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7 **The Findings of Pulmonary Nocardiosis on Chest High Resolution**
8 **Computed Tomography**

9 *A single center experience and review of literature*

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15
16 **Abstract**

17 **Objectives:** Pulmonary nocardiosis is a rare opportunistic infection that is often encountered
18 in immunocompromised patients, in particular those with human immunodeficiency virus
19 (HIV) infection and in solid organ transplant recipients. As the number of
20 immunocompromised patients increase, it is expected that the number of patients with
21 pulmonary nocardiosis will increase. The aim of this study is to review the chest HRCT
22 findings of patients with confirmed pulmonary nocardiosis and to review the imaging
23 features of pulmonary nocardiosis in the literature. **Methods:** We searched the electronic
24 database of the Royal Hospital, Muscat, Oman for patients with a diagnosis of pulmonary
25 nocardiosis between January 2006 and January 2019. Nine patients with pulmonary
26 nocardiosis were identified, but three patients were excluded as no chest HRCT images were
27 available. Patient clinical presentation was recorded and chest HRCT images were
28 retrospectively reviewed. **Results:** The six patients enrolled in the study were male, aged
29 between 29 and 49 years. Three patients were immunocompromised, two of whom had
30 undergone a renal transplant. The main HRCT findings were cavitary nodules/masses, non-
31 cavitary nodules/masses, septal thickening, centrilobular nodules, ground glass opacities,
32 consolidation, pleural effusion, pleural thickening, enlarged lymph nodes and necrotic lymph

33 nodes. **Conclusion:** Pulmonary nocardiosis has various findings on chest CT. Most common
34 are pulmonary nodules and masses. Awareness of these findings can help radiologists to
35 suggest the diagnosis in the appropriate clinical settings.

36 **Keywords:** Nodules; Masses; Lung Infections; Opportunistic Pathogen; Pulmonary
37 Nocardiosis; Computed Tomography.

38

39 **Advances in Knowledge**

- 40 • The findings of this study demonstrate that pulmonary nocardiosis can have different
41 findings on chest CT including pulmonary nodules, masses and consolidation.

42

43 **Application to Patient Care**

- 44 • This study highlights the most common findings of pulmonary nocardiosis on chest
45 HRCT. This can help to establish early diagnosis and to start treatment without delay.

46

47 **Introduction**

48 Nocardiosis is a rare infection caused by a group of aerobic, weekly staining Gram-positive
49 and partially acid-fast bacteria called *Nocardia*, which is found in the water, dust, soil,
50 stagnant matter and decaying vegetation.¹

51

52 Humans contract a *Nocardia* infection mainly by inhalation or direct inoculation through the
53 skin. The most susceptible people to nocardiosis are immunocompromised patients, in
54 particular patients with impaired cell immunity such as patients with human
55 immunodeficiency virus (HIV) infection and solid organ transplant recipients. Approximately
56 one third of nocardiosis cases occur in immunocompetent patients.²⁻⁴ With the increasing
57 number of immunocompromised patients, the number of patients suffering from nocardiosis
58 might increase as well.⁵

59

60 Clinically, patients with pulmonary nocardiosis present with non-specific symptoms such as
61 fever, dyspnoea and productive cough, making the clinical diagnosis difficult. If the correct
62 diagnosis could be made early, patients can be started on treatment without delay. This would
63 prevent the dissemination of the infection to the other parts of the body, especially to the
64 brain, which its associated high mortality rate.^{6,7} Therefore, immediate diagnosis and
65 treatment of pulmonary nocardiosis is essential to decrease disease morbidity and mortality.

66

67 In the literature, there have been few studies on pulmonary HRCT findings in patients with
68 pulmonary nocardiosis.^{2, 8-15} Therefore, the aim of this study was to review the chest HRCT
69 findings in pulmonary nocardiosis and to compare our findings with published studies in the
70 literature.

71

72 **Patients and Methods**

73 The Scientific Research Committee of The Royal Hospital, Muscat, Oman has approved this
74 retrospective single institution study and waived informed consent.

