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A comparison of histopathological appearance with radiological characteristics of usual interstitial pneumonia

Usual interstisyel pnömoninin radyolojik özellikleri ile histopatolojik görünümünün karşılaştırılması

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Özet

Amaç: Pulmoner fibrozisin histolojik bulguları, yüksek çözünürlüklü bilgisayarlı tomografideki (YRBT) radyolojik bulgular ile kuvvetle ilişkilidir ve aynı zamanda buzlu cam görünümü, interstisyel inflamasyon ile ilişkilidir. Biz, usual interstisyel pnömoni (UİP) olan hastalarda YRBT bulguları ile histolojik korelasyonu araştırmayı amaçladık.

Yöntem: Açık akciğer biyopsisi ile UIP tanısı teyit edilen hastaların kayıtları retrospektif olarak incelendi. Semptomların süresi, fizik muayene bulguları, solunum fonksiyon ve difüzyon testi sonuçları ve arteriyel kan gazı analizi sonuçları kaydedildi. İki deneyimli patolog tarafından, tanının teyidi için patoloji örnekleri ATS / ERS kriterleri göz önüne alınarak tekrar incelendi. YRBT görüntüleri de bir radyolog tarafından tekrar değerlendirildi. Klinik, histopatolojik ve radyolojik bulgular kaydedildi ve karşılaştırıldı.

Bulgular: UIP patolojik tanısı olan on hastanın hepsinde mikroskobik bal peteği görünümü vardı. HRCT'de bal peteği görünümü 9 hastada gözlendi, bunların 3 tanesinde kistik oluşumda vardı. Mikroskobik incelemede fibroblastik odakları olan hastalarda HRCT'de traksiyon bronşektazisi vardı.

Sonuç: YRBT bulguları, UIP'li hastalarda mikroskobik bal peteği görünümünü ve fibroblastik odakların varlığını tahminde yardımcı olabilir. Semptomların süresi ile histolojik değişikliklerin derecesi ilişkili değildir.

Anahtar Kelimeler: İdiyopatik pulmoner fibrozis, radyolojik özellikler, histopatolojik özellikler.

Abstract

Objective: Histological findings of pulmonary fibrosis correlate strongly with radiological findings on high-resolution computed tomography (HRCT) and pure ground-glass attenuation correlates with interstitial inflammation. We aimed to investigate histological correlation with HRCT findings in patients with usual interstitial pneumonia (UIP).

Method: The records of patients with UIP confirmed with an open lung biopsy were retrospectively reviewed. Duration of symptoms, findings on physical examination, pulmonary function and diffusion test results, and results of arterial blood gas analysis were recorded. Pathology specimens were reexamined by two experienced pathologists for confirmation of the diagnosis taking into consideration ATS/ERS criteria. HRCT images were also reevaluated by a designated radiologist. Clinical, histopathological and radiological findings were recorded and compared.

Results: Ten patients had a pathological diagnosis of UIP, all of which also had a microscopic honey comb appearance. Honey comb appearance on HRCT was observed in only 9 patients, 3 of which also had cystic formation. Patients with fibroblastic foci on microscopic examination also had traction bronchiectasis on HRCT.

Conclusion: HRCT findings may help predict the presence of microscopic honeycomb appearance and fibroblastic foci consistent with UIP. Duration of symptoms and degree of histological changes are not correlated.

Keywords: idiopathic pulmonary fibrosis, radiological characteristics, histopathololgical characteristics.

Introduction

Idiopathic interstitial pneumonias (IIP) are a heterogeneous group of disorders which result in parenchymal injury through varying patterns of inflammation and fibrosis. The interstitium, which is the primarily involved area in IIP, is the space which lies between the epithelium and the basal membrane of the endothelium. Among the IIP, idiopathic pulmonary fibrosis (IPF) is the most common and most severe form. Although it shows typical histopathological findings of usual interstitial pattern (UIP), the etiology of IPF remains unknown. A diagnosis is usually made after common causes of IPF are excluded, such as toxic drugs, environmental exposure and collagen tissue diseases. Common presenting symptoms are progressive dyspnea and nonproductive cough, and patients usually present after the age of 50. Inspiratory "Velcro" rales are generally heard on chest

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auscultation, whereas 50% of patients have clubbing (1). The prognosis of IPF is poor, with a mean life expectancy of 2.5-3.5 years after a diagnosis is made. The most common radiological finding is peripheral reticular opacities in the posterior and basal areas of the lung along with a honey comb appearance and shrunken lungs (2). High-resolution computed tomography (HRCT) usually reveals interlobular septal thickening, traction bronchiectasis and bronchiolectasis as well as a honey comb and ground glass opacities, frequently located in the base and the periphery of the lung (2-7). Histological findings of IPF include extensive fibrosis with honeycombing as a result of remodeling with extensive scarring surrounded by foci of fibroblastic activity. Smooth muscle hyperplasia is a frequently encountered feature within areas of fibrosis. Such findings are generally either on the septa or subpleural, with patchy involvement of the lung (8,9).

