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SURGICAL LUNG BIOPSY — A GOLDEN STANDARD OF DIAGNOSIS OF IDIOPATHIC INTERSTITIAL PNEUMONIA?

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ХІРУРГІЧНА БІОПСІЯ ЛЕГЕНЬ — ЗОЛОТИЙ СТАНДАРТ ДІАГНОСТИКИ ІДІОПАТИЧНИХ ІНТЕРСТИЦІАЛЬНИХ ПНЕВМОНІЙ?

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Резюме

Проведено незалежний аналіз одних і тих же гістологічних препаратів тканин легень 73 хворих на різні форми ідіопатичних інтерстиціальних пневмоній (ІІП) трьома висококваліфікованими фахівцями патоморфологами, які мають значний досвід роботи у пульмонології. Матеріал для гістологічного дослідження було отримано шляхом проведення відкритої (12 хворих) і відеоторакоскопічної (53) біопсії легень, а також при аутопсії (8).

Аналіз результатів гістологічного дослідження показав, що всі патоморфологи приблизно однаково описують виявлені патологічні зміни в тканинах легень, але інтерпретують їх дещо по різному. У 26,0 % випадків всі учасники дослідження однаково трактували гістологічні зміни, у 49,3 % випадків збігання висновків спостерігалося тільки у двох фахівців і, нарешті, у 24,7 % хворих (кожний четвертий випадок) всі патоморфологи дали різні висновки про нозологічну належність виявлених змін.

Така висока частота різночитань при інтерпретації морфологічних змін тканин легень ставить під сумнів можливості хірургічної біопсії з наступним гістологічним дослідженням препаратів у диференціальній діагностиці різних форм ІІП.

В діагностиці ІІП необхідним є ретельне виключення альтернативних захворювань шляхом мультидисциплінарної дискусії між пульмонологами, радіологами і патологами. В ситуаціях, коли така дискусія є неможливою, хворого слід направити до клініки, в якій працюють кваліфіковані спеціалісти.

Ключові слова: ідіопатичні інтерстиціальні пневмонії, диференціальна діагностика, хірургічна біопсія легень.

Укр. пульмонол. журнал. 2014, № 4, С. 49–52.

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ХИРУРГИЧЕСКАЯ БИОПСИЯ ЛЕГКИХ — ЗОЛОТОЙ СТАНДАРТ ДИАГНОСТИКИ ИДИОПАТИЧЕСКИХ ИНТЕРСТИЦИАЛЬНЫХ ПНЕВМОНИЙ?

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Резюме

Проведен независимый анализ одних и тех же гистологических препаратов тканей легких 73 больных с различными формами идиопатических интерстициальных пневмоний (ИИП) тремя высококвалифицированными специалистами патоморфологами, имеющими значительный опыт работы в пульмонологии. Материал для гистологического исследования был получен путем проведения открытой (12 больных) и видеоторакоскопической (53) биопсии легких, а также при аутопсии (8).

Анализ результатов гистологического исследования показал, что все патоморфологи приблизительно одинаково описывают выявленные патологические изменения в тканях легких, но интерпретируют их в большинстве случаев по-разному. В 26,0 % случаев все участники исследования одинаково трактовали гистологические изменения, в 49,3 % случаев совпадение заключений отмечалось только у двух специалистов и, наконец, у 24,7 % больных (каждый четвертый случай) все патоморфологи дали различные заключения о нозологической принадлежности выявленных изменений.

Такая высокая частота разночтений при интерпретации морфологических изменений тканей легких ставит под сомнение возможности хирургической биопсии с последующим гистологическим исследованием препаратов в дифференциальной диагностике различных форм ИИП.

В диагностике ИИП необходимо исключение альтернативных заболеваний путем мультидисциплинарной дискуссии между пульмонологами, радиологами и патологами. В ситуациях, когда дискуссия невозможна, больного следует направить в клинику, где работают квалифицированные специалисты.

Ключевые слова: идиопатические интерстициальные пневмонии, дифференциальная диагностика, хирургическая биопсия легких.

Укр. пульмонол. журнал. 2014, № 4, С. 49–52.

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Current classification of idiopathic interstitial pneumonia (IIP) is based on certain clinical, radiographic and histopathological features of the disease. Surprisingly, it was an initiative of experts-pathologists to recognize 7 types of IIP not as variations of one disease but as the separate nosological entities which have different characteristics of histological pattern (Tab.) [2, 5].