75

76 We searched The Royal Hospital database for patients with a confirmed diagnosis of
77 pulmonary nocardiosis that were treated between January 2006, and January 2019. We
78 identified nine patients with pulmonary nocardiosis, but three patients were excluded as they
79 did not have chest computed tomography (CT).

80

81 Clinical presentations at presentation and related medical history were documented. The
82 HRCT images were reviewed by a cardiothoracic radiologist with 10 years of experience.
83 The chest HRCT were evaluated for consolidation, centrilobular nodules, nodules/masses,
84 ground-glass opacities, interlobular septal thickening, bronchial wall thickening, cavitation,
85 enlarged hilar/mediastinal lymph node(s) (defined as a short diameter >1 cm) and pleural
86 thickening/effusion. Extrathoracic findings were also recorded if present. The chest HRCT
87 findings were defined according to the Glossary of terms for thoracic imaging proposed by
88 the Fleischner Society.¹⁶

89

90 **Results**

91 *Clinical features*

92 We analysed six patients with pulmonary nocardiosis. All of them were male aged between
93 29 and 49 years (mean age: 40.5, SD \pm 11 years). Three patients were immunocompromised,
94 two of whom had undergone a renal transplant and one was on corticosteroids. Of the
95 immunocompetent patients, one had bronchiectasis and one had gastrobronchial fistula as a
96 complication of gastric sleeve surgery. All patients had respiratory symptoms, including fever
97 (n = 6, 100%) and cough (n = 5, 83.3%), sputum production (n = 3, 50%), dyspnoea (n = 3,
98 50%) and chest pain (n = 3, 50%).

100 **CT findings**

101 The most common CT findings were cavitory nodules/masses (N=4, 66.7%) (Figure 1 A, B),
102 non-cavitory nodules/masses (N=3, 50%) (Figure 1C, Figure 2.), septal thickening (N=4,
103 66.7%), centrilobular nodules (N=3, 50%), ground glass opacities (N=2, 33.3%) and
104 consolidation (N=1, 16.7%) (Figure 1 D). Four patients (66.7%) had enlarged lymph nodes,
105 two of whom had necrotic lymph nodes (Figure 3).

107 **Discussion**

108 Nocardiosis is a rare disease that frequently affects immunocompromised patients, especially
109 patients with impaired cellular immunity related to HIV infection and solid organ
110 transplantation. However, approximately one third of patients with nocardiosis are
111 immunocompetent, which is concordant with our study where three out of six enrolled
112 patients were immunocompetent^{3, 17, 18}

114 Pulmonary nocardiosis accounts for approximately 73-77% of *Nocardia* infection, and
115 usually occurs through direct inhalation of *Nocardia* species.¹⁸ Patients with pulmonary
116 nocardiosis usually have non-specific symptoms, making the clinical diagnosis difficult. The
117 definitive diagnosis is usually based on histopathologic examination and/or culture, which are
118 time-consuming. However, difficulty in isolation and the slow growth of *Nocardia* delay the
119 diagnosis and the initiation of the appropriate treatment. This can lead to disease
120 dissemination and increase the morbidity and mortality related to the disease.^{2, 6, 7}

122 Various HRCT findings have been reported in the literature, including consolidation with or
123 without cavitation, cavitory and noncavitory pulmonary nodules/masses ground glass
124 opacities, centrilobular nodules interlobular septal thickening, a crazy paving pattern, pleural
125 effusion and chest wall extension. Table 2 summarises the studies with more than two cases
126 that reviewed the radiological features of pulmonary nocardiosis since 1995.^{2, 8-11, 13-15} The
127 results of these studies show that the most common HRCT findings are nodules/masses with
128 or without cavitation. The largest study by Balckmon et al.¹⁴ looked at 53 patients with
129 pulmonary nocardiosis; the most common findings by chest CT were airspace disease and
130 nodules. Oszoyoglu et al.¹¹ analysed seven cases of pulmonary nocardiosis after lung
131 transplantation and found that the most common chest HRCT finding was pulmonary
132 nodules, seen in 71% of the patients. Sato et al.¹⁰ reported HRCT findings of 18 patients with

