Radiological Findings of Extensively Drug-Resistant Pulmonary Tuberculosis in Non-AIDS Adults: Comparisons with Findings of Multidrug-Resistant and Drug-Sensitive Tuberculosis

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Objective: This study was designed to describe the radiological findings of extensively drug-resistant (XDR) pulmonary tuberculosis (TB) and to compare the observed findings with findings of drug-sensitive (DS) and non-XDR multidrug-resistant (MDR) TB in non-AIDS patients.

Materials and Methods: From September 1994 to December 2007, 53 MDR TB patients (M:F = 32:21; mean age, 38 years) and 15 XDR TB non-AIDS patients (M:F = 8:7; mean age, 36 years) were enrolled in the study. All of the MDR TB patients had received no treatment or less than one month of anti-TB treatment. In addition, all XDR TB patients received either no anti-TB treatment or only first-line anti-TB drugs. In addition, 141 consecutive DS TB patients (M:F = 79:62; mean age, 51 years) were also enrolled in the study for comparison. Chest radiograph, CT and demographic findings were reviewed and were compared among the three patient groups.

Results: For patients with XDR TB, the most frequent radiographic abnormalities were nodules (15 of 15 patients, 100%), reticulo-nodular densities (11 of 15, 73%), consolidation (9 of 15, 60%) and cavities (7 of 15, 47%) that were located mainly in the upper and middle lung zones. As seen on radiographs, significant differences were found for the frequency of nodules and ground-glass opacity lesions (all $p < 0.001$) (more frequent in DS TB patients than in MDR and XDR TB patients). For the use of CT, significant differences (more frequent in MDR and XDR TB patients) were found for the frequency of multiple cavities, nodules and bronchial dilatation ($p = 0.001$ or $p < 0.001$). Patients with MDR TB and XDR TB were younger as compared to patients with DS TB ($p < 0.001$). Imaging findings were not different between patients with MDR TB and XDR TB.

Conclusion: By observation of multiple cavities, nodules and bronchial dilatation as depicted on CT in young patients with acid-fast bacilli (AFB) positive sputum, the presence of MDR TB or XDR TB rather than DS TB can be suggested. There is no significant difference in imaging findings between patients with XDR TB and MDR TB.

Extensively drug-resistant (XDR) tuberculosis (TB) is an emerging life-threatening infection and is caused by a strain of Mycobacterium tuberculosis that is resistant to any type of fluoroquinolone and at least one of the three following injectable drugs: amikacin, capreomycin or kanamycin in addition to isoniazid and rifampin. Multidrug-resistant (MDR) TB is defined as a strain resistant to at least isoniazid and rifampin (1). According to a previous report (2), XDR TB that

has been transmitted to HIV-infected patients is associated with high mortality; in this study, all (44 patients) patients who underwent HIV testing had positive results and 52 (98%) of 53 patients died. The median survival was 16 days from the time of diagnosis in the 42 patients with confirmed dates of death (2).

Extensive drug-resistant TB can also occur in non-AIDS patients. Four to 19% of MDR TB isolates are in fact XDR strains (3, 4). Non-AIDS XDR TB patients are more difficult to treat as compared to patients with non-XDR MDR TB (5–11). In South Korea, approximately 5–20% of MDR TB patients have been confirmed as having XDR TB in both the public and private sectors (3, 5, 7, 10, 12, 13).

As compared with patients with drug-sensitive (DS) pulmonary TB, non-AIDS patients with MDR TB are younger and the patients have a more frequent history of previous TB treatment and show multiple cavitary lung lesions as seen on CT (14). Although clinical features of XDR TB have been reported (5–11, 13), to the best of our knowledge, the imaging findings of XDR TB have not been reported. Thus, the purpose of this study was to describe the radiological findings of XDR pulmonary TB and to compare the observed findings with findings of DS TB and non-XDR MDR TB in non-AIDS patients.

MATERIALS AND METHODS

Our Institutional Review Board approved this study. Patient informed consent was waived for this retrospective study.

Patients

From September 1994 to December 2007, 65 non-AIDS patients with MDR TB (disease that developed in patients with no history of anti-tuberculous chemotherapy or a history of < one month of therapy) were enrolled in the study. Among the 65 patients, a chest radiograph was available for 53 patients and CT scans were available for 42 patients. Seventeen non-AIDS patients with XDR TB (disease that developed in patients with no history of anti-tuberculous chemotherapy (n = 7) or developed in patients who had a treatment history only with the use of first-line drugs (n = 10)) were enrolled in the study. Among the 17 patients, a chest radiograph was available for 15 patients and CT scans were available for seven patients. Imaging studies were obtained within 60 days of the expectoration of the sputum from which MDR TB or XDR TB organisms were isolated. For comparative purposes, we also enrolled 141 consecutive non-AIDS DS TB (defined as disease with no resistance to any drug) patients from June 2003 to June 2004, for whom anti-tuberculous chemotherapy was never given and in whom both chest radiographic and CT studies were performed within 60 days of TB diagnosis. The sample size of this control group (DS TB patients) was based on power analysis (see Appendix) (15, 16).

