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Differentiation of etiology of nodular changes in high resolution computed tomography (HRCT) in interstitial lung diseases

High resolution computed tomography (HRCT) enables imaging of morphological changes invisible on plain chest radiograms or conventional CT. This is related to thin collimations of the scans and sharp (bone) algorithm of image reconstruction. In HRCT the lung interstitium may be evaluated at the level of the smallest functional unit, namely pulmonary lobule. Nodular changes are among the most frequent morphological changes in interstitial lung diseases. The evaluation of their character and typical features in each interstitial lung disease is very important in differential diagnosis of these diseases.

The aim of the study is evaluation of frequency and character of nodular changes in HRCT in interstitial lung diseases.

MATERIAL AND METHODS

The material comprised a group of 47 patients, 28 men and 19 women, aged between 27 and 68 years, in whom the HRCT examination was performed because of interstitial lung disease. The scanning was performed in supine patients position, and in cases of presence of opacities in posterior, dependant lung areas, additional scanning in prone position was performed. The collimation of scans was 2mm. The scanning was performed from lung apices to the level of diaphragm, with 1 cm spacing.

RESULTS

In 14 patients with sarcoidosis the well-outlined nodules, the diameter of which was from few millimeters up to 1 cm, were associated with peribronchovascular fibrosis in parahilar, seldom subpleural lung regions (Fig.1). In 12 patients with pneumoconiosis, nodules larger than 1 cm, formed irregular conglomerates of masses, bilateral, predominating in posterior lung areas. In 6 cases centrilobular nodules were associated with inhomogeneous ground glass opacities in posterior, paravertebral areas of the lung (Fig. 2). In 3 cases nodules form rosettes. In Wegener's granulomatosis conglomerates of masses, 3 to 5 cm in diameter formed fussing nodular changes (Fig. 3). In 6 cases of pneumoconiosis nodules predominated in upper lung fields, especially in posterior lung areas. In 5 patients nodules were diffused, with associated emphysematous areas and diffuse reduction of vessels.

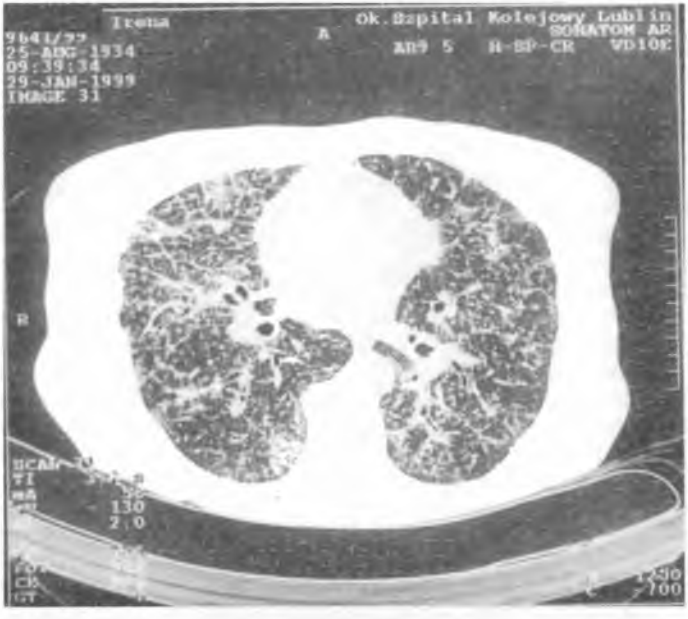

Fig. 1. Diffuse nodules and interstitial fibrosis form the appearance of reticulation

