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Research Article

Keywords: psoriasis, pulmonary, interstitial lung disease, nodules, CT scan

Posted Date: July 20th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1406730/v2

Subclinical High-Resolution Chest CT Scan Features in Psoriasis

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Abstract

Background: Although psoriasis is considered a systemic disease, no clear association has been established between psoriasis and lung diseases. This study aims to detect and describe subclinical pulmonary involvement in psoriasis patients with various degrees of cutaneous manifestations.

Methods: Adult psoriasis patients with no known active pulmonary disease or respiratory symptoms were screened for subclinical pulmonary manifestations and possible parenchymal changes using high-resolution computed tomography (HRCT) scan of the chest. Patients were classified according to the severity of skin manifestations. The clinical characteristics and radiographic findings of these patients were evaluated.

Results: Fifty-nine patients with psoriasis were included, among which 47 (79.7%) had abnormal HRCT scan features. Micronodules were the most common detected lung lesions (66.1%), followed by nonspecific interstitial changes (32.2%), including pleuro-parenchymal band/atelectasis, scarring, and focal ground-glass opacities. Other HRCT findings included emphysematous changes and calcified granulomas. Abnormal HRCT findings correlated with older age and duration of psoriasis but not with the severity of skin manifestations.

Conclusions: Micronodules and minor focal nonspecific interstitial changes were the most detected lung alterations in patients with psoriasis. These findings of the pilot study highlight a possible pulmonary involvement in patients with psoriasis. Larger multicenter studies are needed to clarify these findings further.

Keywords: psoriasis, pulmonary, interstitial lung disease, nodules, CT scan.

Introduction

Psoriasis is a chronic inflammatory and disabling disease [1,2] resulting from genetic, environmental, and immunologic factors [3,4]. It affects 2-3% of the population and is characterized by scaly and erythematous skin patches, papules, and plaques [5,6]. Psoriasis does not only affect the skin but is also known to have a systemic component as it was reported to affect various organs [7], leading to joint disorders [8], enthesitis [9,10], cardiovascular events [11], systemic hypertension [12], diabetes [13], and nonalcoholic fatty liver [14]. It remains controversial whether psoriasis can be considered an independent risk factor for these diseases [15,16]. Patients with psoriasis are routinely screened for well-known prevalent comorbidities, including cardiovascular diseases and diabetes mellitus (7 - 14). However, lung involvement is not routinely investigated unless respiratory symptoms manifest. [17] Hence, asymptomatic, mild parenchymal involvement associated with psoriasis may have been underdiagnosed and, when incidentally found, raises the question of association. [17] Respiratory comorbidities are poorly characterized in psoriasis with conflicting findings [18,19]. Several studies have illustrated a correlation between psoriasis and several types of respiratory comorbidities, such as asthma[17], COPD [20-23] and interstitial lung disease (ILD) [24]. Although there is increasing evidence of an association between psoriasis and lung involvement, data regarding chest CT features in psoriasis remains scarce [24]. Identifying various subclinical parenchymal lung manifestations in psoriasis is significant to a better understanding of the disease spectrum to various confounding factors that might affect the lung parenchyma of these patients who are susceptible to infections [17,18,25-27] and various pulmonary side effects of different therapeutic agents used along the disease course which have been linked to ILD in psoriasis cases [28,29].

This study aims to utilize a high-resolution CT scan of the chest (HRCT) to detect and

describe subclinical pulmonary involvement in patients with psoriasis and explore if such involvement correlates with the severity of psoriatic skin manifestations.

Materials and Methods

Participants, Study Design, and Data Collection:

This single-center observational cross-sectional study was conducted at King Abdullah University Hospital (KAUH), Irbid, Jordan. All adult patients (≥ 18 years) with psoriasis who visited KAUH dermatology clinic between June 1, 2019, and March 20, 2020, were eligible for the study. The study included those diagnosed with various degrees of cutaneous psoriasis. We excluded pregnant female patients, patients with concomitant connective tissue disease, active pulmonary symptoms, uncontrolled cardiac diseases, established pulmonary diseases such as interstitial lung disease (ILD), asthma, or chronic obstructive lung disease (COPD). Patients with psoriasis who received methotrexate or biologic agents for more than two weeks or within six months before the HRCT acquisition were also excluded. The coexistence of connective tissue diseases that might cause ILD was excluded through clinical evaluation and laboratory tests including autoantibodies. Symptomatic asthma cases were screened out using an internationally recognized life quality questionnaire (LQ). [30]

