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Jirapa Deewattanakul

Titawate Tumrasvin

Utis Deesomchok

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The clinical study of septic arthritis due to *Pseudomonas Pseudomallei* in Chulalongkorn Hospital

Jirapa Deewattanakul*

Titawate Tumrasvin* Utis Deesomchok*

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Patients at Chulalongkorn Hospital with septic arthritis caused by Pseudomonas pseudomallei during the period 1972 - 1994 were studied. There were a total of seven cases, four of whom were female. They ranged in age from 22 to 75 years with the most common ages being 40 - 50 years. Most of the patients lived in the central part of Thailand. Mono-articular involvement was commonly seen; joints commonly involved were the knee and elbow. Duration of symptoms before treatment ranged from three days to two months. Extra-articular infections were found in five cases, four of whom had respiratory tract infections and four had skin and soft tissue infections. All of the patients had underlying diseases, including diabetes mellitus, thalassemia and chronic renal failure; 71 percent of the patients had leukocytosis. The infective organism was isolated from the synovial fluid and blood in six and three cases, respectively. An indirect hemagglutination test was performed for five cases and all had titers of over 1:80. The patients were treated with antibiotics and joint drainage with good results; however, there were two deaths.

Key words : *Pseudomonas Pseudomallei, Septic arthritis.*

Reprint request: Deewattanakul J, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

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จรรยา ตีวัฒนากุล, จิตเวทย์ ตุมราศวิน, อุทิศ ตีสมนิช. การศึกษาลักษณะทางคลินิกของโรคข้ออักเสบที่เกิดจากการติดเชื้อ ซูโดโมแนส ซูโดมัลลีไอ ในโรงพยาบาลจุฬาลงกรณ์. จุฬาลงกรณ์เวชสาร 2538 ตุลาคม;39(10): 743-749

จากการศึกษาโรคข้ออักเสบที่เกิดจากการติดเชื้อ *P.pseudomallei* ในโรงพยาบาลจุฬาลงกรณ์ ตั้งแต่พ.ศ. 2525 - 2537 พบผู้ป่วยทั้งหมด 7 ราย เป็นหญิง 4 ราย โดย 3 ราย อายุน้อยที่สุด 22 ปีมากที่สุด 75 ปี อายุผู้ป่วยอยู่ระหว่าง 40 - 55 ปี เป็นส่วนใหญ่ ส่วนมากมีภูมิลำเนาอยู่ในภาคกลางลักษณะอาการของข้ออักเสบเป็นแบบข้อเดียว โดยเกิดที่ข้อเข่า และข้อศอกได้บ่อยที่สุด ช่วงเวลาที่มีอาการก่อนมาโรงพยาบาลอยู่ระหว่าง 3 วันถึง 2 เดือน ผู้ป่วย 5 ใน 7 ราย มีการติดเชื้อในระบบอื่นร่วมด้วย ได้แก่เบาหวาน (5 ราย) *Thalassemia* (2 ราย) และเบาหวานร่วมกับโรคไตวายเรื้อรัง (1 ราย) การตรวจทางห้องปฏิบัติการพบว่า ร้อยละ 71 มีจำนวนเม็ดเลือดขาวในเลือดมากกว่า $10,000$ ตัว / mm^3 และมักมีภาพรังสีของปอดผิดปกติ จากการเพาะเชื้อของน้ำไขข้อสามารถตรวจพบเชื้อ 6 ราย และตรวจพบเชื้อในเลือด 2 ราย มีผู้ป่วย 5 รายที่ได้ตรวจ *indirect hemagglutination test* ซึ่งพบว่าทุกรายมี titer สูงกว่า 1:80 ผู้ป่วยได้รับการรักษาด้วยยาปฏิชีวนะ ร่วมกับการเจาะดูดน้ำไขข้อ พบเสียชีวิต 2 ใน 7 ราย

Melioidosis is an infectious disease caused by *Pseudomonas pseudomallei* (*P.pseudomallei*) which is a gram-negative bacteria bipolarly in the shape of a safety-pin. The organism is a saprophyte normally found in soil, ponds and rice fields. It is occasionally a pathogen for animals. Humans contract the disease through soil contamination of abrasions, ingestion, nasal instillation, or inhalation. Melioidosis was first recognized in Rangoon, Myanmar in 1911 by Whitmore and Krishnaswami.⁽¹⁾ Later, it was found to be endemic in Southeast Asia and surrounding areas.⁽²⁾ The disease can be found in all parts of Thailand, most commonly in the northeastern and the southern parts of the country.⁽³⁾

Melioidosis presents it self in different forms as follows :

1. Disseminated septicemia

The infection spread via the circulation to various organs and appears in the form of multiple abscesses.