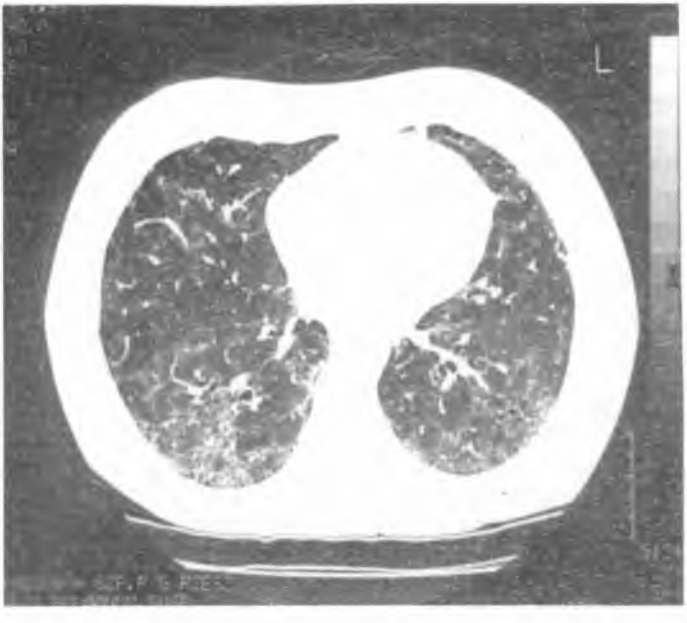

Fig. 2. Diffuse nodular densities with coexisting areas of centrilobular and irregular patchy emphysema. Inhomogeneous densities in posterior parts of the lung

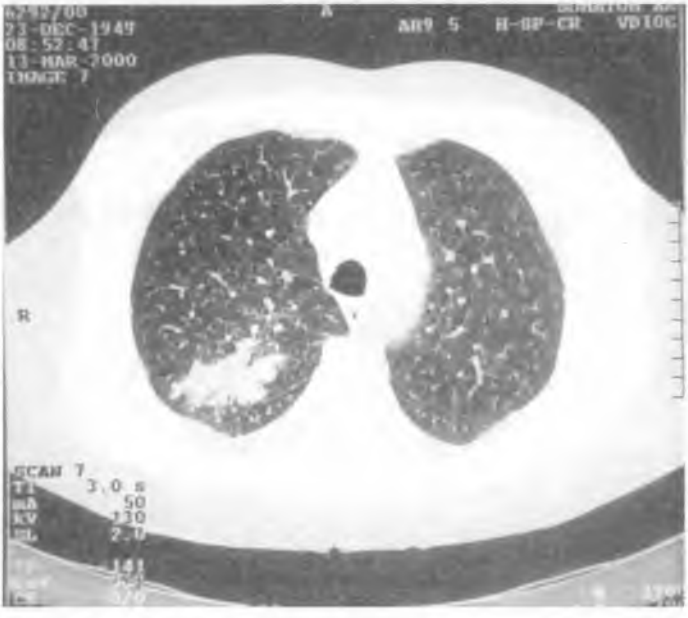

Fig. 3. In posterior part of the right lung a large conglomerate with irregular margins, formed by confluent nodular opacities

DISCUSSION

The small nodule form rounded opacity less than 1 cm in diameter, while the diameter of large nodule is 1 cm or greater. In HRCT nodules are divided into interstitial and air-space nodules, depending on the compartments they affect. Interstitial nodules are usually well-defined, despite their small sizes, of soft tissue density; obscure the edges of vessels and other structures in which they touch (20). Air-space nodules are more often ill-defined, can be of homogenous soft-tissue attenuation, obscuring underlying vessels, or less dense than adjacent vessels, so-called ground glass densities. A clusters or rosette of small nodules may be seen. Despite these differences in appearance, a distinction between interstitial and air-space nodule on the basis of HRCT can be difficult, because many nodular diseases affect both the interstitial and alveolar compartments (20). The distribution or location of small nodules is more valuable in differential diagnosis than their appearance. The nodules may be random, perilymphatic or centrilobular in distribution. Although there may be some overlap between these appearances, in most cases a predominant distribution of nodules is evident on HRCT (20). Centrilobular nodules indicates bronchiolitis, often with associated bronchiolectases (8). The centrilobular distribution of nodules with tree-in-bud pattern is typical in active tuberculosis. Interlobular septal thickening and ground glass opacities may coexist (7). Small nodules with random distribution are often visible in miliary tuberculosis. The nodules may be visible adjacent to small vessels, interlobular septa, pleural surface, but with no consistent and predominant relationship to any of these. The nodules are usually several millimeters in diameter, and well-defined (5,8). The plain chest radiograms may be normal for about 2–6 weeks, and changes are visible only on HRCT, with coexisting ground glass opacities and reticulations (5).