Candidates with a significant history of smoking were screened for undiagnosed clinical COPD using the COPD Assessment Test (CAT). Patients with a CAT score of 10 or more were excluded from the study. [31] Only psoriasis cases with no active respiratory symptoms at the time of the study recruitment were included. Pregnancy was ruled out by submitting a serum beta human chorionic gonadotropin (β-HCG) pregnancy test prior to HRCT scan examination in all female candidates of childbearing age. Electronic medical records of all patients were reviewed for demographic, occupational exposure,

clinical, radiological, and treatment details. Data not available in the medical records were obtained through direct communication with patients and their families. Written informed consent was obtained from all recruited patients prior to study commencement. This study was approved by the institutional review board (IRB) and the research and ethics committee at Jordan University of Science and Technology (#20190178).

CT acquisition and analysis

HRCT of the chest was the method applied to evaluate the involvement of pulmonary parenchyma. Thin-section CT images (1-mm slice thickness) with edge enhancing high special frequency algorithm were acquired at full inspiration (Philips Brilliance 64 slice CT system, Amsterdam, The Netherlands). CT scans were read and evaluated in consensus by our radiologist and pulmonologist authors based on clinical chest radiology standards. Psoriasis area and severity index (PASI)[32] was used to objectively assess the severity of cutaneous psoriasis involvement. Patients were divided according to PASI scores into three groups, mild (less than 5), moderate (5-10), and severe (greater than 10).

The following radiological definitions were used as a guide to characterize HRCT findings: [33,34]

- **Nodule:** well-marginated round opacity and no greater than 3 cm in maximum diameter.
- **Septal thickening:** a computed tomography finding of the increased width of the walls (septa) between the pulmonary lobules.
- **Reticulation/reticular changes:** innumerable interlacing line shadows that suggest a mesh.

- **Ground glass opacity (GGO):** hazy increased opacity or attenuation of the lung parenchyma with preservation of the bronchial and vascular margins.
- **Mosaic changes:** a patchwork of different attenuation regions interpreted as secondary to regional differences in perfusion or air trapping.
- **Emphysema:** focal region or regions of low attenuation without visible walls.
- **Peripheral:** referring to pulmonary structures within 1-2 cm of any visceral pleura.

Statistical Analysis

Data were processed and analyzed using the IBM Statistical Package for Social Sciences Software (SPSS) for Windows, version 23.0. ANOVA test was used to analyze the significant relations between the continuous variables, whereas Chi-Square was used to analyze the suggested relations between the categorical variables. A 2-sided *p*-value of less than 0.05 was considered statistically significant.

Results

A total of 228 patients with psoriasis visited the dermatology clinic at KAUH during the study recruitment period from June 1, 2019, to March 20, 2020. After applying the study criteria, a total of 59 patients were included in the study **(Figure 1).** The mean age was 41.6 years and ranged from 18 to 71 years. More than half of the patients (66.1%) were males. Patients were divided according to the HRCT findings into two groups: One with normal HRCT features and the other with abnormal HRCT findings. **Table 1** describes the demographic characteristics and PASI scores of both groups at the time of the HRCT. The majority of the studied patients (n=47, 79.7%) had abnormal findings in

their HRCT. The group of psoriasis cases with abnormal HRCT findings were older (44.0 vs. 32.6 years, p=0.02) and had psoriasis for a longer duration compared to the group with normal HRCT (14.8 vs. 7.2 years, p=0.044). There was no difference in PASI scores between the two groups.

Lung nodules were the most common parenchymal lung abnormality detected by HRCT scan (39, 66.1%), followed by nonspecific focal interstitial changes including mild pleuroparenchymal band, atelectasis, scarring, focal septal thickening, and minimal parenchymal distortion (19, 32.2%). Other HRCT findings included emphysematous changes (12, 20.3%) and calcified granuloma (10, 16.9%) **(Table 2).** Most lung nodules were less than 6 mm in diameter (87.2%). Only one patient had a nodule measuring more than 8 mm (10 mm). Apart from this patient, all nodules detected in patients with mild cutaneous psoriasis were <6 mm in diameter. None of the (6-8 mm) nodules were detected in the group with mild cutaneous psoriasis, compared to the severe group (3/4, 75%) and moderate group (1/4, 25%). Most of the parenchymal lung changes were noted to be peripheral and predominantly involved the lower lung lobes. A sample of HRCT scans is shown in **Figures 2 (A-D)**. None of the abnormal HRCT findings seem to related to the severity of cutaneous psoriasis manifestations/PASI scores.

