High-resolution computerized tomography changes in diffuse parenchymal lung disease from chronic hypersensitivity pneumonitis related to bird antigen

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ABSTRACT

Background: Chronic hypersensitivity pneumonitis (HP) is the most common cause of diffuse parenchymal lung disease (DPLD) in India. There is no data regarding the avian antigen exposure-associated DPLD from the country.

Methods: Chronic HP from exposure to avian antigen was diagnosed when the high resolution computerized tomography (HRCT) showed features for HP and was supported by the history of exposure to pigeons, the presence of precipitin antibodies (IgG) to avian antigen in high titre with negative rheumatoid factor, antinuclear antibody, and no clinical clue for a collagen vascular disease. The HRCT changes were noted on Likert scale (0–5) in terms of affection of peripheral and/or axial involvement, reticulation, honeycombing, haze, mosaic, traction bronchiectasis, pleural reactions, features of pulmonary hypertension, and air cysts. Cardiomegaly and independent cardiac chamber enlargement were also recorded.

Results: The lower lobes were predominantly (65.6%) affected with similar frequency (78.1) of peripheral and axial parenchymal affection. The parenchymal changes in HRCT were haze or ground-glass opacity (100%), mosaic appearance (93.75%), reticulations (68.75%), traction bronchiectasis (34.3%), air cysts (21.8%), and honeycombing (9.37%). Pleural reactions, though not described so far, were found in 50% of cases. Features of pulmonary hypertension (87.5%), cardiomegaly (50%), left and right atrial enlargement (81.2% and 78.1%), and right ventricular enlargement (31.2%) were the common echocardiography findings.

Conclusion: Chronic HP from avian exposure shows predominantly lower lobe involvement with haze, reticulation, features of pulmonary hypertension, and pleural reactions as common HRCT findings. The likelihood of pulmonary hypertension appears high and although honeycombing is often present, the classical UIP pattern has not been found.

KEY WORDS: Diffuse parenchymal lung disease, forced vital capacity, high-resolution computerized tomography, hypersensitivity pneumonitis

INTRODUCTION

Hypersensitivity pneumonitis (HP) is a disease of lung parenchymal inflammation resulting from inhalation of organic and some inorganic antigens (e.g., low molecular weight chemicals as isocyanates).¹,² It has several clinically described forms as acute, subacute, and chronic depending...
on the dose and duration of exposure;[3] the latter two may present as diffuse parenchymal lung disease (DPLD). Several causes of chronic HP have been unfolded of which exposure to avian antigen, (bird fancier’s lung) and saccharopolyspora rectivirgula (farmer’s lung) are the two common ones.[4] As a prototype, these two conditions have contributed significantly to the knowledge regarding DPLD from chronic HP. Incidentally, in 40% of histologically proven cases of HP, the causative agent remains unidentified.[5,6]

The diagnosis of HP is achieved by clinical, radiological, immunological, and histological evaluations. HRCT chest forms an important investigation for diagnosis of HP; it frequently reveals characteristic findings in cases where the chest x-ray looks normal.[3]

The awareness regarding HP is variable and likely inadequate in several parts of the world, and this fact is unveiled by the recently published ILD-India registry.[7] The revelation leads to a search for HP within the available logistic feasibility by us through detection of HP related to the exposure to avian antigens.[8,9] Here, we present the HRCT characteristics of 37 chronic HP patients that have developed from exposure to avian antigen.

METHODS

This study was done at the Institute of Pulmocare and Research prospectively with proper ethical clearance and written informed consent from the participants. DPLD patients were included as avian antigen-related HP when they had (a) The presence of the history of exposure to the offending antigens (birds, especially, pigeons) and (b) HRCT pattern not showing DPLD characteristics of IPF (idiopathic pulmonary fibrosis) in our evaluation algorithm where a confident exclusion of usual interstitial pneumonia pattern was done through a pooled opinion of a pulmonologist and a radiologist and both agreeing to a possibility of HP-derived DPLD on HRCT, (c) The presence of existence of precipitin antibodies (IgG) to avian antigen in high titer measured by immunocap method,[10] and (d) Negative rheumatoid factor and antinuclear antibody with no historical or clinical suspicion favoring a collagen vascular disease or any other etiology.

