg/mL. Fasting blood glucose was 111 mg/dL, and hemoglobin A1c was 7.3%. Liver and kidney functions were within normal limits. Serum sodium was low at 127 mmol/L and chloride low at 95 mmol/L. Serum total cholesterol was low at 134 mg/dL and triglyceride also low at 52 mg/dL. Urinalysis was normal. The chest plain x-ray film showed the dilation of cardiac shadow with obscured costophrenic angle on the left side (Figure 2B). Electrocardiogram showed regular sinus rhythm with wide QRS, indicative of the left bundle branch block (Figure 2A). Left ventricular ejection fraction determined by cardiac ultrasonography was 50%. The cardiac contractility was good, all valvular functions were normal, and pericardial effusion was approximately 13 mm at the cardiac apex.

The differential diagnoses for pericardial effusion that were listed on the admission were infection including tuberculosis, autoimmune diseases, and metastatic malignancy. Computed tomographic (CT) scan from the thorax, abdomen, to pelvis demonstrated no mass lesions. The pericardial effusion and a small volume of pleural effusion on the left side were shown (Figure 2D, E). Whole-body 2-[^{18}F]fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) disclosed many spotty uptakes with the maximum of standardized uptake value (SUVmax) around 2.0 in the pericardial effusion (Figure 2F, G). No other abnormal uptake was noted systemically. As blood tests for low blood sodium, the measurements of aldosterone, cortisol, adrenocorticotropic hormone (ACTH), and plasma renin activity were all within normal limits. As checkups for autoimmune diseases, antinuclear antibody was positive at 2.84 ratio, Sjogren Syndrome-A (SS-A) positive at 225 U/mL, and cardiolipin antibody positive at 19.3 U/mL. Serum IgG was elevated to 2380 mg/dL and IgG4 was also elevated mildly to 141 mg/dL. Pericardiocentesis was planned as a diagnostic procedure but was not done based on the following reasons: (1) the patient was healthy at the old age and had no symptoms; (2) the volume of pericardial effusion tended to decrease from the initial visit (Figure 2B, 2C); (3) the heart showed good function of expansion in the present volume of pericardial effusion; and (4) the patient denied pericardiocentesis, based on his evaluation of the risk of the procedure. He was thus discharged in several days and followed at the outpatient clinic. He underwent dental treatment (Figure 1B, C), and the pericardial effusion resolved completely in a month. He was healthy in 6 years until the last follow-up at the age of 92 years.

Figure 1. Dental x-rays 2 weeks before the admission (A, maxillary teeth in upper panels, mandibular teeth in lower panels, right-side teeth in left panels, and left-side teeth in right panels), and dental x-rays before (B) and after (C) root canal treatment for chronic apical periodontitis in the first and second premolar teeth 2 months later. Pyocele-like alveolar bone resorption around the apex of mandibular first premolar tooth on the right side (arrows in A, B, and C) is noted in the background of diffuse gingival recession and alveolar bone resorption due to the old age.

Discussion

This healthy aged patient who was followed by a cardiologist showed a small volume of pericardial effusion for 5 years and experienced gradual increase in the pericardial fluid in a month. In the same period, he had persistent mild periodontitis in the background of diabetes mellitus which was controlled around the 7% level of hemoglobin A1c. In parallel with the increase in pericardial effusion, he experienced exacerbation of periodontitis, leading to cheek swelling and mastication problems. Oral administration of antibiotics for a week resulted in relative subsidence of periodontal signs and symptoms and also led to the decrease in pericardial effusion. The sputum tests around this time