133 pulmonary nocardiosis and found that 94.4% patients had a nodule or mass, 77.8 % had
134 ground-glass opacity and 77.8% had interlobular septal thickening. Tsujimoto et al.⁹ found
135 that ground glass opacity and septal thickening were the most common findings seen in
136 85.7% of the patients, followed by bronchial wall thickening and crazy paving seen in 71.4%
137 of the cases. Mehrian et al.¹⁵ analysed 25 patients and found that the most common HRCT
138 findings were pulmonary nodules (96%) and consolidation (76%). More recently, Liu et al.²
139 described nine patients with pulmonary nocardiosis and found that eight of them had
140 consolidation, of which three had cavitation and six had masses/nodules, of which three had
141 cavitation.

142

143 In our study, the most common CT findings of pulmonary nocardiosis were lung
144 nodules/masses, of which four showed cavitation. Four patients had septal thickening and
145 three had centrilobular nodules. Our findings are similar to what has been reported in the
146 literature, however we have noted necrotic lymph nodes in two patients (Figure 3 B), a
147 finding that has not been reported in the literature before.

148

149 The differential diagnosis for pulmonary nocardiosis includes other causes of lung
150 consolidation, cavitation and nodules such as other infections, vasculitis and malignancy.
151 Pulmonary actinomyces is a lung infection that can have similar radiological findings as
152 pulmonary nocardiosis. However, patients with actinomyces are usually immunocompetent
153 who have poor dentition and they are at a higher risk of aspirating infected oropharyngeal
154 secretions. Pulmonary tuberculosis is another pulmonary infection that can present with
155 cavitation. However, cavitation in pulmonary tuberculosis tends to involve the apical
156 segments of the upper lobes and the superior segments of the lower lobes, and there are
157 usually associated tree-in-bud nodules. In the clinical setting of pulmonary infection,
158 nocardiosis should be considered in the differential diagnosis of pulmonary nodules and
159 masses.

160

161 **Conclusion**

162 Pulmonary nocardiosis is a rare infection that commonly occurs in patients with impaired
163 cell-mediated immunity, but can be also seen in immunocompetent patients. On the chest
164 HRCT, pulmonary nocardiosis has a wide spectrum of findings, most commonly lung
165 nodules/masses with or without cavitation. In the appropriate clinical setting, the radiologist

166 should include pulmonary nocardiosis in the differential diagnosis of pulmonary nodules and
167 masses.

168 **Authors' Contribution**

169 RU supervised the work and drafted the manuscript. NP reviewed and edited the manuscript.
170 MB collected the data and revised the manuscript. All authors approved the final version of
171 the manuscript.