All histopathological patterns, listed in the table, doubtlessly, have significant distinctive peculiarities. But in the same time they are not pathognomonic for each taken clinical form of IPP. For example, the histological pattern, called usual interstitial pneumonia or non-specific interstitial pneumonia as well, is often seen in lung manifestation of connective tissue diseases [8]. Diffuse alveolar damage is typical for an acute respiratory distress syndrome regardless of etiology; the histological signs of lymphoid interstitial pneumonia are frequently found in lung disorders due to immunity deficiency conditions [9].

Considering all mentioned above we address ourselves a question: what is a diagnostic value of pathomorphological examination of lung biopsy or autopsy sample in distinction between different forms of IIP?

In order to answer this question we asked three highly qualified pathomorphologists with extensive experience in the field of pulmonary diseases to perform an independent examination of the same histological tissue preparations from patients with different forms of IIP. The following

pathologists participated in the study: professor I. V. Liskina, professor I. V. Gomolyako, professor K. A. Galakhin.

All specialists were aware of the study goals. At the start of the study each of participating experts has been provided with international and national consensus guidelines, containing detailed pathomorphological characteristics of different forms of IIP. Along with histological sample, prepared using hematoxylin and eosin stain, each expert received detailed enough information regarding clinical, radiological, functional and laboratory data and preliminary diagnosis as well (Fig. 1).

The samples from 73 IIP patients were examined (46 males and 27 females, age from 30 to 68 years). The samples for histological examination were obtained by open lung biopsy (12 patients), video-assisted thoracoscopic lung biopsy (53 patients) and autopsy (8 cases).

Based on the results of clinical examination and high-resolution computed tomography (HRCT) data the diagnosis of idiopathic pulmonary fibrosis (IPF) prior to histological examination of tissue specimens was established in 53 patients (72,6 %), idiopathic nonspecific interstitial pneumonia (NSIP) — in 15 (20,5 %), lymphoid interstitial pneumonia (LIP) — in 3 (4,1 %), cryptogenic interstitial pneumonia (CIP) — in 1 (1,4 %) and respiratory bronchiolitis-associated interstitial lung disease (RBILD) — in 1 (1,4 %).

The analysis of histological reports indicated that all experts-morphologists similarly described the changes in lung tissues, but interpreted them in different manner. Unexpectedly, the reports of study participants regarding nosological belonging of revealed abnormalities varied significantly.

An agreement between clinical diagnosis and histological conclusions of all three experts-morphologists was registered only in 15 cases (20,5 %); two experts — in 35 cases (47,9 %) and one — in 15 (20,5 %).

In 8 cases (11 %) there was a complete discordance between clinical diagnosis and all three opinions of the experts. In 4 patients the clinical diagnosis was changed due to histological examination: in 1 case a bronchioloalveolar carcinoma was diagnosed; in 2 patients with clinical diagnosis of LIP there were no histological signs of lymphoid pneumonia but NSIP pattern was found; in 1 patient with NSIP there was a prominent interstitial lymphoid infiltration, typical for LIP. In 4 cases the conclusions of morphologists unanimously contradicted to clinical, radiological and laboratory data. In those cases the clinical diagnosis remained unchanged (further the correctness of this decision has been confirmed during clinical observation and evaluation of treatment response).

In majority of cases the differences in interpretations of histological data stayed within the range of IIP group. For instance, in patient with clinical diagnosis of IPF the pathomorphologist described the histological pattern as NSIP and vice-versa.

The instances when morphological changes had been allocated to completely different nosological entity were

Clinical presentation of patient
Name/Last name_____ Age _____ Identification _____
Complaints:
Dyspnea, grade of dyspnea _____
Cough (dry, with sputum production, volume and character of sputum) _____
Fever _____ Loss of body mass _____
Arthralgia _____
Other _____
History _____
_____
_____

Life history (smoking, professional exposures, concomitant diseases etc.) _____
Chest radiography/ HRCT _____
_____
Spirometry (restriction, obstruction, grade of disorder) _____
_____
Total blood count and other_____
_____
Corticosteroid therapy, dose, effectiveness _____
_____
Conclusion: disseminated lung disease of unidentified etiology.
Presumptive diagnosis:
_____
_____
Histological sample origin _____
_____
Physician _____ Date _____

Fig. 1. Patient' card, containing clinical, radiological, functional and laboratory tests data.