Imaging

All the patients had HRCT of chest done either with 1- or 1.5-mm section algorithm. The HRCT cuts were evaluated on a predecided format by the pulmonologist and radiologist independently. The findings sought on HRCT cuts included the predominant lobe of affection and the standard descriptive changes of the abnormalities noticed for DPLD as reticulation, honeycombing, haze or ground-glass opacity (GGO), mosaic appearance, axial (bronchocentric) or peripheral (pleura apposed) interstitial involvement, traction bronchiectasis, irregular pleural thickening including perilymphatic nodules, features of pulmonary hypertension, air cysts, and cardiac enlargement. Each of the changes was noted on a Likert scale (0–5). Visual impression regarding specific cardiac chamber enlargement (as left atrium, right atrium, and right ventricle enlargement) has been noted too.[11] The findings were charted as per the frequency and the degree of presence (on Likert scale) for each lung and then averaged. We considered coining “transparenchymal bands” for the fibrotic strands traversing more than half the depth of the lung at the respective level. We coined the term “mean strength” of a change as the multiplication result of the frequency (denoted as “f”) and the degree (score in the Likert scale) of the presence (denoted as “d”) for any type of change for calculation. All the patients underwent spirometry and the value of forced vital capacity (FVC) was noted in the percentage predicted. The degree of affection was correlated to the percentage of FVC and the “r” values were charted.

RESULTS

Thirty-seven patients included (male:female = 14:23) with age ranging from 19-76 years (mean + SD 56 + 13 years). Common symptoms of patients were cough (77%) and shortness of breath (92%). The strength of affection for each morphological abnormality was made out as the multiplication of the frequency(f) and degree (d) of affection (f x d) and charted [Table 1] and displayed in Figure 1. The cardiac chamber (right atrium and left atrium) enlargements were also assessed and listed similarly. The co-relationship of the degree of the individual HRCT abnormality to the FVC was also made out [Table 1].

Since the prevalence of the features of PH was very high (87.5%), we decided to look for its association with the different commonly observed morphological changes [Table 2].

DISCUSSION

A female preponderance of chronic HP from avian antigen is known and is also evident in our series.[12,13] The radiological involvements suggest shrunken lung volume...
In only a quarter of the patients unlike IPF where the lungs appear smaller while the lower zones been found to be the predominantly (67.5%) involved. This predominant lower zone involvement does not tally with the previous observations where mid lung and upper lung involvement is predominant in chronic HP\textsuperscript{[14]} Isolated upper lobe involvement was there in 5%, both upper and lower lobe involvement were found in 8% of the patient and involvement of all the lobes (pan parenchymal) was seen in 10% of cases. It is interesting that the distribution of the lung parenchymal involvement of this type of HP includes both the axial and peripheral skeleton equally (81%). This possibly reflects a generalized peripheral bronchiolar affection as the peribronchovascular parenchyma forms a part of the so-called “peripheral lungs.”

The most common type of involvement is haze or GGO (100%) suggesting and ongoing extensive inflammation\textsuperscript{[3]} However, mosaic appearance is found in 94.59% [Figure 2].

This suggests that in most of the times there is bronchiolar obstruction leading to air trapping meaning concomitant small airway pathology\textsuperscript{[15]} The reticulation has been found as next the most frequent parenchymal change (70.27%) [Figure 3] possibly reflecting the progression of inflammation to definitive fibrosis\textsuperscript{[16]}

Table 1: Displays the frequency and degree (in Likert scale) of the morphological changes found on the high resolution computerized tomography chest of the patients. The strength of the affection is made out with multiplying the frequency and degree of involvement. ‘r’ represents the correlation co-efficient between degree of change with FVC

| Nature of changes                        | No. of patients | Frequency of involvement (f) | Degree of involvement (d) | Strength of affection (fxd) | r (between degree of change with FVC) |
|-----------------------------------------|-----------------|------------------------------|----------------------------|------------------------------|---------------------------------------|
| Overall no of patients                  | 37              | -                            | -                          | -                            | -                                     |
| Reduce lung volume                      | 9               | 25%                          | 0.7±1.64                   | 18.75                        | 0.067                                 |
| Lower zone predominant affection        | 21              | 67.5%                        | 3.02±0.87                  | 203                          | 0.128                                 |
| Predominant peripheral                  | 29              | 81%                          | 2.43±0.74                  | 196                          | 0.174                                 |
| Reticular                               | 25              | 70.27 %                      | 1.71±0.77                  | 120                          | 0.0095                                |
| Honeycombing                            | 3               | 9.37%                        | 1.33±0.76                  | 12                           | -0.98                                 |
| Ground glass opacity                    | 37              | 100%                         | 2.86±1.19                  | 286                          | 0.2321                                |
| Mosaic                                  | 35              | 94.75%                       | 2.15±0.86                  | 201                          | -0.3023                               |
| Pleural reaction                        | 19              | 54%                          | 1.9±0.79                   | 102                          | -0.394                                |
| Axial(bronchocentric) Skeleton          | 29              | 81%                          | 2.08±1.06                  | 166                          | -0.022                                |
| Traction bronchiectasis                 | 16              | 43%                          | 1.9±0.83                   | 81                           | 0.2243                                |
| Transparenchymal band                   | 9               | 24.3%                        | 1.3±0.51                   | 32                           | -0.0036                               |
| Features of PH                          | 32              | 87.5%                        | 2.56±0.93                  | 224                          | -0.0722                               |
| Air cysts                               | 9               | 24.3%                        | 1.17±0.85                  | 28                           | -0.123                                |
| Cardiac enlargement                     | 17              | 45.9%                        | 1.32±0.48                  | 59                           | 0.2413                                |
| LA enlargement                          | 30              | 83.7%                        | 2.48±0.83                  | 207                          | -0.0465                               |
| RA enlargement                          | 28              | 75.6%                        | 2.58±0.57                  | 194                          | -0.198                                 |
| RV enlargement                          | 11              | 31.2%                        | 2.3±0.82                   | 71                           | 0.7057                                 |