In the present study, we aimed to investigate histological correlation with HRCT findings in 10 patients with usual interstitial pneumonia (UIP).

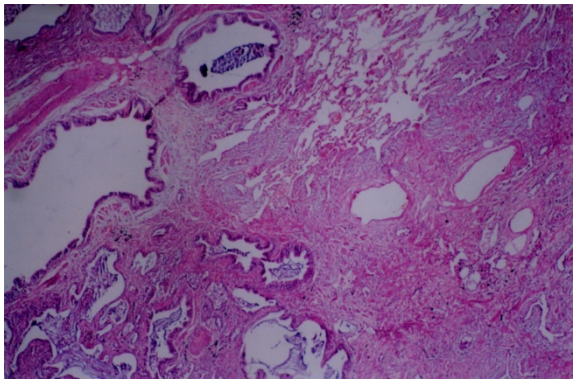

Figure 1. Normal parenchyma replaced by lesions with patchy involvement of the lung.

Material and Methods

In this retrospective study, all the records of patients with who underwent open lung biopsies in our hospital between 2000 and 2003 were systematically reviewed, and those with histopathological findings consistent with UIP were identified. The research was performed according to the World Medical Association Declaration of Helsinki. After evaluating the medical records, patients with evidence supporting the presence of an underlying connective tissue disorder, exposure to environmental agents or drugs known to cause pulmonary fibrosis were excluded from the final analysis.

Information regarding presenting complaints, duration of symptoms (cough, dyspnea), smoking status, occupational history, findings on physical examination (rales, clubbing, etc.), as well as results of Pulmonary Function Test (PFT) and diffusion tests were recorded.

A diagnosis was obtained by transbronchial biopsy in seven patients. If the transbronchial biopsy did not provide a specific diagnosis, patients underwent a surgical (open or thorascopic) lung biopsy. The lung HRCT scan was not used to determine if a patient should undergo a surgical biopsy. Before the surgical biopsy but after the results of the lung HRCT scan and transbronchial biopsy, one pulmonologist rated the certainty of the diagnosis of IPF (as certain, uncertain, or unlikely) and provided an overall clinical diagnosis, even if the diagnosis was uncertain.

HRCT images of all patients were re-evaluated for the presence of ground glass or honey comb appearance, traction bronchiectasis, interlobular septal thickening, pleural irregularities, nodularity, the presence of a cyst or pneumothorax, by an experienced independent radiologist who was blinded to clinical details of the patients involved as well as to the study protocol.

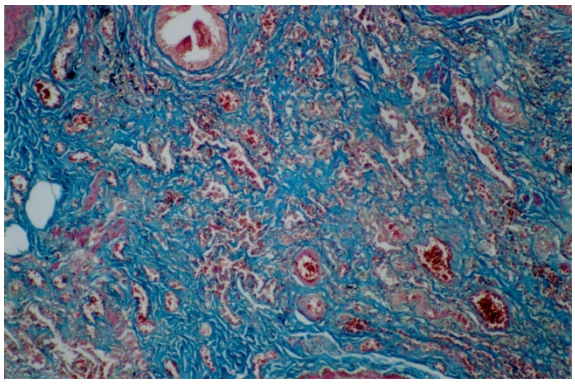

Figure 2. Marked fibrosis in a patient with advanced disease (Masson-Trichrome stain; magnification X100)

The biopsy specimens were also reexamined by two designated pathologists, working independently, to confirm the presence of UIP using the ATS/ERS criteria. Fibrosis was evaluated with mason trichrome stain. The specimens were further assessed with particular attention to specific histological features such honey comb appearance, patchy involvement, fibroblastic foci, smooth muscle hyperplasia, nonspecific interstitial pneumonia (NSIP) and diffuse interstitial pneumonia (DIP)-like areas.