Intervals between DS TB isolation and the initial chest radiographic or CT examination ranged from −52 days to 26 days (median, −1 day; inter-quartile range, −3~0 days) and from −36 days to 49 days (median, 0 days; inter-quartile range, −2~1 days), respectively. Intervals between MDR TB isolation and the initial chest radiographic or CT examination ranged from −58 days to 6 days (median, 0 days; inter-quartile range, −2~0 days) and from −32 days to 47 days (median, 0 days; inter-quartile range, −1~6.8 days), respectively. Intervals between XDR TB isolation and the initial chest radiographic or CT examination ranged from −4 days to 35 days (median, 0 days; inter-quartile range, 0~7.5 days) and from −1 day to 35 days (median, 8 days; inter-quartile range, 0~14 days), respectively. Intervals between TB isolation and a chest radiograph were significantly longer in XDR TB patients than DS TB patients and MDR TB patients ($p = 0.001$ for a chest radiograph and $p = 0.024$ for CT).

Imaging Technique

Posterior-anterior chest radiographs were obtained with the use of a digital radiography system (Revolution XQi ADS_28.4, GE Medical Systems, Milwaukee, WI) with a focal spot size of 1.25 mm, distance from source to detector of 180 cm, 120 kVp and 200–250 mA.

Helical CT scans were obtained by the use of the following equipment. A single-detector scanner was used for 33 patients (HiSpeed Advantage, GE Medical Systems), a four-detector row scanner was used for 40 patients (LightSpeed QX/I, GE Medical Systems), an eight-detector row scanner was used for 59 patients (LightSpeed Ultra, GE Medical Systems), a 16-detector row scanner was used for 30 patients (LightSpeed16, GE Medical Systems), a 40-detector row scanner was used for five patients (Brilliance 40, Philips Medical Systems, Best, The Netherlands) and a 64-detector row scanner was used for five patients (Aquilion, Toshiba, Tokyo, Japan). Other CT scanners were utilized for 18 patients. None of the patients received an intravenous injection of contrast medium. The scanning parameters were 120 kVp and 90–170 mA. Scanning and image reconstruction for single-detector CT was performed with a section thickness of 5 mm, a pitch of 1 and a reconstruction interval of 5 mm. For the 4–64-detector row CT scanners, scanning and image reconstruction was performed with a beam width of 0.625–10 mm and a beam pitch of 0.875–1.675 and scan data were reconstructed with a 2.5-mm section thickness for transverse images. In

both single and multiple-detector CT, data were reconstructed by the use of a bone algorithm. Image data were directly displayed on monitors (four monitors with 1,536 × 2,048 image matrices, 8-bit viewable gray scale and 60-ft-lambert luminescence) of a picture archiving and communication system (PACS) (Pathspeed or Centricity 2.0; General Electric Medical Systems Integrated Imaging Solutions, Mt. Prospect, IL). Both mediastinal (window width, 400 HU; window level, 20 HU) and lung (window width, 1,500 HU; window level, −700 HU) window images were available on the monitors for analysis.

Analyses of Radiographic and CT Findings

Reviews of chest radiographs and CT scans were performed at least two months apart for concern of recall bias. Chest radiographs and CT scans were reviewed in a random order by two independent thoracic radiologists for frequency and extent (involved zones on radiographs or the number of lobes seen on CT images) of lung lesions, and decisions on findings were reached by consensus. If controversy arose, a third reviewer repeatedly reviewed the cases based on the analyses of the previous two reviewers.

For the chest radiographic analyses, we divided each lung into three zones, and each zone was assessed separately. Lesions were considered located in the upper zone if they were located cephalad to the aortic arch, in the lower zone if they were located caudad to the inferior pulmonary vein and in the middle zone if they were located in between the other two areas. The overall extent of each pattern was estimated by calculating the number of the involved zones (six zones for each patient). The observers assessed the extent and presence of lung parenchymal abnormalities including reticulo-nodular opacity, nodule size (a small nodule < 10 mm in diameter; large nodule, 10–30 mm), all nodules (small nodules or large nodules), consolidation and ground-glass opacity (GGO). The number of cavities and the presence or absence of pleural effusion and lymphadenopathy were also recorded. Reticulo-nodular opacity was regarded present when combined reticular and nodular opacity was observed. A nodule was considered present when there was rounded opacity that was well-defined or poorly defined. Consolidation was defined as a homogeneous increase in pulmonary parenchymal opacity that obscured the margins of vessels and airway walls. GGO was defined as an area of hazy increased lung opacity, within which margins of pulmonary vessels may be indistinct. A cavity was regarded present when a gas-filled space was noticed within pulmonary consolidation, a mass or a nodule (17).

On CT scans, the presence of each parenchymal abnormality in each lobe (six lobes: right upper lobe, right

Table 1. Comparisons of Demographic Data among 141 Patients with Drug-Sensitive Tuberculosis, 53 Patients with Multidrug-Resistant Tuberculosis and 15 Patients with Extensively Drug-Resistant Tuberculosis

	DS TB (n = 141)	MDR TB (n = 53)	XDR TB (n = 15)	*P* values
Age, years (mean ± SD)	51 ± 19.1	38 ± 17.5	36 ± 16.5	< 0.001*
	(53, 1.61, 15–85)	(31, 2.41, 15–74)	(30, 4.27, 19–75)	
Sex (M:F)	79 : 62	32 : 21	8 : 7	0.826

Note.— *Kruskal-Wallis test was used to compare three, different groups. DS TB = drug-sensitive tuberculosis, MDR TB = multidrug-resistant tuberculosis, XDR TB = extensively drug-resistant tuberculosis, SD = standard deviation. Numbers in parentheses are median, standard error and range.