Hematogenous metastases also tend to be randomly distributed, although they have a tendency to predominate in the lung periphery and at the lung bases. The nodules are also well-defined, and as with miliary tuberculosis may be seen in relation to small vessels in some locations, reflecting their way of dissemination. The nodules below 3 mm in diameter usually have no relationship to lobular structures. Multiple nodules in histiocytosis X and pneumoconiosis may also appear randomly distributed, and may be difficult to distinguish from the nodules of military infection or metastases. In histiocytosis X, nodular changes are associated with thick- or thin-wall lung cysts (16). Nodules in relation to the parahilar peribronchovascular interstitium, the centrilobular interstitium, interlobular septa and in subpleural location are typical in patients with sarcoidosis, pneumonicniosis and lymphangitic spread of carcinoma. They are also visible in chronic smokers (8,20). This pattern was called perilymphatic, because it corresponds to the distribution of lymphatic vessels in the lung. These disease show different patterns of involvement of the perilymphatic interstitium that allow their differentiation in most cases (4). In patients with sarcoidosis nodules ranging in size from several millimeters to 1 cm or more are visible, most frequently in relationship to the parahilar peribronchovascular interstitium and small vessels. Small clusters of granulomas are visible in these locations. Centrilobular and paraseptal nodules are less frequently seen on HRCT in patients with sarcoidosis. In 15 to 25% of patients with sarcoidosis, large nodules, measuring from 1 to 4 cm in diameter, with irregular margins may be seen. The nodules may cavitate, but it is not frequent (20).

The pneumoconiosis is associated with small nodules, usually measuring from 2 to 5 mm in diameter, which are predominantly localized centrilobular and subpleural on HRCT. They correlate with areas of fibrosis surrounding centrilobular respiratory bronchioles and involving subpleural interstitium. The nodules in relation to peribronchovascular interstitium and thickened interlobular septa are less frequent and less evident than nodules in sarcoidosis and lymphangitic spread of carcinoma. They appear more evenly distributed than in patents with sarcoidosis. In patients with mild coal-worker's pneumoconiosis they are usually visible only in the upper lobes. In patients with silicosis the nodules may calcify (20).

In patients with lymphangitic spread of carcinoma, nodules are the most frequent within the thickened peribronchovascular interstitium and interlobular septa, but are not as profuse as in sarcoidosis. Septal thickening appear nodular (9).

A perilymphatic distribution of nodules is the easiest to diagnose when nodules are visible in a subpleural location, particularly in relation to the fissures, where they can be easily distinguished from pulmonary vessels. Subpleural nodules were described in about 50% of patients with sarcoidosis or lymphatic spread of carcinoma (3,9). Confluent subpleural nodules may result in the appearance of pseudoplaques, linear areas of subpleural opacity, several millimeters in thickness, that mimic the appearance of asbestos-related parietopleural plaques. The presence of pseudoplaques in this disease correlates with the profusion of subpleural nodules (18). Centrilobular nodules are usually separated from the interlobular septa and pleural surface by a distance of several millimeters, and are centered about 5 to 10 mm from the pleural surface. They do not usually occur in relation to interlobular septa or the pleural surfaces as do random or perilymphatic nodules, and subpleural lung is typically spared. This difference can be particularly valuable in distinguishing diffuse centrilobular nodules from diffuse, random nodules (20). Centrilobular nodules are usually related to centrilobular structures, such as small vessels. In most cases centrilobular nodules can be correctly identified by noting their association with small pulmonary artery branches. They typically appear localized perivascular, surrounding or obscuring small pulmonary arteries visible on HRCT. Occasionally the air-filled centrilobular bronchiole can be recognized as a rounded lucency within a centrilobular nodule (20).

Centrilobular nodules can be seen in diseases that primarily affect centrilobular bronchioles or arteries and result in inflammation or fibrosis of surrounding interstitium and alveoli (8). The most frequent causes include diseases of bronchioles, sometimes with dilatation

of centrilobular airways or tree-in-bud. Well-outlined, small peribronchiolar nodules, reflecting the presence of interstitial granulomas, were described in patients with histiocytosis X. Ill-defined centrilobular opacities can occur in patients with endobronchial spread of tuberculosis, bronchopneumonia, hypersensitivity pneumonia, bronchiolitis obliterans, respiratory bronchiolitis or bronchiolectases with surrounding fibrosis in smokers, asbestosis, pulmonary edema and vasculitis. Bronchial spread of carcinoma may also result in centrilobular nodules. They can reflect both interstitial and air-space pathology (20). The large nodule is a rounded opacity, over 1 cm in diameter. The term mass is generally used to describe nodular lesions over 3 cm in diameter.

