

Pyogenic spondylodiscitis caused by atopic dermatitis

Takanori Fukunaga (✉ tfukunaga-nsu@umin.ac.jp)

Iseikai Hospital

Manabu Sasaki

Iseikai Hospital

Koshi Ninomiya

Iseikai Hospital

Gento Moriguchi

Iseikai Hospital

Katsumi Matsumoto

Iseikai Hospital

Haruhiko Kishima

Osaka University

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Abstract

Pyogenic spondylodiscitis (PS) frequently occurs in the elderly or those with risk factors, such as diabetes mellitus (DM), chronic renal disease (CRD), and malignancy. Although we have recorded PS occurring in patients with atopic dermatitis (AD), there have been no reports on the same. This retrospective study aimed to determine whether AD is a potential risk factor for PS. We reviewed the clinical records of 39 patients with PS who were surgically treated. Causative bacteria were identified via blood and operative tissue samples and compared to the underlying diseases and age at onset, for patients with AD, DM, CRD, and malignancy. Consequently, AD was identified as the underlying disease in five patients (12.8%); DM, in 12 (30.8%); CRD, in nine (23.1%); and malignancy, in five (12.8%). *Staphylococcus aureus* was identified as the causative bacteria for all patients in AD (100%), five in DM (41.7%), two in CRD (22.2%), and one in malignancy (20.0%). Age at onset was significantly lower in AD as compared to the other three groups. In this study, the onset of PS in all patients with AD was 50 years, caused by *S. aureus*. These results suggest that AD is risk factor for middle-aged patients with PS.

Introduction

In the past few decades, an increase in the incidence of pyogenic spondylodiscitis (PS) [1] has been reported, attributed to an advancing population and increased number of immunocompromised patients [2, 3]. Predisposing factors for PS have been previously reported as advancing age, diabetes mellitus (DM), intravenous drug abuse, human immunodeficiency virus infection, malignancy, chronic renal disease (CRD), sepsis, recent spinal surgery, and intravascular devices [4–6]. Systemic bacteremia from the primary infected site of the genitourinary tract, respiratory tract, gastrointestinal tract, or oral cavity disseminate PS. Although we experienced the incidence of PS in some patients with atopic dermatitis (AD), there have been no past reports on PS associated with AD. AD is a chronic inflammatory skin disease that is associated with a higher rate of cutaneous and extracutaneous infection. To the best of our knowledge, this is the first report on PS associated with AD.

Methods

Ethical approval for this study was obtained from Iseikai hospital ethics committee (2021-22) and written informed consent was obtained from all subjects before the study. In our hospital, patients suspected of PS underwent blood sampling for bacterial examination at the initial diagnosis, irrespective of the presence of fever. The patients and their families were interviewed about the past and present diseases in detail. When vertebral bone destruction progresses or neurological symptoms emerge, a surgical operation is performed as early as possible, ideally within a few days. The operative tissue samples are then utilized for bacterial examination. Antibiotic medication is not initiated before surgery and if the patient's condition is not severe or has temporarily relaxed at least 3 days before surgery.

We reviewed the clinical records of 39 consecutive patients with PS who were treated during January 2018 and December 2020. We assessed the patients' age, symptoms at initial presentation, causative

bacteria, and medical histories. We focused on patients with AD and on those presenting with the other three diseases, DM, CRD, and malignancy, which are risk factors for PS. Statistical analysis was performed using Dunnett's test, with $P < 0.05$ considered to indicate statistical significance. All methods were carried out in accordance with relevant guidelines and regulations.

Results

Among the 39 patients, the underlying disease was identified to be AD in 5 patients (12.8%) (Group A), DM in 12 (30.8%) (Group D), CRD in 9 (23.1%) (Group C), and malignancy in 5 (12.8%) (Group M) (Table 1). Patients' age of Group A was significantly younger (48.6 ± 4.6 years) than that of Group D (69.9 ± 11.8 years), Group C (74.8 ± 11.6 years), and Group M (73.0 ± 9.0 years) ($P = 0.0038$, $P = 0.0008$, and $P = 0.0053$, respectively). *Staphylococcus aureus* was identified as the causative bacteria in all 5 patients in Group A, 5 of 12 patients in Group D (41.7%), 2 of 9 patients in Group C (22.2%), and 1 of 5 patients in Group M (20.0%).

Table 1
Summary of the underlying diseases in 39 study patients with pyogenic spondylitis

		Atopic dermatitis	Diabetes mellitus	Chronic renal disease	Malignancy
Case number		5 (12.8%)	12 (30.8%)	9 (23.1%)	5 (12.8%)
Patients' Age (years)		48.6 ± 4.6	69.9 ± 11.8 *	74.8 ± 11.6 *	73.0 ± 9.0 *
Causative bacteria	<i>Staphylococcus aureus</i>	5 (100%)	5 (41.7%)	2 (22.2%)	1 (20.0%)
	<i>Staphylococcus epidermidis</i>	0	0	1	0
	<i>Streptococcus</i>	0	0	1	0
	<i>Escherichia coli</i>	0	2	1	0
	<i>Serratia marcescens</i>	0	1	1	1
	<i>Enterococcus faecium</i>	0	0	0	0
	Not identified	0	4	3	3

*: significantly older compared to atopic dermatitis with Dunnett's test

*: the age of Group A was significantly smaller than that of the other group with known risk factors for PS.

