Clinical, Laboratory and Radiologic Evaluations in Patients with Malignant Tuberculous Spondylitis

Bambang Prijambodo[1], Udria Satya Pratama[2]

[1]Professor in Department of Orthopedics and Traumatology, Faculty of Medicine, Universitas Airlangga, Mayjen Prof. Dr. Moestopo 6-8, Surabaya (60286), Indonesia, [2]Student in Department of Orthopedics and Traumatology, Faculty of Medicine, Universitas Airlangga, Mayjen Prof. Dr. Moestopo 6-8, Surabaya (60286), Indonesia

Abstract

Background: Tuberculous spondylitis patient diagnosis still becomes a challenging task in orthopedics. Mycobacterium tuberculosis Beijing strain caused malignant tuberculous spondylitis in most patients (66.7%). Therefore, they proposed scoring system to estimate the prognosis of patients with malignant tuberculous spondylitis with some parameters, including abscess area, erythrocyte sedimentation rate (ESR), number of vertebral destruction, disseminated tuberculosis and infectious Mycobacterium tuberculosis stain.

Objectives: To perform clinical, laboratory and radiologic evaluations in patients with malignant tuberculous spondylitis using scoring system proposed by Yunus and Prijambodo

Methods: This retrospective cohort study was carried out from 2012 to 2015 in patients with malignant tuberculous spondylitis at Dr. Soetomo Teaching Hospital, Surabaya, Indonesia, using Yunus and Prijambodo scoring. Subjects were evaluated in minimum 6 months after surgery. The evaluations included clinical (abscess recurrence), laboratory (ESR) and radiologic (bony fusion in spinal X-ray tomography).

Results: Of eight acute tuberculous patients, only 5 were evaluated. One had moderate prognosis and four had severe prognosis. No abscess recurrence found in patients after 20-month evaluation. ESR was below 20 mm/hour (12.8±7.8) and 80% of patients had bony fusion in spinal X-ray tomography.

Conclusion: Most patients with malignant tuberculous spondylitis with moderate and severe prognosis had better outcomes after 20-month evaluation. Further studies should consider other factors affecting tuberculous spondylitis patient's prognosis including host factor.

Keywords: *malignant tuberculous spondylitis, postoperative evaluation, Yunus and Prijambodo scoring*

Introduction

Mycobacterium tuberculosis commonly causes granulomatous spinal infections. Tuberculosis incidences in developed countries decreased over the past 30 years, with 10% bone and joint involvements and half of which were spinal tuberculosis. Tuberculous spondylitis incidences in Indonesia are still high. 98 tuberculous spondylitis patients were treated at Dr. Soetomo Teaching Hospital, Surabaya, Indonesia, from 1 January 2008 to 31 December 2012 [1].

Tuberculous spondylitis diagnosis still becomes a challenging task in orthopedics. Previous studies reported that Ziehl-Neelsen stain had 87.5% sensitivity and 100% specificity in diagnosing tuberculous spondylitis, while acridine orange had 100% sensitivity [2]. Nevertheless, these methods require a relatively much bacteria (100,000 bacteria/mL). Diagnosis develops by using polymerase chain reaction (PCR) technique from fine needle aspiration with 83.3% sensitivity and 50% specificity [3]. A study found a correlation between malignant/virulence tuberculous spondylitis by measuring abscess and high tumor necrotizing factor alpha (TNF-α) level.

Nevertheless, there was a correlation between increased TNF-α and erythrocyte sedimentation rate

(ESR) that subsequently helped peripheral areas that could not examine TNF-α level. A study found 54.5% of virulent strain PCR positive gyrB gene with 18.2% polydrug-resistance and 9.1% multidrug-resistance, with PCR validation had 83% sensitivity and 80% specificity in diagnosing tuberculous spondylitis. In diagnosing tuberculosis, direct methods, including PCR, require specimens of infected area that are often difficult to obtain or too invasive. Some researchers have tried to detect mycobacterium tuberculosis' DNA in patient's peripheral blood. Studies on PCR with peripheral blood sample are beneficial for tuberculosis diagnosis [4].