When HRCT manifestations were distributed according to the smoking history **(Table 3)**, patients with smoking history were found to be predominately male (34/35, 97.1%), and actively smoking patients were younger than patients who quit smoking or never smoked (p=0.029). Smoking status & duration in all groups was not associated with the duration of psoriasis (p=0.258). Emphysematous changes were mostly seen in patients with a smoking history (10/12, 83.3%). On the other hand, none of the other HRCT findings correlated with the smoking history. When nodules were subdivided according to their size and the numbers of nodules detected in each case, most of the larger-sized

nodules (≥ 6 mm) were detected in patients with a smoking history (4/5, 80%). Most of the cases with a higher number of nodules (>3) detected were among the smoker and ex-smoker groups, whereas more cases with (2-3) nodules were among the group that never smoked (p=0.038).

Discussion

Various manifestations of parenchymal lung involvement have been detected by HRCT in the majority of our psoriasis patients. Lung nodules were the most common lung lesion detected (66.1%); this incidence is markedly higher than the estimated annual incidence of lung nodules in population of the United States in 2012 (6.6/1000 person) [35]. Additionally, out of a total of 24 nonsmokers, (62.5%) were found to have a lung nodule, which is a much higher incidence than that reported by Winter et al. (16.9%) among healthy nonsmokers [36]. Detecting lung nodules did not correlate with smoking history, the severity of psoriatic dermatologic manifestations, or the duration of the disease. Except for one case, all nodules detected in our patients were less than 8 mm in diameter. Almost all lung nodules detected in patients with mild psoriasis were smaller-sized (<6 mm) nodules, whereas larger-sized nodules (≥6 mm) were detected in patients with moderate or severe cutaneous psoriasis. This might indicate that micronodules can be part of the disease's natural course with the potential to progress in relation to the extent of cutaneous involvement.

Most of the detected interstitial lung abnormalities were nonspecific interstitial changes (32.2%). HRCT interstitial changes mainly manifested as parenchymal scarring, pleuroparenchymal band/atelectasis, focal septal thickening, parenchymal distortion, and focal mild ground glass opacity, or a combination of those. Interstitial changes were focal, mild, and scattered with no distinctive pattern and tend to involve the periphery of

the lower lobes and are not associated with lobular distortion or apparent surrounding parenchymal tissue or alveolar involvement. This is the first study to describe such interstitial lung alteration in psoriasis patients. Such changes can be caused by a recent or old infection or as a result of subclinical inflammatory changes. Most associations between psoriasis and ILD were reported as drug-induced pneumonitis secondary to concomitant use of immunosuppressants [29,37]. Nevertheless, a recent study indicated ILD cases in psoriasis with no previous or concomitant exposure to immunosuppressive therapy directed against psoriasis [28].

There is an increasing number of case reports describing the simultaneous existence of psoriasis and ILD. A recent case series described 6 patients with psoriatic arthritis who also developed interstitial lung disease [28]. ILD has not been previously recognized as a psoriasis comorbidity in epidemiologic studies searching for comorbidities in psoriasis, which suggests a low or rare incidence of a clinically relevant ILD in patients with psoriasis. Therefore, chest CT would not be routinely performed as part of psoriasis evaluation. Compared to a large study that included different ethnicities, where the incidence of ILD was found at 98 per 100,000 in a general population[38], a relatively higher prevalence of ILD was also reported in two studies by Kawamoto et al. (8 out of 392, 2%) [17] and Ishikawa et al. [37] (21 out of 447, 4.7%). Higher incidence in the above-mentioned studies and in our study might be attributed to the use of CT scans resulting in detection of more subclinical ILD, in other words, observation bias. Additionally, our study is the first to describe HRCT features in patients with mild and moderate cutaneous psoriasis, mostly managed with topical treatments, in contrast to the study by Kawamoto et al., that only included patients with severe psoriasis who needed biologic agents [17]. None of the above studies concluded a solid association between psoriasis and ILD, and the existence of such an association remains yet to be determined.