Table 2. Presence of Parenchymal Abnormalities among Three Groups as Depicted on Chest Radiographs

	DS TB (n = 141)	MDR TB (n = 53)	XDR TB (n = 15)	*P* values	Meanings†
Reticulo-nodular opacity	112 (79)	40 (75)	11 (73)	0.757	
All nodules	125 (89)	44 (83)	15 (100)	0.187	
Small nodules	123 (87)	43 (81)	12 (80)	0.478	
Large nodules	97 (69)	18 (34)	9 (60)	< 0.001	MDR < DS*
Consolidation	111 (79)	36 (68)	9 (60)	0.122	
GGO lesion	90 (64)	10 (19)	5 (33)	< 0.001	MDR = XDR < DS
Cavities	73 (52)	23 (43)	7 (47)	0.570	DS < MDR = XDR
Multiple cavities	8 (6)	9 (17)	3 (20)	0.021	MDR < DS*
Pleural effusion	81 (57)	16 (30)	5 (33)	0.002	MDR < DS*
Lymphadenopathy	41 (29)	12 (23)	1 (7)	0.140	

Note.— †Meanings were derived from paired comparisons of each of two groups. *XDR TB as compared with MDR TB or XDR TB as compared with DS TB was not significant. Numbers in parentheses are percentages. DS TB = drug-sensitive tuberculosis, MDR TB = multidrug-resistant tuberculosis, XDR TB = extensively drug-resistant tuberculosis, GGO = ground-glass opacity

middle lobe, right lower lobe, upper division of the left upper lobe, lingular division of the left upper lobe and the left lower lobe) was recorded. The observers assessed the extent and presence of tree-in-bud signs (centrilobular nodules less than 10 mm in diameter and branching nodular structures within a secondary pulmonary lobule), small nodules (nodules < 10 mm in diameter), large nodules (10–30 mm in diameter), all nodules (small nodules or large nodules), consolidation, GGO and bronchial dilatation (17). The number of cavities (summed number of cavitating nodules or masses and cavitating consolidation), presence of pleural effusion, pleural thickening, pericardial effusion and lymphadenopathy were also recorded.

Statistical Analyses

Statistical analyses were performed using SPSS software (version 12.0; SPSS, Chicago, IL). The significances of differences of sex and the frequency of each pattern of parenchymal abnormality in the three disease groups were evaluated using the chi-square test. The Kruskal-Wallis test was used to compare differences of age, number of cavities and the extent of involvement (i.e., the number of involved lobes) of each pattern of parenchymal abnormality in the three groups. If significant differences among the three groups were determined with use of the Kruskal-Wallis test, the Mann-Whitney test was used to determine the difference between any two groups. For all statistical values, a p value of less than 0.05 was considered to indicate a statistically significant difference.

RESULTS

Patients Demographics

The demographic data of the three patient groups are summarized in Table 1. The mean age of all patients was 47 years and the age range was 15–85 years. The mean ages were significantly different for the DS TB group (mean age, 51 years; median age, 53 years; age range, 15–85 years, standard error, 1.61), the MDR TB group (mean age, 38 years; median age, 31 years; age range, 15–74

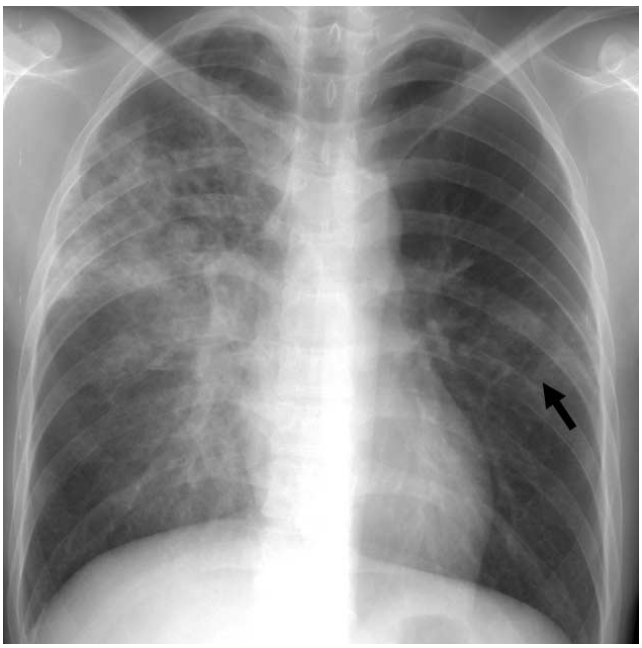


Fig. 1. Findings for extensively drug-resistant pulmonary tuberculosis in 29-year-old man. Posterior-anterior chest radiograph shows nodules, consolidation containing cavities and ground-glass opacity in right lung and reticulo-nodular lesions (arrow) in left middle lung zone.