Table1

Pathomorphological patterns of different forms of II

Clinical diagnosis	Histological pattern	Key histological signs
IPF	Usual interstitial pneumonia	Rough fibrosis, determining a remodeling of structures with frequently found honeycomb areas Foci of proliferating fibroblasts usually located along dense scars Heterogeneous appearance Frequent subpleural and paraceptal localization of histological changes
NSIP	Nonspecific interstitial pneumonia	Cellular pattern corresponds to mild or moderate chronic interstitial inflammation; type 2 pneumocytes hyperplasia in the inflammatory areas Homogenous appearance of inflammation and fibrosis as opposed to heterogeneity seen in UIP Rough fibrosis is usually absent, foci of proliferating fibroblasts
COP	Organizing pneumonia	Organizing fibrosis of distal airways (bronchioles, alveolar ducts and alveoli) Unequal distribution of changes Tissue structure is preserved Homogenous appearance Mild chronic interstitial inflammation
AIP	Diffuse alveolar damage	Diffuse distribution of changes Homogenous appearance Diffuse thickening of alveolar septa due to organizing fibrosis Patchy or diffuse organizing fibrosis within airspaces Hyaline membranes (patchy or diffuse)
RBILD	Respiratory bronchiolitis	Clusters of alveolar macrophages within the lumens of bronchioles Mild bronchiolar fibrosis and chronic inflammation Macrophages present with dusty brown cytoplasm Absence of honeycombing
DIP	Desquamative interstitial pneumonia	Homogenous appearance Clusters of alveolar macrophages Mild or moderate thickening of alveolar septa Mild interstitial chronic inflammation (lymphoid aggregates) Foci of proliferating fibroblasts Absence of honeycombing
LIP	Lymphoid interstitial pneumonia	Diffuse interstitial infiltration of affected areas, mainly located within alveolar septa Infiltrates are composed of T-lymphocytes, plasmocytic cells and macrophages Lymphoid hyperplasia

rare and in all cases such a discrepancy was only made by just one of three study participants. There were in total 219 reports (73 by each expert). In 6 cases (2,7 %) the changes were characterized as those due to diffuse connective tissue disease; 5 (2,3 %) — as hypersensitivity pneumonitis (exogenous allergic alveolitis); 2 (0,9 %) — pulmonary vasculitis; 1 (0,5 %) — sarcoidosis, 1 (0,5 %) — pneumomycosis.

Interobserver variability in determination of histological pattern is presented on Fig. 2.

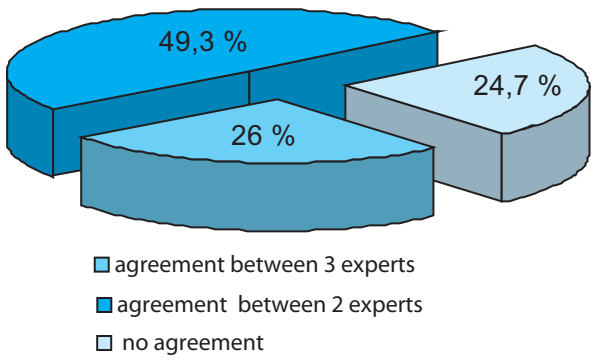

Fig. 2. Interobserver variability in determination of histological pattern.

As it is demonstrated on Fig. 2, in 26 % of cases the study participants similarly interpreted histological abnormalities. In 49,3 % there was an agreement between two experts. And finally, in 24,7 % of cases (each fourth patient) all pathomorphologists made different conclusions regarding pathohistological patterns they found.

Such a high rate of discrepancies in interpretation of histological data makes the value and reliability of surgical lung biopsy doubtful in distinction of IIP forms.

It is worth to mention that diagnostic value of regular chest radiography in IIP patients is quite limited — the sensitivity of this method does not exceed 50 % [4]. At the same time, the implementation of HRCT increased the accuracy of diagnosis up to 90 % [5, 7]. The multislice computed tomography (MSCT) allows to identify and visualize in different regimens the lung structures about 1 mm in size. Sensitivity of this methods approaches 95 % [1, 3].

According to joint ATS/ERS/JRS/ALAT statement on IPF management, published in 2011, the diagnosis of IPF is based on the results of multidisciplinary discussion between pulmonologists, radiologists and pathologists. In situations, when such a dispute is impossible, the patient has to be referred to the hospital, where qualified specialists are available. In our opinion this recommendation should be used in other forms of IIP as well.

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