REVIEW ARTICLE

Mediastinal Adenopathy After COVID-19 Infection

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Abstract

Since the outbreak of the COVID-19 pandemic, there have been myriad signs and symptoms ascribed to this disease process. While some of the most notable features described since the initial months of the pandemic include cough, fever, myalgia, headache, dyspnea/hypoxia, anosmia, and multifocal pneumonia, the pandemic's prolonged continuation has afforded ample opportunity to detect more subtle signs of the disease. Mediastinal adenopathy is one such sign that has been found in many patients with active COVID-19 infection, though the value of this finding in both prognostication and guiding treatment remains unknown. We did a timely brief review of mediastinal adenopathy in COVID-19 infection to shed more light on the potential implications of this finding. We conclude that Mediastinal Adenopathy in hospitalized COVID-19 patients has been associated with higher ICU admissions and higher mortality. Its non-specific nature and confounding etiology may prevent it from being a good marker for prognosticator of COVID-19 disease severity.

Keywords: COVID-19, New-Onset Atrial Fibrillation. NOAF, ACE2, Hypoxia

Introduction

Mediastinal Adenopathy – Definition, Type, Etiology

Mediastinal adenopathy is a non-specific finding of unreliable sensitivity long known to be associated with a variety of intrathoracic pathologies, including but not limited to cancer, sarcoidosis, and infectious processes such as pneumonia and tuberculosis. [1] Arguably the most straightforward definition of mediastinal lymphadenopathy (LAP) is based on size and defines a pathological mediastinal node as measuring at least 10mm or greater along its short axis per imaging [2]. This easily quantifiable measurement is less open to the interpretation necessary to apply the additional/alternative definitions of adenopathy, including loss of ovoid shape, heterogeneous enhancement, and irregular borders, among other criteria [3]. While this finding is of greatest prognostic value when evaluated in the context of cancer staging, there has been evidence to suggest that this may also be a prognosticator of COVID-19 Pneumonia disease severity. [4]

Discussion

Mediastinal Adenopathy in SARS-Co-V2 Infection

The reported incidence of mediastinal lymphadenopathy (LAP) in patients with acute SARS-Co-V2 infection requiring hospitalization varies from 5-29% of the current literature, and there is enough evidence to suggest that LAP does not appear to be an atypical feature of the disease [4,5]. LAP seen in COVID-19 patients at the time of hospital admission, via CT measurement, has been associated with a statistically significant increase in the incidence of inpatient mortality when compared with COVID-19 patients who present to the hospital with no LAP on chest CT [4]. This finding has been replicated, with

pleural effusion and coronary artery calcification also proving to be independent factors that increase the rate of inpatient mortality in the COVID-19 patient population [5].

LAP, advanced age, and the presence of consolidation pattern on CT in COVID -19 have each also been independently associated with an increase in 30-day mortality. Patients with LAP have a statistically significant increase in the presence of at least one of the following co-morbidities: Hypertension, Diabetes Mellitus, COPD, Asthma, Ischemic Heart Disease, Hyperlipidemia, and/or chronic kidney disease. And while ground-glass opacities are the most common finding on CT in all COVID-19 patients, a crazy-paving pattern is a finding more specifically associated (33% vs 14%, p<0.01) with LAP in these patients [6].

Apart from imaging findings, there are important clinical features that differentiate the LAP COVID-19 patient from the non-LAP COVID-19 patient. In LAP patients (vs. non-LAP patients), there have been higher rates of ICU admission (67% vs. 37%), mechanical ventilation (31% vs. 14%), and subjective assessments of disease severity in addition to the statistically significant increase in mortality [7]. Mediastinal adenopathy is a more frequent finding in patients who have advanced past both the initial asymptomatic phase (days 0-2) and initial symptomatic phase (up to day 14) to the progressive phase of COVID-19 in which symptoms linger past two weeks and are typically more severe [8]. When COVID-19 Pneumonia is compared to other viral pneumonias, there is a significant increase in the rate of LAP, pleural effusion, and elevated CRP among COVID pneumonia patients [9].

Despite this, there are multiple examples of studies that alternately describe COVID-19 LAP as an uncommon finding of dubious

significance that simply appears more often in COVID pneumonia compared to non-COVID pneumonia [10,11,12]. One study found no statistical difference in the length of hospitalization or rate of ICU admission when comparing LAP vs. non-LAP COVID patients, though LAP was associated with decreased duration of cough [13]. This latter finding might be explained by the possibility that LAP patients exhibit a more rapidly progressive severity of symptoms that prompts them to present to the hospital earlier in their course, hence leading to a shorter duration of cough. However, this finding has not been specifically studied to provide a definitive explanation.

Mediastinal Adenopathy and Imaging

While mediastinal adenopathy (LAP), defined by a short-axis length of 1cm or greater, can be detected on a CT scan, a PET scan has the unique ability to identify abnormal metabolic activity in mediastinal nodes that may not be enlarged. Because of this, COVID-19 infection has also been diagnosed as a consequence of PET scans in cancer patients. Some patients showed increased FDG uptake in mediastinal and carinal nodes that were of normal size per CT measurement, which then prompted COVID testing. This demonstrates that even when LAP is not present, there can still be increased nodal metabolic activity that, if detected, should increase clinical suspicion for possible COVID infection [14]. The maximum standardized uptake value [SUV (max)] of fluorodeoxyglucose in PET imaging is used as an indicator of localized glucose metabolism in tissues. And though some associations have been made between higher SUV (max) of mediastinal nodes and increased length/severity of COVID-19 clinical course, this remains a poorly validated area of research in need of further study before it can be reliably used to aid management. Because FDG uptake in mediastinal nodes has been shown to remain elevated even in

patients who have both clinically recovered from COVID-19 pneumonia and cleared the infection per CT scan, the utility of a costly PET scan as a COVID-19 diagnostic tool is low and arguably best reserved for those patients who are already receiving PET scans for other well-validated indications [14,15]. Endosonographic modalities have been found to be a great tool for diagnosing these patients [16].

At best, it would seem that the detection of LAP by CT in the absence of overt COVID-19 symptoms or the detection of increased PET activity of normally-sized mediastinal nodes in cancer patients might merit an increased clinical suspicion for sub-clinical COVID-19 infection. The meta-analysis published by Bao et al. [17] confirms that thin-section chest CT has higher COVID-19 detection rate among symptomatic patients. It is within this narrow set of circumstances that testing of these asymptomatic individuals for COVID-19 may be indicated. However, Valette et al. [18] has reported a prevalence (66%) of mediastinal adenopathy in small sample size (n=15), which is higher than previously reported data from China (3-5%) [19] but comparable to data from Italy (58%) [20]. There is a need for larger observational studies [21,22] to shed further light on this important disease entity.

Conclusion

We conclude that while Mediastinal Adenopathy in hospitalized COVID-19 patients has been associated with higher rates of ICU admissions and 30-day mortality, it remains too non-specific a finding with too many confounding etiologies to be reliably used as a prognosticator of COVID-19 disease course severity. Moreover, how such a prognostication should change the management of a patient with acute COVID-19 pneumonia is not clear. It would likely necessitate a large-scale clinical trial showing

the benefit of possibly administering earlier steroids and/or antivirals on the basis of LAP before the finding of mediastinal adenopathy can be considered to be of reliable clinical significance. At this time, the evidence supports our recommendation that patients with an incidental finding of mediastinal adenopathy with no proven SARS-Co-V2 infection should at least get tested for the disease, as LAP has been associated with subclinical SARS-Co-V2 infection.

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