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Retrospective Study Comparing the Characteristics of NTM Vertebral Osteomyelitis and Tuberculous Vertebral Osteomyelitis

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Background

- Nontuberculous mycobacteria (NTM) are ubiquitous in our environment, but scarcely cause significant disease. However, infections such as NTM pulmonary disease, lymphadenitis, skin and soft tissue infections, or osteomyelitis may occur in rare cases.
- While most cases of NTM osteomyelitis are caused by direct inoculation due to trauma, penetrating injuries, or contamination during surgical procedures in immunocompetent patients, various degrees of immunosuppression are found in many patients with NTM vertebral osteomyelitis. In previous studies, *M. avium* complex was the most frequently identified NTM species causing vertebral osteomyelitis, followed by *M. xenopi*, *M. fortuitum*, *M. abscessus*, *M. kansasii*, and *M. simiae*.
- NTM osteomyelitis is clinically, radiologically, and histologically difficult to differentiate from tuberculous (TB) osteomyelitis due to its subacute course and granulomatous nature. Since TB is much more common, NTM osteomyelitis is often misdiagnosed as TB osteomyelitis, and patients are usually started on empiric antituberculous therapy. Since identifying the culprit pathogen in mycobacterial culture takes a long time, NTM osteomyelitis is often aggravated due to inadequate treatment.
- The aim of our study was to compare the characteristics of NTM vertebral osteomyelitis to TB vertebral osteomyelitis in order to aid in the clinical differentiation of the two diseases.

Methods

- A retrospective review was performed to identify patients who were diagnosed with either NTM vertebral osteomyelitis or TB vertebral osteomyelitis between January 2004 and July 2020. Due to the scarcity of cases, we performed a multicenter study including 5 referral hospitals located in South Korea.
- Patients who met both of the following criteria were selected: (1) radiologic findings consistent with vertebral osteomyelitis; and (2) positive NTM or TB cultures on biopsy of the affected bone or surrounding abscesses.
- Data such as demographic characteristics, underlying diseases, symptoms and signs, laboratory findings, radiologic findings, and pathologic findings were acquired. Cases with extra-spinal involvement were recorded, as well as whether the patient received surgical treatment for the vertebral osteomyelitis.

Results

Table 1. Baseline characteristics of patients with NTM and TB vertebral osteomyelitis

	Total (N = 124)	NTM (N = 19)	TB (N = 105)	*P* value
Age at diagnosis (years)	59.9 ± 18.6	68.0 ± 14.5	58.5 ± 18.8	0.01
Male	50 (40.3)	10 (52.6)	40 (38.1)	0.24
Underlying diseases				
Hypertension	50 (40.3)	11 (57.9)	39 (37.1)	0.09
Diabetes mellitus	29 (23.4)	4 (21.1)	25 (23.8)	> 0.99
Solid organ cancer	7 (5.6)	1 (5.3)	6 (5.7)	> 0.99
Chemotherapy within 6 months	0 (0)	0 (0)	0 (0)	
Liver cirrhosis	1 (0.8)	0 (0)	1 (1.0)	> 0.99
Chronic kidney disease	13 (10.5)	2 (10.5)	11 (10.5)	> 0.99
HIV infection	1 (0.8)	1 (5.3)	0 (0)	0.15
Steroid use within 1 month	7 (5.6)	4 (21.1)	3 (2.9)	0.01
Immunosuppressant use within 1 month	6 (4.8)	3 (15.8)	3 (2.9)	0.046
Solid organ transplant	2 (1.6)	1 (5.3)	1 (1.0)	0.28
Stem cell transplant	1 (0.8)	1 (5.3)	0 (0)	0.15
Previous vertebral surgery	23 (18.5)	9 (47.4)	14 (13.3)	< 0.001
Symptoms and signs				
Pain	118 (95.2)	18 (94.7)	100 (95.2)	> 0.99
Any neurologic symptoms	33 (26.6)	7 (36.8)	26 (24.8)	0.27
Motor weakness	27 (21.8)	6 (31.6)	21 (20.0)	0.26
Sensory loss	19 (15.3)	3 (15.8)	16 (15.2)	> 0.99
Bladder or bowel dysfunction	12 (9.7)	2 (10.5)	10 (9.5)	> 0.99
Laboratory results				
WBC (/μL)	6915 (5875-8908)	7800 (6225-11385)	6900 (5700-8780)	0.09
ESR (mm/hr)	66 (41-93)	51 (34-80)	67 (44-93)	0.11
CRP (mg/dL)	4 (1-6)	3 (1-5)	4 (2-6)	0.61
IGRA test performed	51 (41.1)	7 (36.8)	44 (41.9)	
IGRA positive	39 (76.5)	1 (14.3)	38 (86.4)	< 0.001
MRI findings				
Spine involved				
Cervical	7 (5.6)	1 (5.3)	6 (5.7)	> 0.99
Cervicothoracic	2 (1.6)	0 (0)	2 (1.9)	> 0.99
Thoracic	39 (31.5)	4 (21.1)	35 (33.3)	0.42
Thoracolumbar	18 (14.5)	3 (15.8)	15 (14.3)	> 0.99
Lumbar	58 (46.8)	11 (57.9)	47 (44.8)	0.29
Number of involved vertebral bodies	2.7 ± 1.3	2.6 ± 1.2	2.7 ± 1.3	0.81
Abscess formation	99 (79.8)	15 (78.9)	84 (80.0)	> 0.99
Soft tissue inflammation	84 (67.7)	16 (84.2)	68 (64.8)	0.12
Subligamentous spread	51 (41.1)	9 (47.4)	42 (40.0)	0.55
Disc space sparing	36 (29.0)	7 (36.8)	29 (27.6)	0.42
Pathologic findings	90 (72.6)	15 (78.9)	75 (71.4)	
Chronic granulomatous inflammation	53 (58.9)	5 (33.3)	48 (64.0)	0.04
Caseous necrosis	16 (17.8)	1 (6.7)	15 (20.0)	0.29
Inflammation only	27 (30.0)	8 (53.3)	19 (25.3)	0.06
Extra-spinal involvement	59 (47.6)	8 (42.1)	51 (48.6)	0.60
Lung	43 (34.7)	4 (21.1)	39 (37.1)	0.20
Lymph nodes	9 (7.3)	1 (5.3)	8 (7.6)	> 0.99
Other joints	9 (7.3)	3 (15.8)	6 (5.7)	0.14
Central nervous system	2 (1.6)	0 (0)	2 (1.9)	> 0.99
Other sites	12 (9.7)	2 (10.5)	10 (9.5)	> 0.99
Surgical treatment	54 (43.5)	8 (42.1)	46 (43.8)	0.89