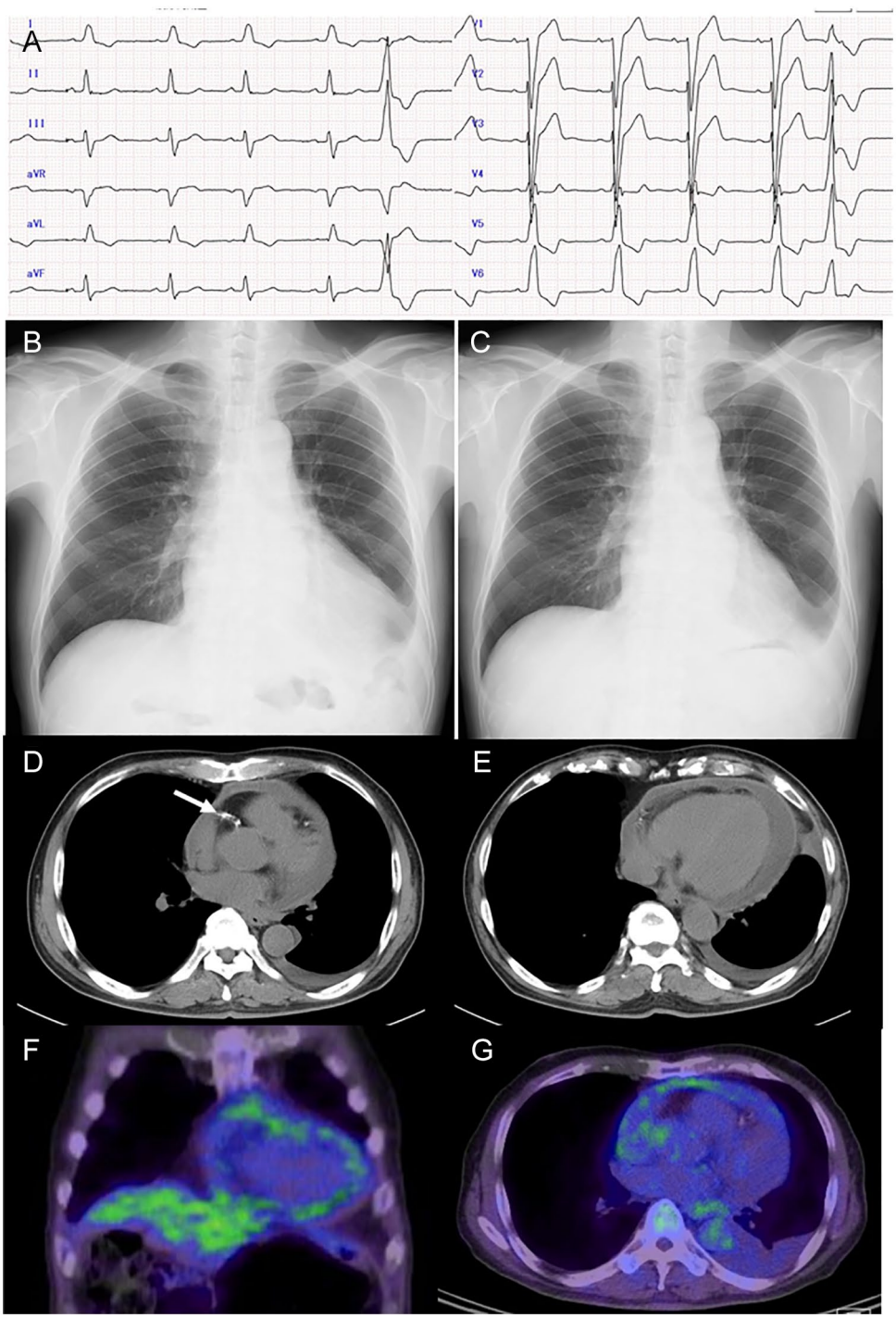

Figure 2. Electrocardiogram (A), chest plain x-ray (B), and computed tomography (D, E) on the day of admission, fluorodeoxyglucose positron emission tomography (FDG-PET) 4 days later (F, G), and chest plain x-ray 11 days later at outpatient visit (C). Not regular sinus rhythm at pulse rate of 65 beats per minute with left bundle branch block and an isolated ventricular extrasystole (A), cardiac shadow enlargement which decreased spontaneously in 11 days (B, C), pericardial effusion (D, E) and coronary stent (arrow in D), and multiple uptake sites in the pericardium in the coronal image (F) and axial image (G) of FDG-PET.

detected a large number of *Streptococcus* species. The temporal association of the increase in pericardial effusion with the exacerbation of periodontitis suggests causal relationship of periodontitis and pericardial effusion after the other causes have been excluded in the differential diagnoses. Oral *Streptococcus* species which are famous for causing infective endocarditis might be responsible for pericardial effusion in this patient, although the evidence is weak. In this context, the causal relationship of oral bacteria with pericarditis would be further supported by the previous study that the same bacterial strains by DNA typing with oral bacteria were identified in the pericardial fluid of 22 subjects at forensic autopsy.[25]