Statistical analysis was performed with Dunnett's test, with $P < 0.05$ considered to indicate statistical significance.

In Group A, the spinal level affected by infection ranged from the cervical to the lumbar spine (Table 2). *Methicillin-susceptible S. aureus* (MSSA) was detected in the operative tissue samples of all five patients and in the blood samples of the four patients. It was also detected on the skin of three patients (Case #1, 3, and 4). Case 1 underwent bacterial examination on the skin immediately before surgery, and dermatologists examined the other two cases for >1 year before. One patient (Case #4) had used ointment, including steroids and antibiotics, but had not taken oral steroids before the onset of AD.

Table 2

Summary of the five study patients with pyogenic spondylitis caused by atopic dermatitis

Case	Age	Gender	Affected	Usage of	Bacterial culture examination		
	(years)		spinal level	steroid	Tissue sample	Blood	Skin
1	55	M	C4/5	None	MSSA	MSSA	MSSA
2	47	M	T10/11	Ointment	MSSA	MSSA	NE
3	51	F	L4/5	None	MSSA	ND	MSSA
4	49	F	L5/S1	None	MSSA	MSSA	MSSA
5	41	M	L5/S1	None	MSSA	MSSA	NE

MSSA: *methicillin-susceptible Staphylococcus aureus*, ND: not detected, NE: not examined

Discussion

AD is a chronic inflammatory skin disease that often causes bacterial skin infections. The innate immune system of the epidermis essentially protects against the development of cutaneous infections. However, the skin of patients with AD is susceptible to infection owing to the reduction of cell-mediated immunity and the developed deficiency in the antimicrobial peptides barrier on the skin [7–9]. The skin of patients with AD is highly colonized with toxin-producing *S. aureus* [10]. The skin lesion is colonized by *S. aureus* in up to 90% of the patients compared to that in 5–30% of healthy controls. Since *S. aureus* is tightly bound to the inflammation site of the skin, scratching of the skin disturbs the skin barrier and promotes its colonization [11].

AD is associated with a high rate of incidence of extracutaneous infections in various organs [12]. Correlation between AD and extracutaneous infections has not been sufficiently examined until recently. According to a previous study on a large population in the United States, the ears, respiratory tract, and urinary tract are the frequently affected sites for infection in patients with AD [13]. The bone and joint infection has also been noted; however, the concrete infected site has not been described. As far as we could find, there have been only two reports with concrete descriptions presenting with osteomyelitis of the hip and distal phalanges in children with AD [14, 15].

Although the mechanism of extracutaneous infection in patients with AD remains unknown, some past papers have documented the possibility of hematogenous dissemination of *S. aureus* infection.

This study suggested that AD is associated with the incidence of PS. MSSA infection was confirmed in the operative tissue samples of all five cases and the blood samples of the four cases. The same bacterium was also detected on the skin of all three patients examined. The spinal level of infection ranged from the cervical to lumbar spine. These results suggested that PS is potentially induced through hematogenous dissemination from the cutaneous infection.

We had not experienced patients with PS and AD until 2018. The number of patients with AD in Japan has demonstrated an increasing trend in recent years. According to the Ministry of Health, the number of patients with AD increased from 0.40 million in 1999 to 0.51 million in 2017 [16]. Previous age–period–cohort (APC) analyses suggest that the period effect for AD demonstrated an increasing trend from 2002 owing to an increase in the population of the urban areas in Japan. The cohort effects for AD increased rapidly for cohorts born in the years 1950 to 1980. This tendency has been attributed to factors, such as rapid urbanization, increasingly westernized lifestyles, and improved standards of living and education [17, 18]. It is probable that the recent higher prevalence of AD will provide us with a greater number of cases of patients with PS and AD.

An accurate diagnosis of PS is relatively difficult at the early stage of the disease. Previous studies have reported that a median interval from the onset of symptoms to diagnosis is 26 days [19]. The delayed diagnosis of PS can be attributed to its nonspecific symptoms, such as back pain and fever, which are often observed in other common diseases too. Additionally, a sign of infection is difficult to recognize by imaging studies at the early stage; therefore, the knowledge of the risk factors for PS is essential to cite PS as a differential diagnosis. Advanced age is one of the risk factors. In this study, the mean age of the patients without AD was ~70 years, whereas that of the patients with AD was around 50 years. The age of onset was significantly smaller in patients with AD. In our cases, the prevalence of AD was equivalent to that of malignancy, which is a risk factor for PS. Therefore, we considered that AD should be regarded as a risk factor for PS, especially at the middle age.

There are some limitations in this study. For instance, this is a retrospective study conducted on few cases at a single institution. Not all patients underwent a bacterial examination of the skin at the initial diagnosis, and there was no way to ensure that the same bacterium caused both cutaneous and extracutaneous infection. However, this study does provide some helpful insights for the correct diagnosis of PS associated with AD.

Conclusions

Clinicians should regard AD as one of the risk factors for PS when symptoms and spinal imaging studies indicate the possibility of PS at the initial diagnosis. Although PS is highly prevalent among patients at an advanced age, it can be induced in the younger generation with AD. However, further large-scale prospective studies are warranted to obtain more evidence for PS with AD.

Declarations

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Author contributions

TF designed and conducted the study, GM and KN analyzed the data, KM and HK and MS revised the manuscript. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data availability statement

All data generated or analysed during this study are included in this published article.

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