A large population-based study from Denmark demonstrated a strong association between psoriasis and the risk of sarcoidosis [39]. Many cytokines, such as IL-23/IL-17 axis, were found to play a central role in the pathogenesis and development of psoriasis. IL-23/IL17 axis was also found to be elevated in other connective tissue diseases that involve the lungs, such as rheumatoid arthritis and inflammatory bowel disease, which might give an insight into their role in the development of lung diseases that are associated with autoimmune conditions [37,39]. Clinically available anti-IL17 and anti-IL 23 have been shown to be effective not only in treating the cutaneous manifestation of psoriasis, but they were also reported to be effective in reducing ILD severity in psoriatic patients. Kawamoto et al. [17] found that the inhibition of the IL-23/IL-17 axis ameliorated not only psoriasis skin lesions but also ILD changes. That observation was supported by serial chest CT scans and suggested a possible common mechanism between the development of psoriasis and ILD. A recent study by Miyachi et al. [40] reported a case showing improvement in ILD during psoriasis by IL-23/IL-17 inhibition. Although these studies support that inhibition of this pathway with biologic agents may be effective for psoriasis-associated ILD, few other studies reported that biologic agents might potentially induce ILD [17 39,41-47]. In our study, there were no ILD changes detected in the two patients who had biologic agents.

Emphysema and calcified granulomas were also common HRCT findings in our study group. Although our study included psoriasis cases with no respiratory symptoms or established diagnosis of COPD, emphysematous changes were a common HRCT manifestation in our study population (20.3%), indicating a large proportion of undiagnosed COPD in psoriasis patients, predominantly in cases with smoking history. Almost all cases with a smoking history were male (97.1%). The emphysematous changes detected in the two nonsmoker cases were very mild and involved the upper

lobes. Both cases were females with cutaneous psoriasis who had no history of smoking or related exposure history, but they seemed to have symptoms consistent with possible underlying reactive airway disease. This common finding of subclinical CT-evidence emphysema is concordant with a meta-analysis that concluded that patients with psoriasis have a two-fold higher risk of developing COPD, particularly in patients with a severe form of psoriasis [21]. Taking into consideration the significantly higher prevalence of smoking among psoriasis patients [48], and that the severity of psoriasis was found to be proportionate to a high number of cigarettes smoked per day [22,23]. Whether the correlation between smoking and COPD events is circumstantial or casual in psoriasis patients remains to be answered [23]. The degree of emphysematous changes in our study did not correlate with disease duration or the severity of psoriasis skin manifestations/PASI scores.

This study has several limitations. Firstly, it was cross-sectionally designed and performed in a single center using a single CT technique (HRCT) to evaluate the lung parenchyma. The sample size was small. Laboratory data did not include various inflammatory markers that may contribute to a possible link between psoriasis and parenchymal lung involvement. Future larger and prospective studies are therefore needed.

Conclusions:

The study showed a high incidence of detected lung nodules and focal nonspecific interstitial lung changes in HRCT scans of patients with psoriasis. A larger scale study with objective radiologic assessment using software analysis might be helpful to look for subtle early changes in the lung parenchyma to better clarify the underlying pathophysiology of parenchymal abnormalities in patients with psoriasis.

Compliance with Ethical Standards:

All procedures performed in this study involving human participants were reviewed and ethically approved by the Institutional Review Board (IRB) and the research and ethics committee at Jordan University of Science and Technology. This study was conducted following the 1975 Helsinki declaration, as revised in 2008, and its later amendments or comparable ethical standards.

Author Contribution:

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Data Availability:

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Informed consent:

Written informed consent was obtained from all individual participants included in the study.

Declaration of interests:

The authors declare that they have no competing interests.

Funding:

This study was supported by a grant from the Deanship of Research at Jordan University of Science and Technology, Irbid, Jordan. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

No writing assistance was utilized in the production of this manuscript.

Acknowledgment:

We gratefully acknowledge all dermatology residents and healthcare workers involved in diagnosing and treating psoriasis patients in KAUH. A preprint has previously been published (https://www.researchsquare.com/article/rs-1406730/v1) and an updated version has been provided.

Figure 1. A Flow chart indicating the inclusion and exclusion flow.

Figure 2. A, Peripheral focal pleuroparenchymal band/atelectasis in the left upper lobe. **B,** Faint ground-glass opacities in the right and left upper lobes and interlobular septal thickening (irregular linear reticular opacity) in the left upper lobe periphery. **C,** Subpleural interstitial thickening/scaring, right lower lobe. **D,** Paraseptal emphysematous (subpleural) changes in the right lower lobe with linear atelectasis/scaring and focal septal thickening, prominent in the left lower lobe.