In the differential diagnoses, he did not have any sign of autoimmune diseases while he had the background of positive antinuclear antibody, SS-A, and cardiolipin antibody. Carcinomatous pericarditis is difficult to be excluded completely. The patient had no findings in upper and lower digestive tract endoscopic examinations and showed no mass in the thoracic, abdominal, and pelvic CT. FDG-PET showed pericardial uptakes, suggestive of inflammation or metastatic cancer,[26-31] but detected no other abnormal uptake in the whole body. Under the circumstances, the possibility of carcinomatous pericarditis would be low because pericardial effusion resolved spontaneously in this patient. This study also supports that FDG-PET would be useful to determine the unknown cause of pericardial effusion although the examination is expensive at cost.[26-31]

As a tendency in aged people, the present patient did not have any symptoms such as fever and general fatigue. However, it should be noted that his pulse rate increased to 65 beats per minute, compared with his usual status around 50. Cheek swelling on the right side in this patient would not be noticed in the background of skin loosening in the cheek which is often seen in aged people. An increase in the pulse rate was a sign of his illness, together with CRP elevation and relative increase in neutrophils in the not-so-elevated white blood cell count.

To analyze similar cases, PubMed and Google Scholar were searched for the key words: pericarditis (pericardial effusion) and periodontitis (periodontal disease). The Japanese literature was searched for the same key words in the bibliographic database of medical literature in Japanese (Igaku Chuo Zasshi, Japana Centra Revuo Medicina, Ichushi-Web), published by the Japan Medical Abstracts Society (JAMAS, Tokyo, Japan). Old literature was collected from references cited in the articles identified during the literature search. Table 1 summarizes 8 patients with sufficient description,[17-24] together with the present case. The 9 patients, including the present patient, were 5 men and 3 women with the age at the initial visit ranging from 19 to 86 years (median, 45 years) while the sex and the age of the remaining one person were not described. All showed pericardial effusion and pericardiocentesis was done in 4 patients. Mediastinitis was noted in 5 patients, and constrictive pericarditis in 3. All 9 patients, except for the present patient (case 9), underwent surgical interventions such as thoracotomy and pericardial drainage. As for the dental diagnoses, 5 patients had teeth caries frequently in the mandibular molar teeth while 4 patients were described to have periodontitis or suspected of periodontitis.

Causative agents were described in all 9 patients except for one (case 6). *Fusobacterium nucleatum*, *Peptococcus magnus*, *Pseudomonas* species, *Actinomyces odontolyticus*, and methicillin-sensitive *Staphylococcus aureus* were identified in pericardial fluid which was obtained by pericardiocentesis or pericardiectomy. *Actinomyces* was identified in the pericardial soft tissue mass which was resected in 1 patient (case 4). *Streptococcus* species which was isolated from the sputum was suspected of a causative agent in the present patient (case 9) who did not undergo surgical procedures such as pericardiocentesis. In another patient, causative agents were stated as aerobic and anaerobic flora of pus (case 5). Pathogens in oral bacterial flora can travel from the oral cavity to the pharynx and directly reach the mediastinum in severe purulent oral conditions. On the other hand, oral pathogens can enter the bloodstream and reach the pericardial space in periodontitis with alveolar bone destruction, as seen in the present patient.[16,32,33]

The present patient, as well as the other patients in the literature, indicates that periodontal diseases would serve as a precipitating factor for the development of not only the well-known infective endocarditis but also pericardial effusion or pericarditis. In the other fields of medicine, for instance, in ophthalmology, periodontal diseases may also cause endogenous endophthalmitis by probable bloodstream infection with *Aspergillus* and *Acanthamoeba*.[32,33] Oral hygiene should be checked in medical interview and systemic evaluations of patients with pericardial effusion. The earlier detection of oral problems would lead to the earlier diagnosis of pericardial effusion and hence to the earlier treatment to avoid devastating results such as mediastinitis and constrictive pericarditis which were described in the literature.[17-24]

Table 1. Review of 8 Patients With Pericarditis in Association With Periodontitis, Including the Present Patient.