The correlation coefficient “r” of these changes with FVC has been charted. RV: Right ventricle, FVC: Forced vital capacity, RA: Right atrium, LA: Left atrium, PH: Pulmonary hypertension

Table 2: Association of the common parenchymal high-resolution computerized tomography changes with features of pulmonary hypertension

| Types of changes | r     |
|------------------|-------|
| Feature of PH    |       |
| Mosaic           | 0.51  |
| Haze             | 0.579 |
| Reticulation     | 0.090 |

Variable degree of pleural thickening even mimicking a perilymphatic nodule has been seen up to 54% of cases [Figures 1 and 4]. They may actually signify an extension of peripheral peribronchiolar parenchymal inflammation within a secondary lobule to start with and followed by further extension and coalescence that may embrace the visceral pleura. Although the frequency of affection of the axial and peripheral skeleton remains the same, the weight of the peripheral affection is higher and can be explained from the fact that the depth of the subpleural parenchyma is likely to be more than the paraxial parenchymal areas.

This particular change has not been described in literature and the described pathogenesis needs histological validation. The other lung changes noted are as follows: (a) traction bronchiectasis (43%), (b) transparenchymal bands (24.3%), and (c) air cysts as 24.3% [Figure 5].
In addition to the pulmonary parenchymal changes, we have noted the marked involvement of the heart been assessed from the mediastinal window. They include (a) cardiac enlargement (45.9%), (b) right atrial enlargement (75.6%) [Figure 6], and (c) left atrial enlargement (83.7%).

Taking into consideration the criteria laid out for pulmonary hypertension on radiological evaluations (both chest X-ray and CT chest)\textsuperscript{[17,18]} 87.5% of our patients had the presence of pulmonary hypertension [Figure 4], and this can explain the high frequency of right atrial enlargement in HRCT chest in our series. This high prevalence of the suggestive presence of pulmonary hypertension is also a noteworthy feature in our patients.

GGO has been found to be the strongest entity followed by the features of pulmonary hypertension. If the GGO has been regarded as the morphological description of the ongoing inflammation, the high prevalence of the presence of PH in these patients may indicate some mechanistic association for the development of secondary PH. We have tried to look at the correlation of different morphological change with the presence of PH [Table 2]. This elaborates that the association of the presence of PH is weak with fibrotic features (reticulation and honeycombing) compared to inflammation (GGO). This observation demands further research.

As for any DPLD, the FVC remains an acceptable parameter to indicate the degree of involvement.\textsuperscript{[19]} We considered looking for the co-relationship of all the morphological descriptions independently with FVC. The honeycombing showed the best negative association. This implies that
the element of fibrosis is highest in honeycombing and honeycombing denotes an advanced stage of the disease or a kind of protracted chronic active state.\(^\text{[20]}\) We had only one patient who showed soft ill-defined classical centriflobular nodules; the entity appears distinctly less in frequency. We also described a change as BOOP.\(^\text{[21]}\) We have also tried to see the relative strength of the different HRCT abnormalities in our series. The relative presence of the different changes compared to the maximum possible value has been depicted in Figure 1.

The biggest limitation of our study is about the diagnostic accuracy for chronic HP as we did not have any histological proof. In our series, all the participants had the history of contact with pigeons and the IgG precipitin titer was very high as 63.53 ± 37.4 (mean ± SD). We have observed a titre of 30 mgA/L by immunoCAP method to be highly specific for the group of chronic HP-induced DPLD patients.\(^\text{[10]}\) However, in a state of no histological proof, the demonstration of lymphocyte predominance (over 50%) in bronchoalveolar lavage could have made the diagnostic claim further strong.\(^\text{[22]}\) Incidentally, the lack of invasive exercise in the diagnostic algorithm of DPLD has been a reality in India.\(^\text{[27]}\) We have also excluded the possibility of a collagen vascular disease in our patients clinically and through universal testing of the rheumatoid factor and antinuclear antibody.

CONCLUSION

Chronic HP from exposure to birds causing DPLD appears very much present and quite prevalent in pulmonary practice in our part of the world. HRCT features may be useful to diagnose them with pleural reactions and features favoring the presence of pulmonary hypertension.

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Conflicts of interest

There are no conflicts of interest.

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