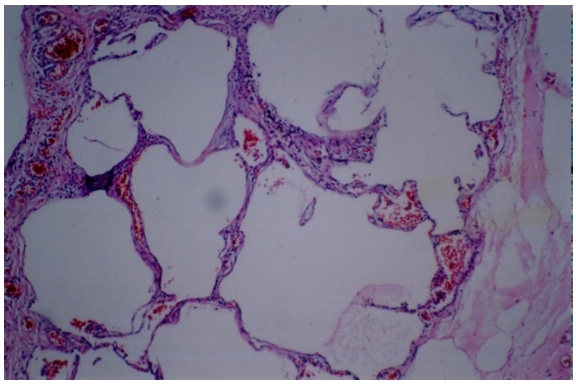

Figure 3. "Honey comb lung" appearance caused by the presence of small cystic spaces (H&E stain, magnification x100)

Results

Of all the records reviewed, a secondary cause of pulmonary fibrosis was not identified in 10 patients, 5 male and 5 female, who were presumed to have IPF, with a mean age of 52 years (22-71). All patients presented with either dyspnea, cough, or both. Demographic and clinical characteristics of the patient population have been summarized in table 1.
PFT and HRCT images were available for all 10 patients. Although an open biopsy was obtained for all 10 patients, 7 of them had also undergone a transbronchial lung biopsy (6 with nonspecific findings, 1 with findings consistent with fibrosis of peribronchial lung parenchyma). Open lung biopsies were obtained from a single location in five cases and from two different locations in the remaining five cases, which were prepared on an average of 8 hemotoxylin and eosin–stained slides (range 4-14 slides).

Histopathologically, all patients had patchy involvement and varying degrees of honey comb appearance, 9 (90%) had fibroblastic foci and 8 (80%) had smooth muscle hyperplasia. A diffuse interstitial pneumonia (DIP) pattern was observed in 6 patients (60%) whereas a NSIP pattern was encountered in 4 patients (40%). A Masson body was detected in only 1 of the specimens (table 2).

The presence of 3+ honey-comb appearance, cystic formation and widespread fibroblastic foci in patients with a short duration of symptoms (1-4 months) suggest that extent of histopathological findings are not correlated with duration of symptoms.

With regard to HRCT findings of patients with microscopic honey comb appearance, 9 (90%) also had radiological findings consistent with honey comb appearance, 3 had accompanying cystic formation and all had traction bronchiectasis with interlobular septal thickening in the subpleural area along with pleural thickening/irregularity (table 3).

The most commonly encountered histopathological findings were focal or diffuse fibroblastic foci with a patchy distribution accompanied by a honey comb appearance. Only 1 patient did not have a fibroblastic focus. This patient was also the only case which did not have a honey comb or ground glass appearance on radiological imaging.

Smooth muscle hyperplasia, which is a nonspecific finding which has been reported in association with asthma, chronic airway disorders, malignancies, bronchiectasis and fibrosis scarring, was a feature of UIP in 80% of our cases. Considering the disruptive effect UIP has on normal histology and physiology, this result is not really unexpected.

NSIP-pattern, which is characterized by uniform thickening of alveolar septa as a result of chronic inflammation and collagen-type fibrosis, was only seen in 4 cases.

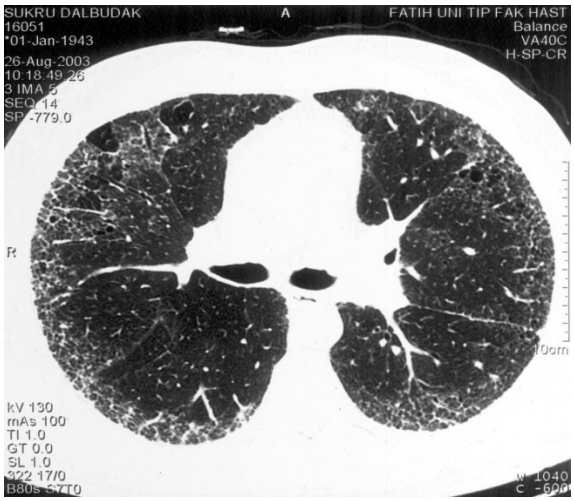

Figure 4. Peripheral honey comb appearance in a HRCT of one of the cases

Discussion

IPF is a progressive disorder with a poor prognosis. Since many treatable disorders with more favorable prognoses may mimic IPF, a lung biopsy is essential in patients clinically suspected to have IPF. However, recent retrospective studies have shown HRCT to be quite specific at making a diagnosis, without the need for an open lung biopsy (5, 6, 10-14). The aim of this study was to determine the value of clinical and radiological findings in diagnosis IPF.

IPF is more frequently reported in males (16,17), the majority of patients with IPF are older than 60. In our study the number females and males were equal, and the mean age was 52. Patients commonly present with long-standing (months or years) dyspnea, initially with exertion, but which may have progressed to the point where the patient becomes dyspneic at rest.

All our patients had dyspnea and/or cough. Duration of symptoms ranged from 1 month to 7 years. Smoking is strongly associated with IPF, particularly for individuals with a smoking history of more than 20 pack-years (18). In our study, especially male patients had a history of smoking (four of five male patients).