Table 3. Extent of Parenchymal Abnormalities and Number of Cavities in Three Groups as Depicted on Chest Radiographs

	DS TB (n = 141)	MDR TB (n = 53)	XDR TB (n = 15)	*P* values	Meanings
Reticulo-nodular opacity	1.13 ± 0.88	1.58 ± 1.54	1.47 ± 1.13		
	(1, 0.07, 0–5)	(1, 0.21, 0–6)	(2, 0.29, 0–3)	0.233	
Small nodules	1.48 ± 1.02	1.55 ± 1.42	1.53 ± 1.13		
	(1, 0.09, 0–5)	(1, 0.20, 0–6)	(2, 0.29, 0–4)	0.851	
Large nodules	0.96 ± 0.92	0.43 ± 0.69	0.80 ± 0.78		
	(1, 0.08, 0–5)	(0, 0.10, 0–3)	(1, 0.20, 0–2)	< 0.001	MDR < DS*
Consolidation	1.20 ± 1.03	1.08 ± 0.98	1.20 ± 1.32		
	(1, 0.09, 0–5)	(1, 0.13, 0–3)	(1, 0.34, 0–4)	0.746	
GGO lesion	0.89 ± 0.92	0.36 ± 0.83	0.53 ± 0.83		
	(1, 0.07, 0–5)	(0, 0.12, 0–4)	(0, 0.22, 0–2)	< 0.001	MDR < DS*
Number of cavities	0.63 ± 0.81	0.68 ± 0.96	0.80 ± 1.15		
	(1, 0.07, 0–5)	(0, 0.13, 0–4)	(0, 0.30, 0–4)	0.943	

Note.— *XDR TB as compared with MDR TB or XDR TB as compared with DS TB is not significant. Numbers represent mean ± standard deviation of involved zones. Numbers in parentheses are median, standard error and range. DS TB = drug-sensitive tuberculosis, MDR TB = multidrug-resistant tuberculosis, XDR TB = extensively drug-resistant tuberculosis, GGO = ground-glass opacity

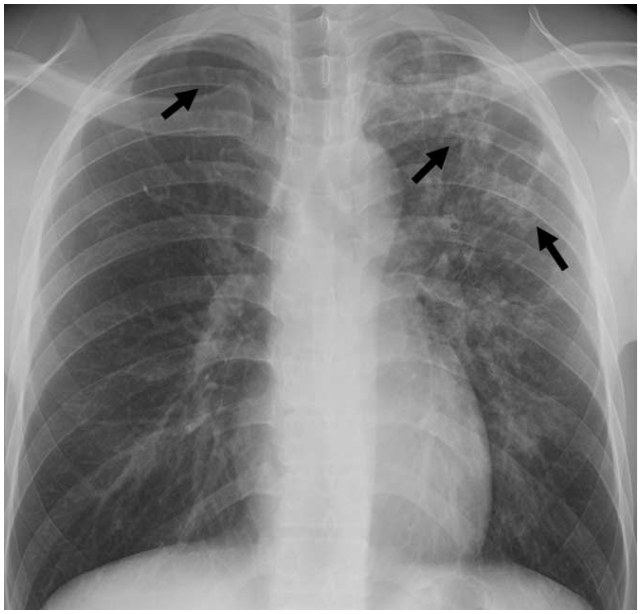
years, standard error, 2.41) or the XDR TB group (mean age, 36 years; median age, 30 years; age range, 19–75 years, standard error, 4.27). Patients with DS TB were older as compared to patients with MDR TB or XDR TB ($p < 0.001$). There was no significant age difference between patients with MDR TB and XDR TB. The sex ratio was not significantly different among the three groups.

Imaging Findings

Chest Radiographic Findings

The radiographic findings of the three patient groups with TB are summarized in Tables 2 and 3, and the radiographic findings for XDR TB patients are described in Table 4. For XDR TB patients, the most frequent patterns of lung involvement were all nodules (small nodules or large nodules, 15 of 15 patients, 100%), reticulo-nodular densities (11 of 15, 73%) and consolidation (9 of 15, 60%). Cavities were observed in seven (47%) patients (Table 2). All of these patterns for parenchymal lesions were predominantly located in the upper and middle lung zones (Table 4) (Figs. 1 and 2).

The most common finding in all three groups was all nodules (observed in 89%, 83% and 100% for patients with DS TB, MDR TB and XDR TB, respectively) (Table 2) (Figs. 1–3). The frequency of GGO and pleural effusion was significantly higher in patients with DS TB as compared to patients with MDR TB and XDR TB ($p < 0.001$). Multiple cavities were more frequently observed in MDR TB and XDR TB patients as compared to DS TB patients ($p = 0.021$) (Figs. 1 and 2). Large nodules ($p < 0.001$) and GGO lesions ($p < 0.001$) were more extensive in DS TB patients as compared to MDR TB patients (Table



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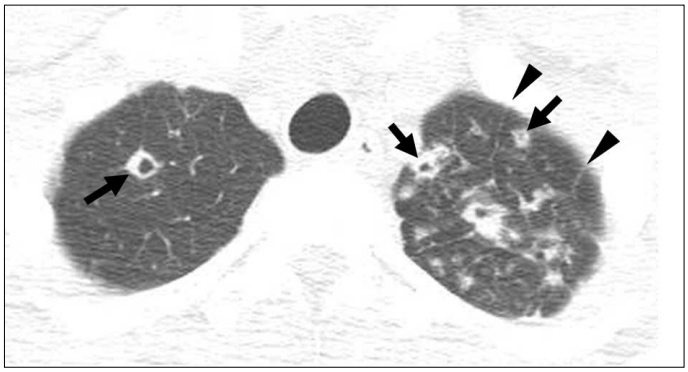