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Figures

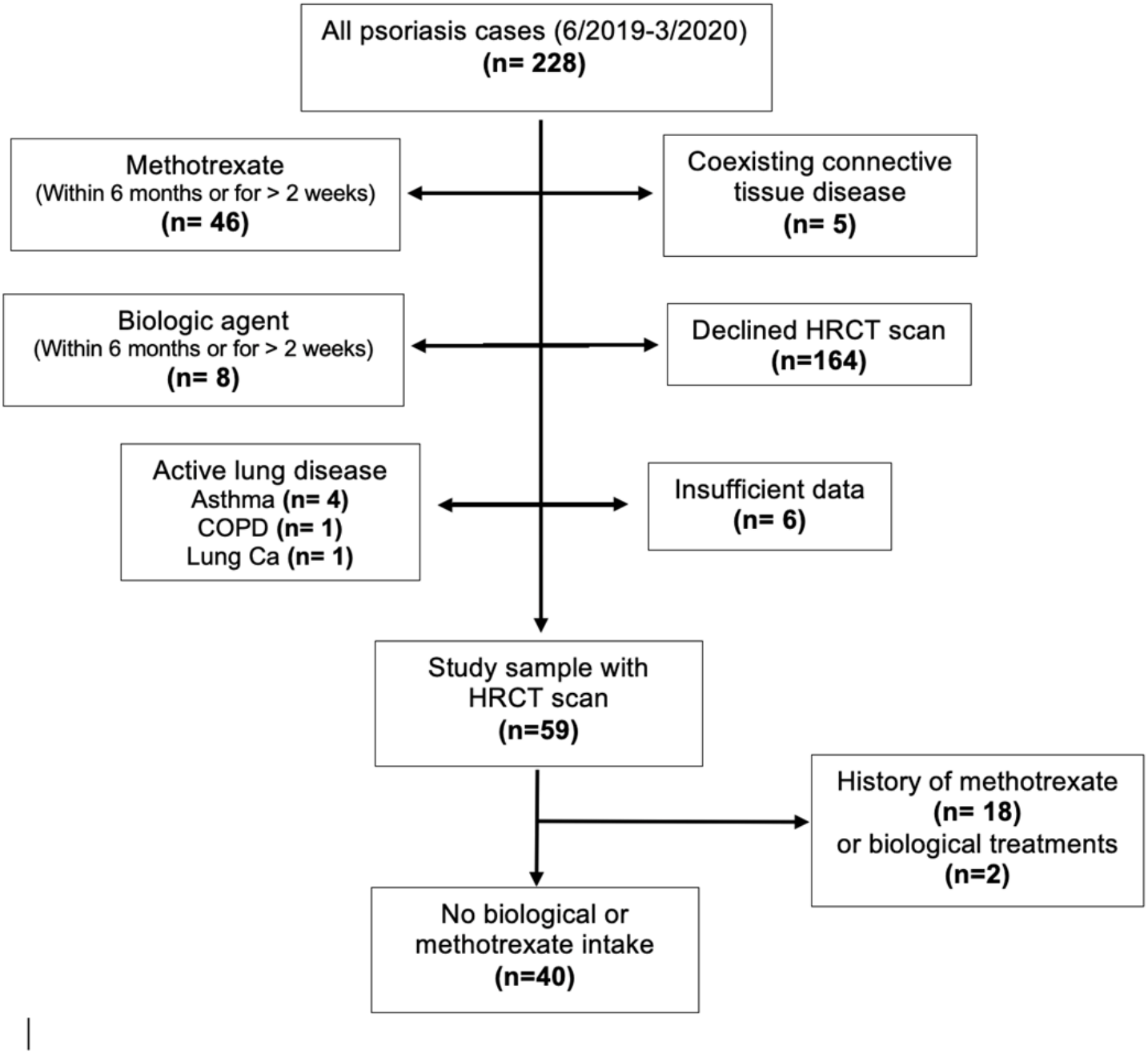

Figure 1

A Flow chart indicating the inclusion and exclusion flow.

Figure 2

A, Peripheral focal pleuroparenchymal band/atelectasis in the left upper lobe. **B,** Faint ground-glass opacities in the right and left upper lobes and interlobular septal thickening (irregular linear reticular opacity) in the left upper lobe periphery. **C,** Subpleural interstitial thickening/scaring, right lower lobe. **D,** Paraseptal emphysematous (subpleural) changes in the right lower lobe with linear atelectasis/scaring and focal septal thickening, prominent in the left lower lobe.

Supplementary Files

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- Tablespsoriasis720.pdf