A restrictive ventilatory defect with decreased DLCO is a common physiologic pattern among patients with IPFs. Half of our patients had restrictive pattern. Decreased DLCO was seen in all measured patients.

Several studies (15,18) have shown that the diagnostic accuracy of IPF ranges from 71% to 100% when HRCT findings are typical of UIP (ie, subpleural, basal predominance, presence of reticular abnormality, and honeycombing with or without traction bronchiectasis).

In a study by Kazerooni et al, histopathological findings were correlated with HRCT findings in patients with IPF (4). The most common feature on HRCT was the presence of a honey comb appearance, although findings such as traction bronchiectasis, subpleural interlobular septal thickening as well as pleural thickening and irregularity were also present in all patients. A study by Hunninghake et al produced similar findings (15).

In support of findings from a study by Katzenstein et al., our results have shown patchy involvement and honey-comb appearance to be a constant finding in patients with IPF. As has been reported in the literature, our patients had peripheral involvement with radiological findings consistent with subpleural interlobular septal thickening and pleural irregularities in areas with pathological findings depicting subpleural fibrosis.

A recent study has shown that UIP pattern on HRCT is highly accurate for the presence of UIP pattern on surgical lung biopsy. If there is not honeycombing, but the imaging features otherwise meet criteria for UIP, the imaging features are regarded as representing possible UIP, and surgical lung biopsy is necessary to make a definitive diagnosis (19).

In the revision of the IIP classification, cryptogenic fibrosing alveolitis is removed, leaving IPF as the sole clinical term for this diagnosis. Surgical lung biopsy is not required in patients with UIP pattern on HRCT (20).

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Table 1. Demographic and clinical characteristics of the study population

Patient no.	Gender	Smoking history	Packet-year	PFT findings	Duration of symptoms	DLCO	DLCO/VA
1.	M	+	15	Restrictive	3 years	32	61
2.	M	+	25	Restrictive	4 months	57	86
3.	F	-	-	Restrictive	2 years	54	83
4.	F	-	-	Normal	15 years	55	73
5.	F	-	-	Normal	7 years	70	89
6.	M	?	?	Restrictive	3 months	?	?
7.	M	+	30	Normal	2 months	49	66
8	M	+	10	Normal	1 month	65	97
9.	F	?	?	?	10 years	?	?
10.	F	-	-	Restrictive	1 year	?	?

PFT, Pulmonary Function Test; DLCO, Diffusing capacity for carbon monoxide; VA: alveolar ventilation

Table 2. Histopathological characteristics of UIP cases

Patient no	Honey comb	Patchy involvement	Fibroblast focus	Smooth muscle hyperplasia	NSIP pattern	DIP pattern	Masson body	Additional findings
1	3+	+	Focal +	-	-	-	-	Dystrophic ossification
2	3+	+	Widespread +	Widespread +	-	-	-	-
3	3+	+	Widespread +	Widespread +	-	1+	-	Dystrophic ossification
4	3+	+	Widespread +	Widespread +	1+	2+	-	-
5	3+	+	Widespread +	Widespread +	-	2+	-	-
6	3+	+	Widespread +	Widespread +	-	-	-	-
7	3+	+	Widespread +	Widespread +	-	2+	-	-
8	2+	+	Widespread +	Widespread +	2+	2+	-	-
9	1+	+	-	-	1+	-	Focal +	-
10	1+	+	Focal +	Focal +	1+	1+	-	Congestion

UIP, usual interstitial pneumonia; NSIP (nonspecific interstitial pneumonia); DIP, diffuse interstitial pneumonia

Table 3. HRCT findings of UIP cases

Patient no	Honey comb	PBT	TB	ILST	ILIT	PT	Band	Ground glass	Nodule	Hyperinflation	PNX	Cyst
1	+	+	+	+	+	+	+	+	+	+	+	+
2	+	+	+	+	+	+	+	+	+	+	-	-
3	+	+	+	+	+	+	+	+	+	+	-	-
4	+	+	+	+	+	+	+	+	+	-	-	-
5	+	+	+	+	+	+	+	+	+	+	-	-
6	+	+	+	+	+	+	+	+	-	-	+	-
7	+	+	+	+	+	+	+	+	+	-	-	+
8	+	+	+	+	+	+	+	+	-	+	-	+
9	-	+	+	+	+	+	+	-	+	+	-	-
10	+	+	+	+	+	+	+	+	+	-	+	-

PBT, peribronchial thickening; TB, traction bronchiectasis; ILT, interlobular septal thickening, ILIT, interlobular interstitial thickening; PT, pleural thickening and irregularity; PNX, pneumothorax

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