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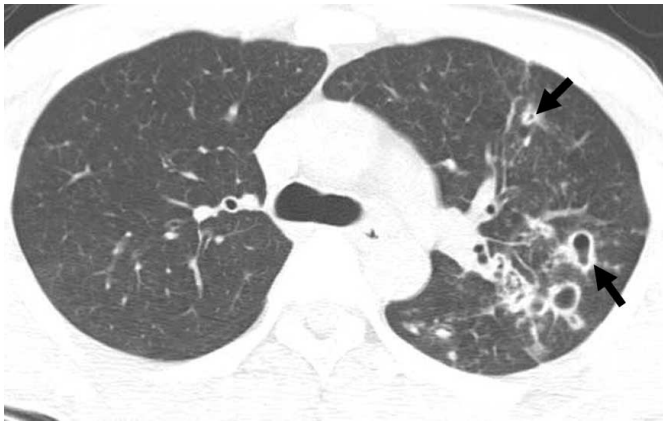

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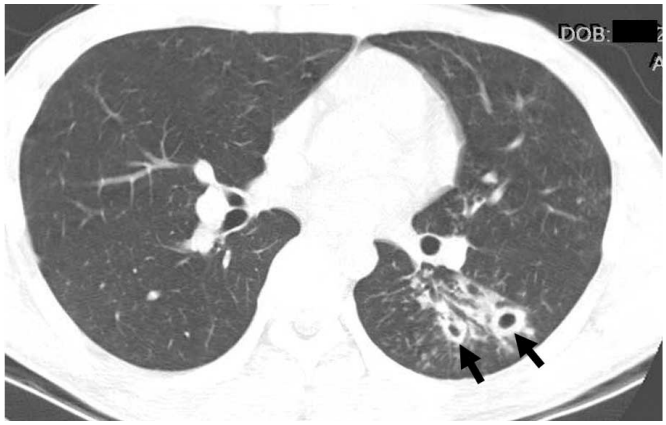

D

Fig. 2. Findings for extensively drug-resistant pulmonary tuberculosis in 22-year-old man.
A. Posterior-anterior chest radiograph shows small nodular lesions, reticulo-nodular lesions and cavitating nodules (arrows) mainly in left upper and middle lung zones and in right apex.
B-D. Transverse CT (2.5-mm section thickness) scans obtained at levels of great vessels (**B**), main bronchi (**C**) and left basal trunk (**D**), respectively, show small nodules and cavitating nodules (arrows) mainly in left upper lobe and superior segment of left lower lobe. Also, note mild interlobular septal thickening (arrowheads) in left upper lobe.

3). There was no significant difference in the radiographic findings between MDR TB and XDR TB patients.

CT Findings

The CT findings of the three patient groups with TB are summarized in Tables 5 and 6. For XDR TB patients, the most frequent patterns of lung involvement were all nodules (6 of 7 patients, 86%), and the tree-in-bud sign (5 of 7 patients, 71%). Cavities were observed in three (43%) patients. All of these patterns of parenchymal lesions were predominantly located in the upper and lower lobes (Table 4) (Fig. 2).

The most common pattern in the three groups was all nodules (observed in 93%, 98% and 86% of DS TB, MDR TB and XDR TB patients, respectively) (Table 5) (Figs. 2 and 3). Large nodules were more commonly observed in MDR TB patients (71%, mean extent 1.19 lobes) as compared to DS TB patients (50%, mean extent 0.83 lobes) ($p = 0.015$) (Tables 5 and 6). The extent of small nodules was significantly larger in patients with MDR TB as compared to patients with DS TB ($p = 0.049$) (Table 6). Multiple cavities were also more commonly observed in patients with MDR TB (40%) as compared to patients with DS TB (15%) ($p < 0.002$) (Fig. 2). The mean number of cavities for DS TB, MDR TB and XDR TB patients were 1.38, 2.45 and 4.86, respectively (Table 6). Bronchial dilatation was more common in XDR TB patients (43%, mean extent 0.43 lobe) and MDR TB patients (55%, mean

Table 4. Chest Radiographic and CT Findings of Extensively Drug-Resistant Pulmonary Tuberculosis

Patterns	Radiographic Findings (n = 15)								Patterns	CT Findings (n = 7)							
	Laterality		Zonal Involvement							Laterality		Involved Lobes					
	Uni	Bi	RU	RM	RL	LU	LM	LL		Uni	Bi	RU	RM	RL	LU	Li	LL
RN opacity (n = 11)	9	2	10	1	0	6	4	1	TBS (n = 5)	3	2	3	0	1	1	1	1
All nodules (n = 15)	5	10	10	3	3	6	5	4	All nodules (n = 6)	4	2	6	0	3	2	1	1
Small nodules (n = 12)	4	8	9	3	2	3	4	2	Small nodules (n = 6)	4	2	6	0	3	2	1	1
Large nodules (n = 9)	8	1	4	2	1	4	1	0	Large nodules (n = 6)	5	1	3	0	1	2	0	1
Consolidation (n = 9)	9	0	6	5	2	3	2	0	Consolidation (n = 3)	2	1	2	1	1	1	0	0
GGO (n = 5)	5	0	0	2	1	3	2	0	GGO (n =0)	0	0	0	0	0	0	0	0
Cavity (n = 7)	5	2	6	1	0	2	2	1	Cavity (n = 3)	2	1	3	0	0	1	1	1

Note.— Uni = unilateral, Bi = bilateral, RU = right upper, RM = right middle, RL = right lower, LU = left upper, LM = left middle, Li = lingular division, LL = left lower, RN = reticulo-nodular, GGO = ground-glass opacity, TBS = tree-in-bud sign

Table 5. Presence of Parenchymal Abnormalities in Three Groups as Depicted on CT Images