Case no. /sex/ age at onset	Presenting symptoms	Diagnosis of pericardial effusion	Pericardiocentesis	Findings in pericardial effusion	Other sites involvement	Oral cavity findings and treatment	Treatment	Outcome and complications	Authors
1/Male/49	Cough, chest pain, orthopnea, diarrhea	Ultrasonography Chest plain x-ray	No	Leukocytes *Fusobacterium nucleatum*	None	Dental caries and pyorrhea	Antimicrobials Pericardiectomy for constrictive pericarditis	Healthy in 3 weeks	Truant et al[17]
2/Male/30	Fever, chest pain, cough, dyspnea	Ultrasonography Chest plain x-ray	Yes	Gram-positive cocci Neutrophils *Peptococcus magnus*	Mediastinitis (necrotic purulent debris)	Carious molars with apical abscess Tooth extraction	Antimicrobials Thoracostomy tube insertion Thoracotomy, pericardial stripping for constrictive pericarditis, mediastinal lavage	Healthy in 2 months	Plelps and Jacobs[18]
3/Unknown/-	Left cheek and neck swelling Dyspnea	Chest plain x-ray Emergency surgery	No	*Pseudomonas* from mediastinal drain	Mediastinitis	Carious teeth, mouth floor pus Total teeth extraction	Antimicrobials Thoracotomy Mediastinal and pericardial drains	Healthy	Zachariades et al[19]
4/Female/41	Chest pain Dyspnea Weight gain	Chest plain x-ray Ultrasonography CT	Yes	Neutrophils No acid-fast bacilli	Mediastinitis	Suspicious of periodontal disease	Antimicrobials Pericardial drain *Actinomyces* in pericardial soft tissue mass extirpation Thoracostomy tube insertion	Healthy in 3 years	Fife et al[20]
5/Male/40	Left mandibular and neck swelling Hoarseness, fever, dysphagia	Chest plain x-ray CT	No	Not available	Mediastinitis	Left submandibular abscess from molars Aerobic and anaerobic flora of pus Mandibular molar extraction	Antimicrobials Tracheostomy Mediastinotomy Thoracotomy	Healthy Ankylosing spondylitis Both hip replacement 3 months earlier	Pappa and Jones[21]
6/Female/19	Left cheek and submandibular swelling Chest pain and dyspnea next day	Chest plain x-ray CT	No	Pus	Mediastinitis Reactive (aseptic) ascites	Left mandibular carious second molar and semi-impacted third molar Incisional drainage of buccal abscess	Antimicrobials Thoracotomy Thoracic drain	Not described	Rallis et al[22]
7/Male/61	Dyspnea, cough Fever, chest pain	Chest plain x-ray Ultrasonography	Yes	Pus Gram-positive cocci *Actinomyces odontolyticus*	None	Suspicious of periodontal disease Dentures	Antimicrobials Pericardial drain	Chemotherapy and radiation for right upper lobe squamous carcinoma Dead from lung cancer	Mack et al[23]
8/Female/56	Chest pain	Ultrasonography CT	Yes	Pus Neutrophils MSSA	Infective thoracic aortic aneurysm	Periodontitis	Antimicrobials Thoracotomy Aortic arch replacement Pericardiectomy for constrictive pericarditis	Healthy in 8 months	Sato et al[24]
9/Male/86	Right cheek swelling	Chest plain x-ray Ultrasonography CT, FDG-PET	No	Not available	Right pleural effusion	Mandibular periodontitis on the right side *Streptococcus* in sputum	Antimicrobials	Healthy in 6 years	This case

Abbreviations: CT, computed tomography; FDG-PET, fluorodeoxyglucose positron emission tomography; MSSA, methicillin-sensitive *Staphylococcus aureus*.

Authors' Note

Data are available upon reasonable request from the corresponding author.

Author Contributions

T.M., as an ophthalmologist, suggested periodontal origin of illness and wrote the manuscript. C.N.M., as an orthodontist, suggested periodontal origin of illness. N.M., as a professor emeritus of ophthalmology, presented history of illness. A.M., as a dentist, treated the patient. M.M. and H.I., as cardiologists, examined and followed the patient. All authors approved the final version of the manuscript.

Declaration of Conflicting Interests

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Ethics Approval

Ethics committee review was not applicable due to the case report design, based on the Ethical Guidelines for Medical and Health Research Involving Human Subjects, issued by the Government of Japan.

Informed Consent

Oral informed consent was obtained from the patient for his anonymized information to be published in this article.

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