Single nodules must be distinguished from carcinoma. In differential diagnosis the character of the margins of the nodule is essential. The smooth margins suggest benign process. Irregular, spicular margins are typical in carcinoma, but are also sometimes visible in inflammatory pseudotumors (19). Apart from evaluation of margins HRCT enables reliable assessment of relations of tumor and bronchi, which may be helpful in biopsy (10).

The presence of air-bronchogram or cystic lucencies is typical of malignant lesions, especially adenocarcinoma (19). Because the fluid and mucus produced by the tumor is of low attenuation, after contrast infusion, angiogram sign can be seen; contrast-enhanced pulmonary vessels appear denser than the surrounding opacified lung (20).

Large nodule may be visible in different interstitial lung diseases, or diseases involving air-spaces. Conglomerates of small nodules are visible in sarcoidosis, pneumoconiosis, inflammatory changes, infractions (13). They may be associated with parenchymal bands, interlobular septal thickening or ground glass opacities, suggesting active process (13). They usually predominate in upper lobe and peribronchovascular areas, and often have irregular shapes, surrounding central bronchi and vessels, with small discrete nodules in their periphery. Large confluent nodules may be seen in sarcoidosis, silicosis and histiocytosis X (13,20). The large nodule can cavitate. The relationship of nodules and vessels is better assessed on thicker, 10 mm contiguous sections. HRCT allows better evaluation of cavitations, especially in small nodules, as well as the assessment of nodules adjacent to the pleural surface (6).

Nodular changes are most typical HRCT finding in sarcoidosis, lymphangitic spread of carcinoma, pneumoconiosis, military tuberculosis and histiocytosis X. In sarcoidosis and lymphangitic spread of carcinoma the nodules are usually associated with increased reticulation, in other diseases the nodules dominate. In sarcoidosis nodules are small, well-defined with characteristic perilymphatic distribution, adjacent to pleural surface, main fissures, localized along thickened interlobular septa and vessels (14,17). Bilateral nodules dominate in middle and upper lung areas; in most cases they are grouped in parahilar and peribronchovascular areas, with relative sparing of subpleural areas (17). The typical findings of lymphangitic spread of carcinoma on HRCT are smooth of beaded central peribronchovascular interstitial thickening. They may be associated with nodular or smooth interlobular septal thickening, resulting in characteristic reticulation. In pneumoconiosis nodules may calcify and predominate in centrilobular, subpleural lung areas (11,14,20). In the course of the diseases the number of nodules increases, confluent nodules may result in large nodules, irregular conglomerates and parenchymal distortion. They usually are localized in central and peripheral areas of upper lobes (12). In sarcoidosis, lymphangitic spread of carcinoma and pneumoconiosis the nodules are perilymphatic. The predominant location of nodules and presence of fibrosis are essential in differential diagnosis. In sarcoidosis the nodules predominate along central peribronchovascular cuffs and in subpleural areas. In lymphangitic spread of carcinoma paraseptal and peribronchovascular localization dominates. In pneumoconiosis the nodules are mainly centrilobular and subpleural (14).

In lymphangitic spread of carcinoma and pneumoconiosis the nodules are usually evenly diffused, the pattern less frequent in sarcoidosis (14,17). Conglomerates in sarcoidosis show air bronchogram, which is not seen in pneumoconiosis. The septal thickenings are main findings in

lymphangitic spread of carcinoma, in sarcoidosis they are less evident. In many cases differentiation between sarcoidosis and lymphangitic spread of carcinoma is impossible.

The pneumoconiosis may be distinguished from lymphangitic spread of carcinoma based on different localization of nodules. In pneumoconiosis nodules are bilateral and symmetrical. Nodular septal thickenings are usually absent (14,17).