Masuda et al., in their study in 104 pulmonary tuberculosis patients, found 35.4% of them were positive for acid bacillus testing, 62.5% were positive for culture testing and 14.5% were positive for PCR of peripheral blood. Mycobacterium tuberculosis bacterial virulence is obtained by evaluating its morbidity and mortality [5]. One of the causes of treatment failure in tuberculosis is the presence of Beijing strain that inhibits therapy effectivity. Beijing strain in 33% of Indonesian patients. In experimental animal model, Beijing strain shows high virulence level, severe tissue damage and lower survival rate. Tuberculous spondylitis is clinically divided into two: malignant/virulence tuberculous spondylitis and non-malignant/virulence tuberculous spondylitis. Malignant/virulence tuberculous spondylitis causes severe and multiple damages, skip lesion, higher ESR and abscess [1].

Malignant/virulence tuberculous spondylitis was caused by Mycobacterium tuberculosis Beijing strain as much as 66.7%. Tuberculous spondylitis with large abscess is dominated by Beijing strain as much as 80%, with abscess size 300-1000 mm. Tuberculous spondylitis with ESR 50-100 mm is found in Beijing strain as much as 71.4%. Tuberculous spondylitis with 2-level vertebral destruction is caused by Beijing strain as much as 75% and 60% with multilevel damage and all malignant/ virulence tuberculous spondylitis with disseminated tuberculosis caused by Mycobacterium tuberculosis bacteria [6].

Masuda *et.,al* (2016) in their research proposed a classification or scoring system in assessing tuberculous spondylitis with clinical virulence. Parameters measured in the study were: abscess size, vertebral destruction, disseminated tuberculosis/skip lesion that can be evaluated with MRI, high ESR and Mycobacterium tuberculosis strain that can be detected with PCR test [5]. We can estimate prognosis of each tuberculous spondylitis case from those parameters.

Method of Research

This retrospective-cohort study used malignant tuberculous spondylitis patients participated in the study conducted by Eviyanti *et.,al* (2018). All samples were followed up and evaluated for their clinical, laboratory and radiologic outcomes. New malignant tuberculous spondylitis patients diagnosed during the study period were evaluated for their scores and outcomes [1]. Malignant tuberculous spondylitis patients were treated at Dr. Soetomo Teaching Hospital, Surabaya, Indonesia, from April 2013-June 2015. The inclusion criteria were male and female malignant tuberculous spondylitis patients with paravertebral abscess, multiple spinal collapse and/ or disseminated tuberculous spondylitis and ESR below 20 mm/hour.

We evaluated bony fusion in spinal X-ray tomography, ESR and abscess recurrence. Primary data were obtained from clinical, laboratory and radiologic evaluation results in tuberculous spondylitis patients with anti-tuberculosis drugs, former surgery procedures and classified based on scoring system (Table 1). Secondary data (patient identity, medical history and medication history) were obtained from medical records at Dr. Soetomo Teaching Hospital, Surabaya, Indonesia [7]. The data were categorized based on bony fusion in X-ray, ESR and abscess recurrence. The outcome results were compared with the predicted prognosis scores to test the scores' clinical reliability and usefulness. We processed the data using SPSS 20 SPSS, Inc., Chicago, IL.) [8].

Result

Of 8 samples, only 5 samples could be evaluated (Table 2). Three samples were excluded since one of them refused to participate in the study, while two others suffered from loss of control. Table 3 showed subjects' characteristics by sex, age, abscess size, ESR, vertebrae corpus destruction, skip lesion, Mycobacterium tuberculosis strain based on PCR test results, prognosis classification based on clinical, laboratory and radiologic

evaluations minimum 6 months after surgery. The subjects' average age was 25.8±8.32, average abscess size was 1704.40±1979.50 mL and average ESR was 81.00±19.46 mm/hour.