	DS TB (n = 141)	MDR TB (n = 42)	XDR TB (n = 7)	*P* values	Meanings
Tree-in-bud signs	97 (69)	37 (88)	5 (71)	0.046	DS < MDR
All nodules	131 (93)	41 (98)	6 (86)	0.369	
Small nodules	124 (88)	40 (95)	6 (86)	0.380	
Large nodules	71 (50)	30 (71)	6 (86)	0.015	DS < MDR*
Consolidation	91 (65)	30 (71)	3 (43)	0.319	
GGO	35 (25)	7 (17)	0 (0)	0.191	
Bronchial dilatation	26 (18)	23 (55)	3 (43)	< 0.001	DS < MDR = XDR
Cavities	51 (36)	29 (69)	3 (43)	0.001	DS < MDR*
Multiple cavities	21 (15)	17 (40)	2 (29)	0.002	DS < MDR*
Pleural effusion	36 (26)	10 (24)	3 (43)	0.561	
Pleural thickening	16 (11)	4 (10)	3 (43)	0.038	DS = MDR < XDR
Pericardial effusion	6 (4)	4 (10)	1 (14)	0.271	
Lymphadenopathy	46 (33)	6 (14)	2 (29)	0.069	

Note.— *XDR TB as compared with MDR TB or XDR TB as compared with DS TB is not significant. Numbers in parentheses are percentages. DS TB = drug-sensitive tuberculosis, MDR TB = multidrug-resistant tuberculosis, XDR TB = extensively drug-resistant tuberculosis, GGO = ground-glass opacity

extent 0.67 lobe) as compared to DS TB patients (18%, mean extent 0.34 lobe) ($p < 0.001$). Tree-in-bud signs were more commonly ($p = 0.046$) and extensively ($p = 0.010$) involved in MDR TB patients (88%, mean extent 2.33 lobes) as compared to DS TB patients (69%, mean extent 1.55 lobes). Pleural thickening was more frequently observed in XDR TB patients (43%) as compared to DS TB (11%), and MDR TB (10%) patients. Except for the pleural thickening, no significant differences were determined for frequency and extent of parenchymal abnormalities between MDR TB patients and XDR TB patients with the use of CT.

DISCUSSION

In our study, as compared to involvement for MDR TB patients, as seen on chest radiographs, large nodules and GGO lesions were more frequently observed and showed more extensive involvement. Multiple cavities were more common in MDR TB and XDR TB patients as compared to DS TB patients. With the use of CT, large nodules, bronchial dilatation and multiple cavities were observed more frequently in XDR and MDR TB patients as compared to DS TB patients. In addition, the number of cavities involved and the number of lobes containing small nodules were higher in MDR TB patients as compared to DS TB patients. Thus, for MDR TB or XDR TB patients as compared to DS TB patients with the use of CT, parenchymal lesions that were more extensive were seen. GGO lesions were more frequently observed for DS TB patients as compared to MDR TB or XDR TB patients as seen on chest radiographs. However, for the use of CT, there was no significant difference in the frequency of GGO lesions among the three groups. Chest radiographs did not accurately show disease processes (more frequent and