In sarcoidosis and pneumoconiosis septal thickenings are less intense than in lymphangitic spread of carcinoma, and reticulations are not main HRCT finding. In sarcoidosis, pneumoconiosis and fibrosis the distortion of lung architecture is frequent, while in lymphangitic spread of carcinoma the lung architecture remains unchanged, and the shape and size of lobules are preserved (14).

The nodules in histiocytosis X are peribronchial and centrilobular. They are usually below 5 mm in diameter. Larger nodules are not frequent. The amount of nodules depends on the intensity of the disease. Their margins are irregular, especially if cystic lesions surround them. They may be solid or show small, central lucency, representing dilated central bronchioles surrounded by granulomas and interstitial thickening. Both nodules and cysts may be the only findings on HRCT, but usually they coexist. This is an important feature, enabling differentiation of histiocytosis from other nodular interstitial lung diseases.

CONCLUSIONS

HRCT enables imaging of nodular changes in miliary tuberculosis, before they are visible on radiograms. Perilymphatic nodules are typical in sarcoidosis, lymphangitic spread of carcinoma and pneumoconiosis. In sarcoidosis, nodules predominate along the peribronchovascular cuffs and in subpleural regions, in lymphangitic spread of carcinoma they are septal and peribronchovascular. In pneumoconiosis, nodules are centrilobular and subpleural. The assessment of character and localization of nodules in interstitial lung disease is not sufficient in reliable differentiation, but may be helpful in differential diagnosis in association with other HRCT findings.

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SUMMARY

High resolution computed tomography (HRCT) enables imaging of morphological changes invisible on plain chest radiograms or conventional CT. This is related to thin collimations of the scans and sharp (bone) algorithm of image reconstruction. In HRCT the lung interstitium may be evaluated at the level of the smallest functional unit, namely pulmonary lobule. Nodular changes are among the most frequent morphological changes in interstitial lung diseases. The aim of the study is evaluation of frequency and character of nodular changes in HRCT in interstitial lung diseases. HRCT enables imaging of nodular changes in miliary tuberculosis, before they are visible on radiograms. Perilymphatic nodules are typical in sarcoidosis, lymphangitic spread of carcinoma and pneumoconiosis. In sarcoidosis nodules predominate along the peribronchovascular cuffs and in subpleural regions, in lymphangitic spread of carcinoma they are septal and peribronchovascular. In pneumoconiosis nodules are centrilobular and subpleural. The assessment of character and localization of nodules in interstitial lung disease is not sufficient in reliable differentiation, but may be helpful in differential diagnosis in association in other HRCT findings.

Różnicowanie etiologii zmian guzkowych w tomografii komputerowej wysokiej rozdzielczości (TKWR) w schorzeniach śródmiąższowych płuc

Tomografia komputerowa wysokiej rozdzielczości (TKWR) umożliwia uwidocznienie zmian morfologicznych niewidocznych na radiogramach klatki piersiowej oraz w klasycznej tomografii komputerowej. Związane jest to z cienką kolimacją i zastosowaniem ostrego (kostnego) algorytmu rekonstrukcji obrazu. W TKWR widoczna jest struktura miąższu płuc na poziomie najmniejszej jednostki funkcjonalnej płuc, tj. zrazika płucnego. Zmiany guzkowe są jednymi z najczęstszych zmian morfologicznych w chorobach śródmiąższowych płuc. Celem

pracy jest ocena częstości występowania i charakteru zmian guzkowych w badaniu TKWR wybranych schorzeń śródmiąższowych płuc. TKWR umożliwia uwidocznienie zmian guzkowych w rozsiewie prosówkowym gruźlicy, zanim stają się one widoczne na radiogramach. Guzki o lokalizacji okołolimfatycznej są typowe dla sarkoidozy, *lymphangitis carcinomatosa* i pylicy krzemowej. W sarkoidozie guzki przeważają wzdłuż centralnych mankietów okołooskrzelowonaczyniowych i w obszarach podopłucnowych, w *lymphangitis carcinomatosa* zlokalizowane są przegrodowo i okołooskrzelowonaczyniowo, w pylicy krzemowej są one głównie środkowozrazikowe i podopłucnowe. Analiza charakteru i rozmieszczenia guzków w chorobach śródmiąższowych nie jest wystarczająca w różnicowaniu, jednak bardzo pomocna w diagnostyce różnicowej w połączeniu z innymi objawami TKWR.