Male subjects were fewer than female subjects (40% vs 60%). Figure 1 showed 40% samples suffered from 2-level vertebrae corpus destruction and 60% had more than vertebrae corpus destruction level 2.

Figure 3 showed that Mycobacterium tuberculosis Beijing strain mostly infected tuberculous spondylitis subjects (60%). No subjects had good prognosis (0%), 20% had moderate prognosis and 80% had bad prognosis (Figure 4). No subjects had abscess recurrence (0%) after being clinically evaluated 20 months after surgery. The subjects' average ESR was 12.80±7.79 mm/hour. Most samples had bony fusion in spinal X-ray tomography (80%) after being radiologically evaluated 20 months after surgery (Figure 6).

Table 1. Yunus & Prijambodo classification in tuberculous spondylitis

Parameters	Value	Score	%	Beijing	%	Non- Beijing
Abscess	<300	1	22.2	1/6	16	1/3
	300-1000	2	55.6	4/6	66	1/3
	>1000	2	22.2	1/6	16	1/3
ESR	<50	0				
	50-100	1	77.78	5/6	84	2/3
	>100	2	22.2	1/6	16	1/3
Destruction	1 level	0				
	2 level	1	33.3	3/6	48	1/3
	>2 level	2	66.7	3/6	48	2/3
Skip lesion	Yes	2	11.1	1/6	16	0/3
	No	0	88.9	5/6	84	3/3
PCR	Beijing	4	66.7	6		6
	Non-Beijing	2	33.3	3		3

Annotation:

<4 : good prognosis

4-6 : moderate prognosis

>6 : bad prognosis

Table 2. Research data

No.	Name	Sex	Age	Abscess size	EMR	Corpus destruction	Skip Lesion	PCR	Yunus & Prijambodo scoring	Evaluation time (months)	Abscess recurrence	EMR evaluation	Bony fusion
1	Veranatul	F	19	253	94	2 vertebra	(-)	NB	5	24	(-)	19	(+)
2	Yurliani	F	22	2843	105	3 vertebra	(-)	NB	8	17	(-)	20	(-)
3	Sani	F	40	4665	69	2 vertebra	(-)	B	8	19	(-)	16	(+)
4	Sogol	M	22	375	81	5 vertebra	(-)	B	10	21	(-)	6	(+)
5	Rodandi	M	26	386	56	6 vertebra	(-)	B	9	19	(-)	3	(+)
6	Sukarni	F	48	816	121	2 vertebra	(-)	B	9	Drop out	Drop out	Drop out	Drop out
7	Sri Wahyuni	F	29	455	55	5 vertebra	(-)	B	9	Drop out	Drop out	Drop out	Drop out
8	Ummi	F	30	372	52	3 vertebra	(-)	NB	7	Drop out	Drop out	Drop out	Drop out

Table 3. Subjects' characteristics

Subjects' characteristics	
Sex	L = 40% P = 60%
Age (year)	25.8±8.32
Abscess size	1704.40±1979.50 mL
ESR	81.00±19.46 mm/hour
Corpus destruction	2 level = 40% > 2 level = 60%
Skip lesion	Yes = 20% No = 80%
PCR	B = 60% NB = 40%
Yunus & Prijambodo scoring	Good prognosis = 0% Moderate prognosis = 20%
Evaluation	Bad promotion = 80% 20.00±2.65 months
Abscess recurrence	Recurrence = 0% No recurrence = 100%
EMR evaluation	12.80±7.79 mm/hour
Bony fusion	Fusion = 80% No fusion = 20%

Discussion

Tuberculous spondylitis patients' morbidity and mortality could be estimated by determining patient's prognosis. Nevertheless, this diagnosis still becomes a challenging task in orthopedics.

Tabassum & Haider (2016) in their research argued that tuberculous spondylitis is clinically divided into two: malignant/virulence tuberculous spondylitis and non-malignant/virulence tuberculous spondylitis [9]. Mycobacterium tuberculosis Beijing strain mostly causes malignant/virulence tuberculous spondylitis (66.7%) that eventually results in severe and multiple damages, skip lesion, high ESR and abscess [10].

