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Research Article

Imaging and enhancement characteristics of coccidioidomycosis nodules assessed by dynamic contrast-enhanced computed tomography

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Abstract

Objective: To describe the dynamic contrast-enhanced CT (DCECT) appearance of pulmonary nodules related to infection with coccidioidomycosis.
Methods: Retrospective review of a database of DCECTs identified a subset of patients with pulmonary nodules related to coccidioidomycosis. General and DCECT imaging characteristics of these nodules were evaluated.
Results: 16 of the 44 nodules identified (36.4%) showed enhancement on DCECT imaging. The majority (74.9%) of enhancing nodules demonstrate delayed (3 or 4 min) peak enhancement. The majority (88.6%) of the 44 nodules were either smooth or lobulated in appearance. Only 1 (2.3%) of the nodules was cavitary. 19 (43.2%) of the nodules had adjacent satellite nodules. DCECT can be a useful study to help characterize pulmonary nodules in areas with endemic Coccidioides with an expected false-positive rate of ~30–40%. Biopsy could potentially be averted in 60–70% of nodules by evaluating with DCECT prior to tissue sampling.
Conclusion: When combined with morphological, serological, clinical, and historical information DCECT can be a powerful tool for reducing the number of benign nodules being biopsied and/or resected.

Keywords: Coccidioidomycosis; Dynamic contrast enhanced CT (DCECT); Pulmonary nodule; Biopsy

1. Introduction

Evaluation of the solitary pulmonary nodule (SPN) poses a significant challenge in radiology. This challenge has been growing in scope due to increasing identification of SPNs secondary to increasing utilization of computed tomography (CT). The results of the National Lung Screening Trial (NLST), a study demonstrating a 20% reduction in lung cancer mortality in certain high-risk patients screened with annual low dose CT (LDCT), have opened the door to CT screening in the United States [1]. As lung cancer screening programs take shape, more SPNs will be identified, further exacerbating the impact of SPNs on the healthcare system.

CT is a powerful tool for identifying pulmonary nodules; however, it is not very good at distinguishing between benign and malignant nodules. Many of the nodules identified with CT will be benign leading to a large number of "false positives" necessitating further workup and additional cost. For example, the false positive rate of baseline screening LDCT in the NLST was 26.6% [1]. One of the tools in the medical imager's arsenal for evaluation of SPNs is dynamic contrast-enhanced CT (DCECT). DCECT involves scanning the SPN prior to and at various time intervals following the infusion of intravenous iodinated contrast. The basic premise for DCECT

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hinges on the assumption that there are differences in vascularity between benign and malignant nodules providing an opportunity to distinguish between the two [2−4]. Studies have shown that malignant pulmonary nodules enhance more than benign nodules [5−7]. A large multicenter study evaluating the utility of DCECT for distinguishing between benign and malignant SPNs identified an enhancement threshold of 15 Hounsfield units (HU); enhancement of less than 15 HU was a strong predictor of benignity whereas 167 of 171 malignant nodules identified by the study demonstrated enhancement of greater than 15 HU [4].

Our practice is located in Arizona, in the southwestern United States and within the endemic range of the soil fungus Coccidioides (Cocci), which also includes arid regions of Mexico, Central America, and South America [8]. Inhalation of Cocci spores can result in infection (coccidioidomycosis) which is common in immunocompetent patients and the incidence is highest among the elderly and has been increasing dramatically in recent years, presumably due to a combination of drought, population growth, and new construction resulting in soil disturbances [9,10].

The most common manifestations of coccidioidomycosis are pulmonary. Cocci accounts for up to 30% of cases of community acquired pneumonia in our region [11]. Like most endemic fungal pneumonias, coccidioidomycosis manifests as granulomatous inflammation and often presents with nodules and lymphadenopathy on imaging. Often Cocci will leave behind one or several pulmonary granulomas following an acute infection. Unfortunately these nodules rarely calcify which can make them extremely difficult to differentiate from lung cancer [12]. Cocci granulomas represent up to 50% of SPNs in our region [13].

Because of the high prevalence of benign non-calcified granulomas in our region, a large proportion of the SPNs we encounter in our practice are benign. One of the tools we use to help increase our specificity when dealing with SPNs is DCECT, and we have routinely been using the DCECT protocol used by Swenson et al. [4] to risk-stratify SPNs. We performed a retrospective review of this database (from 2005 to 2013 comprising more than 500 CT scans) and identified the nodules which were definitively attributed to Cocci in order to evaluate the DCECT imaging characteristics of Cocci granulomas.

2. Materials and methods

To be eligible for an SPN-protocol DCECT at our institution the nodule must be solid, be between 0.8 and 3 cm in diameter, and not have any other findings indicating benignity (benign calcifications, macroscopic fat). All DCECT examinations performed between 1/1/2005 and 1/31/2013 were enrolled in our retrospective review. For detailed description of the DCECT protocol used at our institution, please see the "Materials and methods" section of Swenson et al. [4]. Cases where the nodule in question was identified as being coccidioidomycosis, either by tissue sampling or by a combination of serologic analysis and clinical validation, were selected and the DCECTs of these nodules were reanalyzed. The unenhanced and dynamic contrast-enhanced images of the nodules obtained at 1, 2, 3 and 4 min were reviewed. The average nodule attenuation (HU) from each acquisition was recorded. An attenuation difference greater than 15 HU between the unenhanced and any of the enhanced 1, 2, 3 or 4 min time points was considered a positive study. For the positive examinations the time period which demonstrated the highest degree of enhancement (peak enhancement) was also recorded. The percentage of positive nodules demonstrating peak enhancement at each individual acquisition was calculated. The morphology of the nodules was also evaluated with attention to location, size, calcification, shape/margins, cavitation, and presence of satellite nodules. The medical record was also interrogated for information concerning Cocciserological studies, any available pathological specimens, and follow-up imaging.

3. Results

A total of 44 nodules met criteria for inclusion in this analysis. Of these the diagnosis of coccidioidomycosis was histopathologically confirmed in 15 cases while the rest were confirmed with various combinations of serological analysis and clinical history. Of the 44 nodules identified, 16 (36.4%) had positive DCECT exams. Of the 16 positive nodules, 1 (6.3%) demonstrated peak enhancement at 1 min, 3 (18.8%) at 2 min, 5 (31.3%) at 3 min, and 7 (42.2%) at 4 min 25.1% of the positive nodules demonstrated early (1 or 2 min) peak enhancement, whereas 74.9% showed late (3 or 4 min) peak enhancement (see Table 1).

The gender of the patients was evenly distributed with 23 female and 21 male patients. The average age of the patient was 65 years old (35−83 y/o). The average age of the 16 patients with DCECT-positive nodules was 67. 41 of the 44 patients with nodules had Cocciserological studies drawn around the time of the DCECT. 15 (36.6%) had positive IgM and 28 (68.3%) had positive IgG titers for Cocci. 6 (40%) of the 15 patients with positive IgM had a positive DCECT whereas 9 (32.1%) of the 28 patients with positive IgG had a positive DCECT. Interestingly, of the 15 histopathologically proven Cocci cases only 6 had positive Cocciserological studies. All 44 of the patients had definitively benign disease on follow-up, either histopathologically proven Cocci, decreased size of the nodule on follow-up, or a stable nodule for at least 2 years.

Histopathologically, all biopsied or resected nodules universally showed features characteristic of pulmonary

Table 1
Number of nodules demonstrating peak enhancement (>15 HU) at 1, 2, 3, and 4 min.

1 min	1/44
2 min	3/44
3 min	5/44
4 min	7/44

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