172

173 **Conflict of Interest**

174 The authors declare no conflicts of interest.

175

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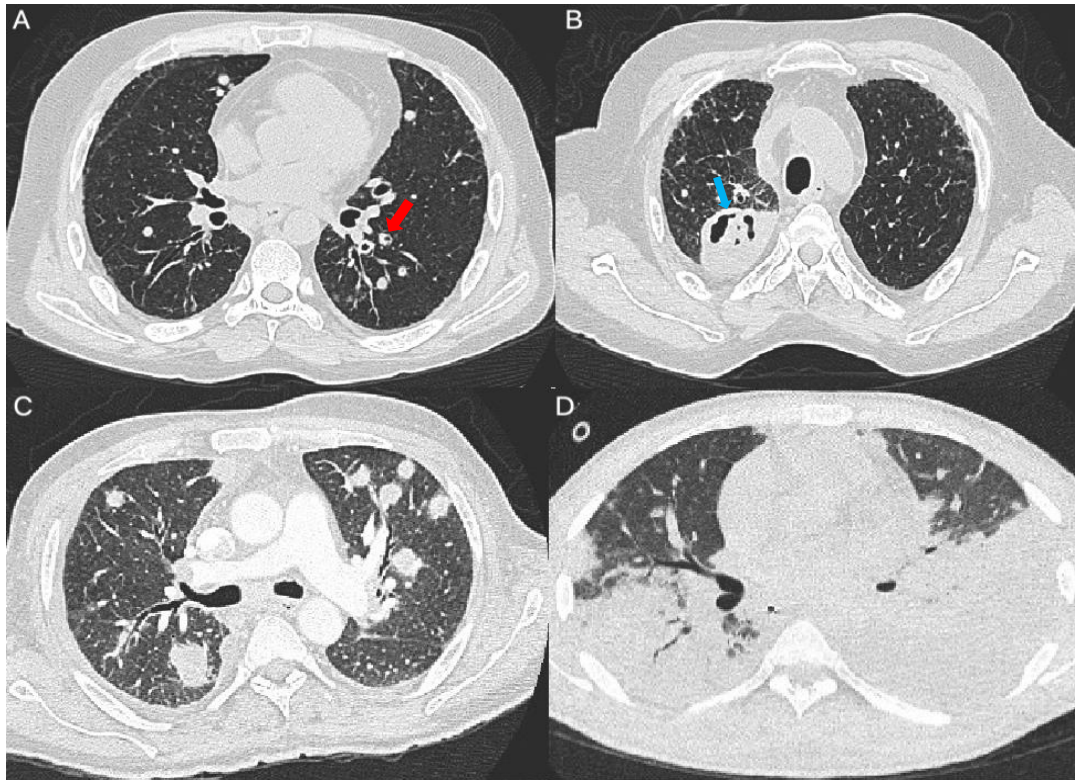
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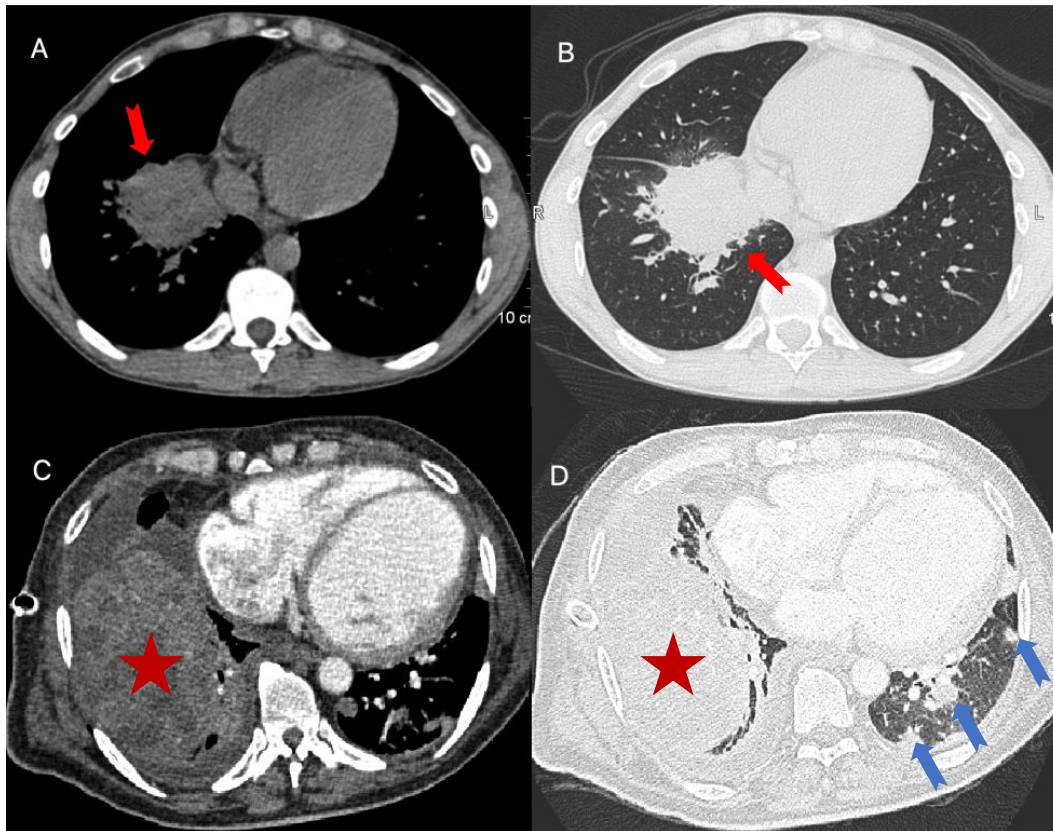
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230