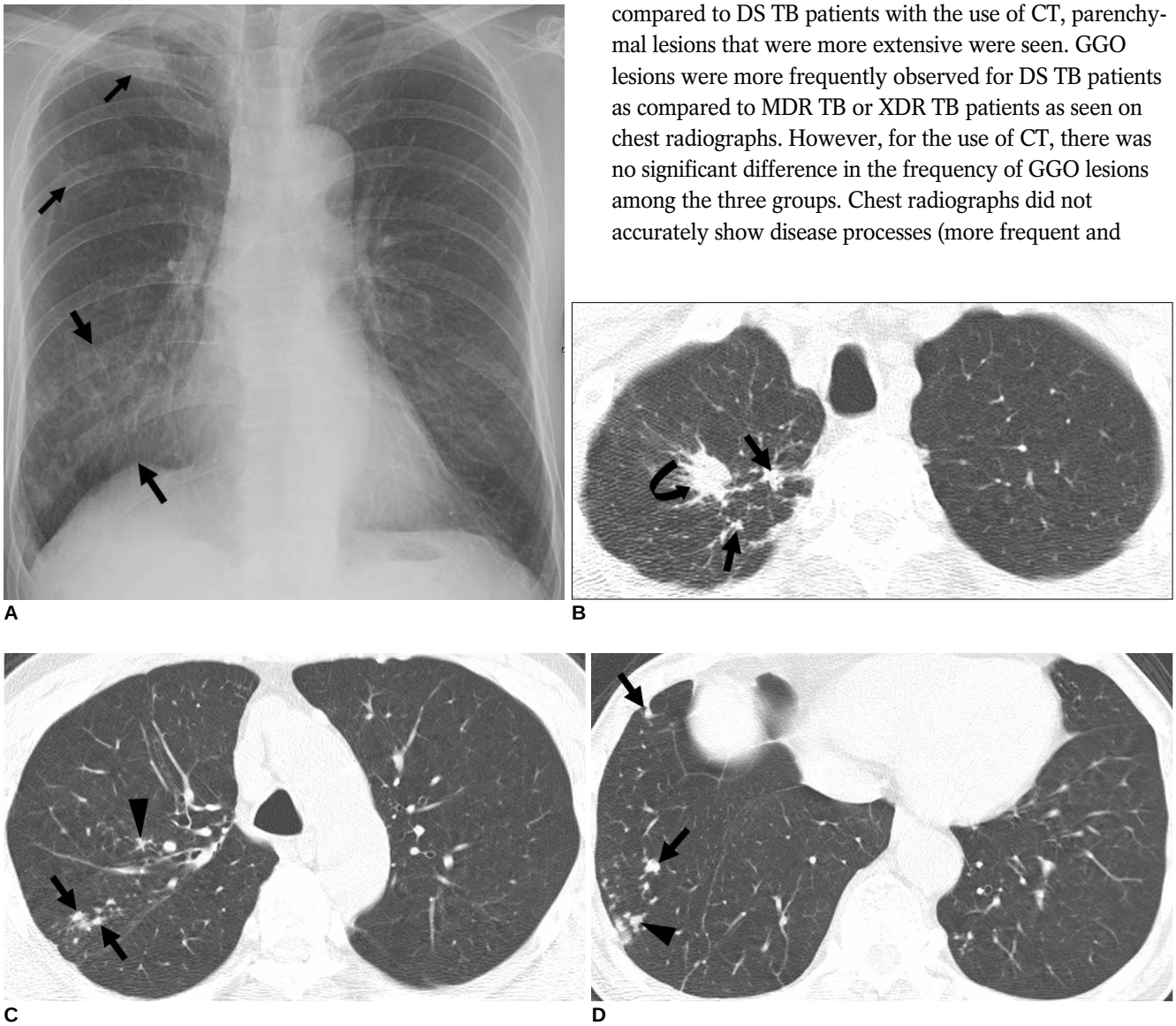

Fig. 3. Findings for drug-sensitive tuberculosis in 70-year-old man.
A. Posterior-anterior chest radiograph shows small nodular lesions (small arrows) in right upper lung zone and variable-sized nodules and reticulo-nodular lesions (large arrows) in right lower lung zone.
B-D. Transverse CT (2.5-mm section thickness) scans obtained at levels of great vessels (**B**), aortic arch (**C**) and liver dome (**D**), respectively, show small nodules (arrows), tree-in-bud signs (arrowheads) and nodules (curved arrow) in right upper lobe and right lower lobe.

Table 6. Extent of Parenchymal Abnormalities and Number of Cavities in Three Groups as Depicted on CT Images

	DS TB (n = 141)	MDR TB (n = 42)	XDR TB (n = 7)	*P* values	Meanings
Tree-in-bud signs	1.55 ± 1.53 (1, 0.13, 0–6)	2.33 ± 1.71 (2, 0.26, 0–6)	1.00 ± 1.00 (1, 0.38, 0–3)	0.010	DS = XDR < MDR
Small nodules	2.21 ± 1.58 (2, 0.13, 0–6)	2.88 ± 1.70 (3, 0.26, 0–6)	1.86 ± 1.57 (1, 0.60, 0–4)	0.049	DS < MDR*
Large nodules	0.83 ± 1.04 (1, 0.09, 0–5)	1.19 ± 1.13 (1, 0.18, 0–5)	1.00 ± 0.58 (1, 0.22, 0–2)	0.069	
Consolidation	1.13 ± 1.15 (1, 0.10, 0–5)	1.17 ± 1.03 (1, 0.16, 0–3)	0.71 ± 1.11 (0, 0.42, 0–3)	0.453	
GGO	0.57 ± 1.29 (0, 0.11, 0–6)	0.21 ± 0.57 (0, 0.09, 0–3)	0.00 ± 0.00 (0, 0, 0)	0.153	
Bronchial dilatation	0.34 ± 0.84 (0, 0.07, 0–4)	0.67 ± 0.72 (1, 0.11, 0–3)	0.43 ± 0.54 (0, 0.20, 0–1)	< 0.001	DS < MDR*
Number of cavities	1.38 ± 5.99 (0, 0.50, 0–50)	2.45 ± 4.87 (1, 0.75, 0–30)	4.86 ± 11.14 (0, 4.21, 0–30)	< 0.001	DS < MDR*

Note.— *XDR TB as compared with MDR TB or XDR TB as compared with DS TB is not significant. Numbers represent mean ± standard deviation of involved lobes. Numbers in parentheses are median, standard error and range. DS TB = drug-sensitive tuberculosis, MDR TB = multidrug-resistant tuberculosis, XDR TB = extensively drug-resistant tuberculosis, GGO = ground-glass opacity

extensive involvement of nodular lesions for MDR and XDR TB patients) observed with the use of CT. These findings were probably due to limited resolution and a summation effect of overlapping lesions associated with the use of chest radiography. The inferior capability of chest radiography as compared to CT to distinguish between MDR TB and DS TB has also been reported in previous studies (18–20).

It has been reported that multiple cavities and bronchiectasis are more frequently observed in MDR TB patients as compared to DS TB patients (14, 21). Our results were similar to previous results. Fishman et al. (18) have reported that although the overall radiographic findings and patterns of MDR TB patients and DS TB patients are similar, there are significant differences among patients depending on how MDR TB is acquired. Most patients with primary drug resistance (in this study all of 33 patients were HIV-positive and the mean CD4 count in these patients was 108 cells/μL) showed a primary form of TB with abnormalities such as noncavitary consolidation, pleural effusion and lymphadenopathy. Cavitary disease was more common in patients who acquired MDR TB secondary to noncompliance with therapy (63% [17 of 27 patients] of the patients were HIV-positive, and the mean CD4 count in these patients was 194 cells/μL). Cavitation was less frequent in patients with MDR TB who were HIV-positive and excessively immunocompromised as compared to HIV-negative and immunocompetent patients.