2. Localized infection with or without septicemia.

3. Chronic form

The infection commonly involves the lungs, skin and salivary glands.

4. Asymptomatic

Even though no symptom is found, there is high serum activity due to the presence of the organism.

Melioidosis can imitate other common infectious diseases as well as tuberculosis and carcinoma of the bones and joints.^(4,5)

The purpose of this study was to determine the clinical manifestations of septic arthritis

due to *P. pseudomallei* in Chulalongkorn Hospital, particularly in the Medical Service Section.

Material and Methods

Seven adult patients with *P. pseudomallei* arthritis who were admitted to Chulalongkorn Hospital, Bangkok, during the period January 1982 to February 1994 were studied. All of these arthritic patients were diagnosed as having *P. pseudomallei* arthritis owing to the presence of the either one the following characteristics:

1. Gram staining of the synovial fluid showing gram-negative bacilli with bipolar staining
2. Synovial fluid culture being positive for *P.pseudomallei*
3. Hemoculture being positive for *P. pseudomallei*

The records of the patients were reviewed. Information was obtained regarding age, sex, residence, time of increased prevalence, pattern and site of the arthritis, and underlying diseases. Laboratory evaluations included white blood cell (WBC) count, gram staining and culture of synovial fluid, hemoculture, chest x-ray, and indirect hemagglutination test for melioidosis (IHA).

Results

Of the seven patients, four were females thus giving a female to male ratio of 1.3 : 1. Age range was from 22 to 75 years, with the most common ages being from 40 to 50 years. Five patients lived in the central part of Thailand, one in the eastern part of the country and one in the northeastern part. Most of the patients were

admitted to the hospital during the period September to December.

The arthritis mostly involved only one joint, as was the case in five patients; in the other two more than one joint was involved. The joints commonly involved were elbows and knees; others were the ankle and metatarsophalangeal joints. One patient had periarticular cellulitis. Extra-articular infections were found in five patients. Of those five patients, four had respiratory tract infections; four had skin and soft tissue infections; and one had a urinary tract infection. All patients had underlying diseases. Diabetes mellitus was found in five patients. Two patients had thalassemia and one had diabetes mellitus with 3 chronic renal failure. The duration of symptoms before treatment ranged from three days to two months.

Five patients (71%) had white blood cell counts of more than 10,000 per cubic millimeter, with a predominance of neutrophils. Urinalysis was within normal limits in all but one patient who had a urinary tract infection. Gram's staining of the synovial fluid revealed gram-negative bacilli with bipolar staining in one case. *P. pseudomallei* was isolated from the synovial fluid and blood in six and three cases, respectively. An indirect hemagglutination test was done in five patients and all had titers higher than 1:80.

All patients were managed with appropriate antibiotics and joint drainage. Needle aspiration was sufficient in all but one case which needed surgical drainage. Five patients responded well to the treatment, but two others died. Hemoculture was positive in one of the two patients who died.

Discussion

Septic arthritis in melioidosis is relatively uncommon.^(6,7) The incidence of septic arthritis due to *P.pseudomallei* has been quite low in Chulalongkorn Hospital; in 12 years, only seven cases have been diagnosed. The incidence of melioidosis in Bangkok, which is in the central part of Thailand, is lower than in the north-eastern part.⁽³⁾ Most of our patients lived in the central part of the country. The peak incidence of melioidosis is usually in the rainy season (June to October),⁽³⁾ but in this study most of the patients were seen in the period September to December. The onset of septic arthritis in melioidosis may be acute, subacute, or chronic. Cases of septic arthritis due to *P.pseudomallei* may present with isolated articular involvement or multiple organ involvement.⁽⁸⁾ Most of our patients had infection sites other than the joints, mostly the respiratory tract, skin and soft tissue. This may indicate the route of infection via the respiratory tract and skin. Monoarthritis was the most common joint pattern, occurring in 70 percent of the patients. The joints commonly involved were the knee and wrist. The articular features of our patients were the same as those previously reported in other series.^(3,6-8)