Most subjects in this study were females (60%), with age ranged from 19 to 40 (25.8±8.32). The subjects' abscess sizes were varied from 235 mL to 4,665 mL. This abscess is formed from the accumulation of reactive liquefaction and exudation products of leukocytes, caseous material, bone debris and bacillary tubercle. Some patient's symptoms cannot be seen until paravertebral abscess developed. In this stage, patient will have back pain complaint that may be visible and palpable in physical examination. Recurrent infections may wider abscess in the lumbar region as it expands to a new region with lowest pressure that subsequently forms a skin tract below inguinal ligament or gluteal region [11].

The subjects' average ESR were varied from 56 mm/hour to 105 mm/hour (81.00±19.46 mm/hour). ESR examination tends to be simpler and can be performed in the peripheral areas compared to TNF-α examination. Prasetyo and Prijambodo in their study found no correlation between abscess size and TNF-α. Their study also found a correlation between increased TNF-α level and ESR.

The subjects' corpus destructions were varied from 2 to 6 vertebrae corpus, and 60% of which suffered from more than 2 vertebrae corpus destruction. The higher the destruction level accompanied by larger kyphosis angulation, the longer the spondylitis disease experienced by the patient. Bone destruction occurs due to bone lysis that subsequently makes bone to be softer and flattened due to gravitation and thoracolumbar muscle pull. Bone destruction is exacerbated by secondary ischemia as results of thromboembolism, periarteritis and endarteritis [12]. Since gravitational transmission load in the thoracic vertebrae is more located in the anterior half of vertebral body, more compression lesions are found in anterior vertebral body that subsequently causes vertebral body to be flatter than its posterior [13].

In this study, Mycobacterium tuberculosis Beijing strain mostly infected tuberculous spondylitis patients (60%). This strain mostly caused malignant tuberculous spondylitis (66.7%). Beijing strain mostly dominated tuberculous spondylitis with large abscess (80%), with size ranged from 300 to 1,000 mL. This strain also caused tuberculous spondylitis with ESR 50-100 mm/hour (71.4%), 2-level vertebrae destruction (75%) and multilevel destructions (60%). In addition, this strain mostly caused malignant tuberculous spondylitis with disseminated tuberculosis.

Some parameters included in the study were abscess size, ESR, vertebral destruction, disseminated tuberculosis/skip lesion and infectious Mycobacterium tuberculosis. We found no good prognosis (0%), 20% moderate prognosis and 80% bad prognosis. All subjects had no abscess recurrence after being clinically evaluated 20 months after surgery. The subjects' average ESR was 12.80±7.79 mm/hour, and most subjects had bony fusion in spinal X-ray tomography (80%). The results of clinical, laboratory and radiologic evaluations showed most subjects with moderate or bad prognosis had better outcomes after being evaluated 20 months after surgery [14]. Therefore, further studies should consider other factors affecting tuberculous spondylitis patient's prognosis including host factor.

The host factor is patient's immunity to resist Mycobacterium tuberculosis infection. This depends on age, sex, nutrition status toxic factor and comorbidities. As infants and children, both males and females have weak immunity, and will only increase after puberty. Malnutrition (both in children and adults) will decrease resistance to disease [15]. Tobacco smokers and alcoholic are toxic factors that will lower immune system, as well as other corticosteroid or other immunosuppressant. Comorbidities like HIV, diabetes, leukemia also increase tuberculosis risk [16].

Conclusion

20-month clinical evaluation after surgery in acute tuberculous spondylitis patients showed no abscess recurrence and average ESR was 12.80±7.79 mm/hour (all subjects had ESR lower than 20 mm/hour). Most subjects had bone fusion in spinal X-ray tomography (80%).

Source of Funding : *This paper is funded by authors' money without any sponsorship*

Conflict of Interest*:* There is no conflict of interest due to this research publication.