Our results differed from the findings reported by Fishman and colleagues (18). In our study, all patients were HIV-negative and had primary drug resistance. However, cavities were more common and extensive in XDR TB patients or MDR TB patients than in DS TB patients. Moreover, nodules depicted on CT were the most frequent lung abnormalities observed and had involvement that was more extensive in XDR TB or MDR TB patients than in DS TB patients. Thus, cavitary lesions and nodules were the predominant CT patterns of lung abnormalities in non-AIDS XDR and MDR TB patients. These observations indirectly corroborate the findings of a previous report where the most important determinant of radiologic patterns of parenchymal abnormalities was patient immunity (i.e., HIV sero-positivity and a decreased CD4 count < 200 cells/μL) rather than the drug-resistance intensity of the organisms involved (22).

In South Korea, TB remains a major public health threat and an economic burden. A national survey disclosed 35,269 new cases (73 of 100,000 population) in 2005 (23). MDR TB strains occurred in 3% of new cases and in 14% of previously treated cases (24) and approximately 5–20% of MDR TB patients were confirmed as having XDR TB (5–11, 13). In our institution, we saw 366 patients with MDR TB over 13 years, and of these 366 patients, 52 (14%) were confirmed as having XDR TB infections.

Drug resistance can develop during inadequate antituberculous chemotherapy that enables selection of drug-resistant organisms (acquired resistance). Radiological findings might show inadvertently progressed features with an ongoing infection (chronic TB infection) during the development of acquired resistance. Thus, we have included only patients who had a primary resistant form of

MDR TB (who had received no or less than one month of anti-TB treatment) and XDR TB patients (who had received no or less than one month of anti-TB treatment or received only first-line anti-TB drugs).

In our study, there was no difference in imaging findings in terms of frequency and extent of each parenchymal abnormality between XDR TB patients and MDR TB patients except for pleural thickening. Therefore, it does not seem to be possible to differentiate between MDR TB and XDR TB based on imaging findings alone. The clinical significance of the difference in the frequency of pleural thickening was not clear. For DS TB and MDR TB, the frequency of pleural thickening was not different (11% versus 10%). For XDR TB patients, the frequency was 43% (in three of seven patients). The small number of XDR TB patients might has been one of factors for such a difference, but a further study with more cases is required.

Age was significantly different among the three groups. Patients with DS TB (mean age, 51 years) were older than patients with MDR TB (mean age, 38 years) or XDR TB (mean age, 35 years). We do not know the precise cause of this difference. One possible reason may be the year in which effective anti-TB drug therapies (such as rifampin therapy) were started. In South Korea, rifampin-based regimens were given first in the private sector during the 1980s, and the current 6-month, four-drug (including rifampin) regimen became standard in the national tuberculosis plan in 1990. Elderly patients likely acquired the organisms in the past when the circulating bacilli were susceptible to the current regimen, whereas young patients likely acquired the bacilli more recently, when the bacilli were more likely to be resistant. Other related factors (drug resistance in young adults) may be due to decreased patient immunity caused by the declining BCG effect (most older people in South Korea received BCG vaccinations) and an unhealthy lifestyle (lack of exercise and sudden excessive weight loss to maintain a thin body habitus) in young adults.

This study has several limitations. First, as our study was retrospective in design, not all patients underwent both chest radiography and CT. Moreover, patients were selected over a long period and the times of selection for the three groups were different. Although we selected patients over a long period, we still found only a small number of patients with XDR TB. Thus, the difference in imaging findings among DS TB, MDR TB, and XDR TB patients might be underestimated. However, the number of XDR TB cases in non-AIDS patients is extremely small. Second, selection bias may also have existed in our study. As our institution is a tertiary referral hospital, patients with more grave symptoms or cases that were more complicated might have been selectively included. Third, the exact time between symptom onset and an imaging study in our study could have not been provided owing to a long period of patient selection and the retrospective design. Instead, we were aware of interval between sputum acid-fast bacilli (AFB) isolation and the imaging studies. Imaging findings of pulmonary tuberculosis may depend on the chronicity or disease-ongoing period. A further study on imaging findings of XDR TB in consideration of chronicity of the disease needs to be performed.

In conclusion, MDR and XDR pulmonary TB in non-AIDS patients is characterized with the use of CT by more extensive parenchymal lesions of the post-primary form of TB containing multiple cavities than DS tuberculosis and is more frequently observed in young patients. Thus, when young non-AIDS patients have culture-positive AFB and show multiple cavities, nodules and bronchial dilatation as depicted on CT, the presence of MDR or XDR TB infection should be considered. The disease pattern and extent of MDR and XDR TB are similar.

Appendix

The sample size of the control group (DS TB patients) was determined based on the use of formulas described by Fleiss et al. (16) for unequal sample size analysis. According to previous studies about the comparison of radiological findings among MDR, XDR and DS TB patients (5, 14), the most significantly different radiological finding was multiple cavitation, which was predicted to be 0.15 for DS TB, 0.6 for MDR TB and 0.6 for XDR TB. The estimated total patient number determined by use of the chi-squared test for multiple proportions was 203 by using a power of 0.90, alpha of 0.05 and the above proportional settings. From the given patient number for MDR TB and XDR TB of 68, we determined that the minimum required sample size for DS TB patients was 135.

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