Table 1⁽⁷⁾ shows a comparison of the clinical features of our patients with those from Srinakarind Hospital, which is in the northeastern part of Thailand. The articular features of the two series are similar. Monoarthritis associated with soft tissue and respiratory tract infections are the main features of septic arthritis caused by *P.pseudomallei*.

Table 1. Comparison of the clinical manifestations of our patients with those from Srinakarind Hospital in Khonkaen province.

	Chulalongkorn H.	Srinakarind H.
Age	40-50 yrs.	40-50 yrs.
Sex ratio	F:M 1.3:1	F:M 2:1
Residence	Mostly from the central part	all from the northeast
Bones & Joints Manifestation	Mostly monoarthritis (knee,elbow)	Mostly monoarthritis
Underlying diseases	All cases (mostly DM,thalassemia,CRF)	Most cases (DM,thalassemia,CRF)
Duration	2 days - 3 months	3 days - 5 months
Other sites of infection	Respiratory tract (4/7) Skin & soft tissue (4/7)	Respiratory tract (2/21) Skin & soft tissue (2/21)
Laboratory		
1. WBC	>10,000 (5/7) 5,000-10,000 (2/7)	5,000-10,000
2. UA	WBC>5 cells (1/7) Normal (6/7)	Normal (all)
3. Synovial fluid gram staining	Positive (1/7)	Positive (7/21)
4. Synovial fluid culture	Positive (6/7)	Positive (3/21)
5. Hemoculture	Positive (3/7)	Positive (1/21)
6. Melioid titer	>1:80 (all)	>1:80 (all)
7. Treatment	Antibiotics and joint aspiration (6/7) surgical drainage (1/7)	Antibiotics, joint aspiration and surgical drainage
8. Outcome	Death (2/7) (H/C positive in one patient)	Death (1/21) (H/C positive)

Melioidosis is usually associated with other diseases, such as diabetes mellitus, chronic renal failure, urolithiasis, thalassemia, and hematologic malignancies.^(4,7,9) All our patients had underlying diseases, including diabetes mellitus, thalassemia, and chronic renal failure.

The definitive diagnosis of melioidosis can be made by specimen culture. Six of the seven cases in this series had synovial fluid cultures that grew *P. pseudomallei*. Identification of the gram-negative bacilli, which are shaped like a safety-pin, by gram staining of the synovial fluid was infrequent. In only one case could the organism be so identified. Hemoculture was positive in three cases and associated with the severity of the disease. The septicemic patients who had positive hemoculture were associated with very high mortality rates despite optimum therapy.⁽¹⁰⁾ In areas where melioidosis is endemic, diagnosis of the active disease by serologic tests should be made with care. In Thailand, an IHA titer of > 1:80 yields 90 percent sensitivity and 88 percent specificity in the diagnosis of active melioidosis.⁽¹¹⁾ A single titer of > 1:640 is highly suggestive of active disease. All our patients in whom IHA was detected had titers higher than 1:80. There was no correlation between the titer and the severity, but a rising titer may be helpful in diagnosing a recurrence of disease activity.⁽¹²⁾

Joint aspiration together with the administration of appropriate antibiotics enabled effective management of the septic arthritis in melioidosis in our cases. Only one case needed open drainage. Two patients died, one with

multiple sites of infection, and the other from septicemia, which is usually associated with high mortality.

In conclusion, septic arthritis due to *P. pseudomallei* was mostly manifested as monoarthritis involving knee and elbow joints, with extra-articular infections such as that of the skin and respiratory tract. The patients had underlying diseases. An IHA titer was helpful in the diagnosis of melioidosis. The diagnosis of articular melioidosis should be kept in mind in assessing patients with monoarthritis and multiple organ infections and an underlying disease, especially for patients from an area where the disease is endemic.

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