Ethical Clearance *:* This study obtained research ethical certificate from The Ethical Committee Dr. Soetomo Teaching Hospital Surabaya, Indonesia.

References

1. Evayanti LG, Kalanjati VP, Machin A. A rare widespread tuberculous spondylitis extended from the T5-T10 levels–a case report. In: IOP Conference Series: Materials Science and Engineering. IOP Publishing; 2018. p. 12323.
2. Chu G, Zhang H, Huang J, Wei HU, Wang Y, Kahaer A. Brucellar and tuberculous spondylitis: a comparative study of their imaging features. Chinese J Infect Dis. 2015;(6):335–8.
3. Gunawan H, Mukti I, Mudjanarko SW, Rahmawati LD, Pranoto A. Correlation of radiographic damage and central obesity in ankylosing spondylitis: A cross sectional study. Obes Med. 2019;14:100091.
4. Lacerda C, Linhas R, Duarte R. Tuberculous Spondylitis: A Report of Different Clinical Scenarios and Literature Update. Case Rep Med. 2017;2017.
5. Masuda T, Horiba M, Hirose T, Nakano S, Moroi A, Seki E, et al. Clinical investigation of 6 cases of tuberculous spondylitis. Kekkaku:[Tuberculosis]. 2016;91(11–12):709–15.
6. Gibson J, Coucher J, Coulter C, Eather G. Pleuropulmonary tuberculosis with spinal lesions due to metastatic malignancy differentiated definitively on imaging. BMJ Case Reports CP. 2018;11(1):e226160.
7. Sari NIP, Mertaniasih NM, Maruyama F. Application of serial tests for Mycobacterium tuberculosis detection to active lung tuberculosis cases in Indonesia. BMC Res Notes. 2019;12(1):313.
8. Santosa H, Putra GS, Yuniarta TA, Budiati T. Synthesis and Molecular Docking Studies of N'-benzoylsalicylhydrazide derivatives as antituberculosis through InHA enzym inhibition. Indones J Pharm. 2018;29(4):198–205.
9. Tabassum S, Haider S. Frequency of magnetic resonance imaging patterns of tuberculous spondylitis in a public sector hospital. Pakistan J Med Sci. 2016;32(1):171.
10. Ngadino S, Koerniasari E, SA S. Evaluation of antimycobacterial activity of Curcuma xanthorrhiza ethanolic extract against Mycobacterium tuberculosis H37Rv in vitro. Vet world. 2018;11(3):368.
11. Chernyaeva E, Rotkevich M, Krasheninnikova K, Yurchenko A, Vyazovaya A, Mokrousov I, et al. Whole-genome analysis of mycobacterium tuberculosis from patients with tuberculous spondylitis, Russia. Emerg Infect Dis. 2018;24(3):579.
12. van den Bosch MH, Ascone G, Di Ceglie I, Walgreen B, Sloetjes AW, Lindhout E, et al. P073 High LDL levels lessen bone destruction during antigen-induced arthritis by inhibiting osteoclast formation and function. BMJ Publishing Group Ltd; 2019.
13. Matsumoto T, Abe M. TGF-β-related mechanisms of bone destruction in multiple myeloma. Bone. 2011;48(1):129–34.
14. Winias S. Effect of cynammyldehyde from cinnamon extract as a natural preservative alternative to the growth of Staphylococcus aureus bacteria. Indones J Trop Infect Dis. 2015;2(1):38–41.
15. Yanardag H, Tetikkurt C, Bilir M, Demirci S, Canbaz B, Ozyazar M. Tuberculous Spondylitis: Clinical Features of 36 Patients. Case Reports Clin Med. 2016;5(10):411.
16. Frederika E, Mareta A, Poetranto D, Wulandari L, Setyoningrum RA, Setyowati LL, et al. Identification of influenza viruses in human and poultry in the area of larangan wet market sidoarjo-east java, indonesia. Indones J Trop Infect Dis. 2013;4(4):30–4.