231 **Figure 1: A, B.** A 42-year-old male post renal transplant. CT chest (lung window siting)
232 shows bilateral multiple pulmonary nodules of variable sizes; some of the nodules show
233 central cavitation (red arrow). A cavitory mass in the posterior segment of the right upper
234 lobe (blue arrow). **C.** A 59-year-old male with pulmonary nocardiosis. CT chest (lung
235 window siting) shows bilateral multiple pulmonary nodules of various sizes, some of the
236 nodules show a ground glass hallow. **D.** A 28- year-old male with glomerulonephritis on
237 steroid. CT chest (lung window siting) shows bilateral lower lobe consolidation and bilateral
238 pleural effusions.

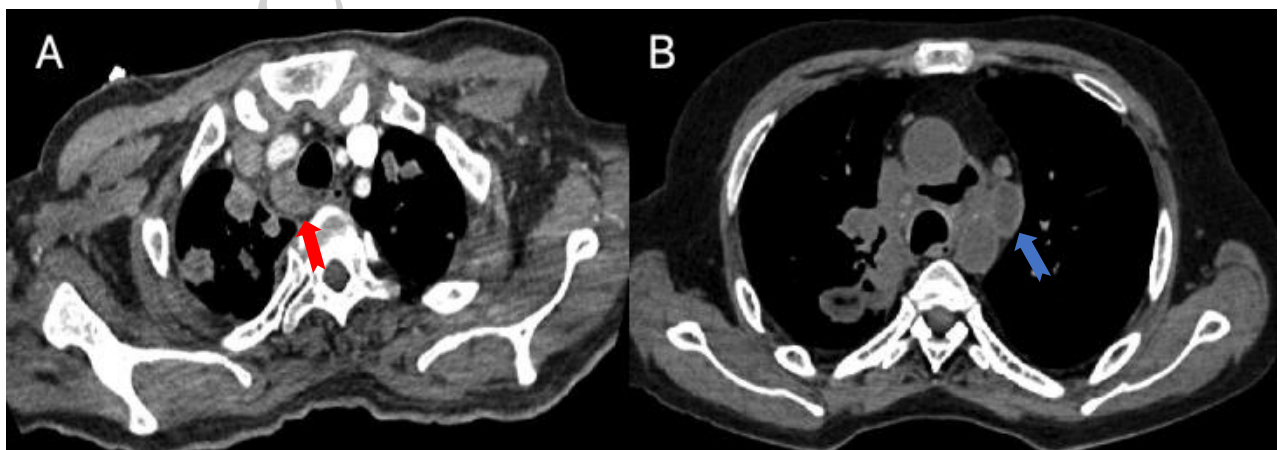
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241 **Figure 2:** A 29-year-old male post renal transplant. CT chest (mediastinal window A, lung
 242 window B) shows a mass surrounded by ground glass halo in the right lower lobe (red
 243 arrow). A 59-year-old male with pulmonary nocardiosis. CT chest (mediastinal window C,
 244 lung window D) shows a mass with areas of low attenuation in the right lower lobe (red star)
 245 associated with a right pleural effusion. Pulmonary nodules are also seen in the left lower
 246 lobe (blue arrow).

247



248

249 **Figure 3:** A 59-year-old male with pulmonary nocardiosis. CT chest (mediastinal window A)
 250 a right paratracheal lymph node (red arrow). A 42-year-old male with pulmonary nocardiosis.
 251 CT chest (mediastinal window B) shows a necrotic mediastinal lymph node (blue arrow).