Data are expressed as mean ± standard deviation, median (interquartile range), or number (%).

Results

- A total of 19 patients with NTM vertebral osteomyelitis and 105 patients with TB vertebral osteomyelitis were included. Among the patients diagnosed with NTM vertebral osteomyelitis, *M. intracellulare* (52.6%) and *M. abscessus* (26.3%) were the most common pathogens.
- The mean age of patients was significantly older in the NTM vertebral osteomyelitis group (68.0 vs. 58.5 years, $P = 0.01$). Previous steroid or immunosuppressant use was more frequent in the NTM vertebral osteomyelitis group (21.1% vs. 2.9%, $P = 0.01$; 15.8% vs. 2.9%, $P = 0.046$, respectively), as was a history of vertebral surgery (47.4% vs. 13.3%, $P < 0.001$).
- Symptoms such as back pain or neurological signs (motor weakness, sensory loss, and bladder or bowel dysfunction) were similar between the two groups.
- Inflammatory markers such as WBC count, erythrocyte sedimentation rate, and C-reactive protein were also similar between the 2 groups, although the proportion of patients with positive interferon-gamma release assays (IGRA) was significantly higher in the TB vertebral osteomyelitis group (14.3% vs. 86.4%, $P < 0.001$).
- Radiologic (MRI) findings were also similar, with lumbar involvement being the most common in both groups (57.9% vs. 44.8%, $P = 0.29$). Upon pathologic examination, chronic granulomatous inflammation was more frequently seen in TB vertebral osteomyelitis patients (33.3% vs. 64.0%, $P = 0.04$), while inflammation alone was more common in NTM vertebral osteomyelitis.
- Approximately 40% of patients in each group received surgical treatment. Although there was no significant difference in survival after 1 year, survival at last follow-up (median, 24 months) was significantly lower in the NTM vertebral osteomyelitis group (75.0% vs. 98.8%, $P = 0.02$).

Conclusions

- Differentiating NTM and TB vertebral osteomyelitis through clinical signs can be challenging, since the patient characteristics and presenting symptoms of the two diseases are very similar.
- NTM vertebral osteomyelitis should be considered in older patients with a history of immunosuppression or previous vertebral surgery.
- While the pathologic and radiologic findings of NTM vertebral osteomyelitis were similar to that of TB, granulomatous inflammation and positive IGRA tests were more common in TB than NTM vertebral osteomyelitis.