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Multiple focal pulmonary, pancreatic and renal lesions in a young patient with Hodgkin's disease detected by multi-slice computed tomography – a case report and literature review

Extranodal forms of lymphomas may be primary or secondary; the incidence of the latter is slightly lower. Individual organs and systems are mainly involved by direct spread through nodal infiltrations; metastatic foci through blood are rarer. The CT extranodal changes are mostly described in non-Hodgkin's lymphomas. If present in Hodgkin's disease, they affect: the spleen, bone marrow, bones, nasopharyngeal cavity and liver.

The authors present the multi-slice CT features of lesions found in a 22-year-old female patient with Hodgkin's disease treated with chemo- and radiotherapy several months earlier whose CT scan showed coexisting multifocal secondary lesions in the lungs, kidneys and pancreas complicated obstructive jaundice.

CLINICAL COURSE OF THE DISEASE AND MULTI-SLICE CT FINDINGS

A 22-year-old female patient with the diagnosis of Hodgkin's disease was referred to chest CT due to infiltrative parenchymal changes observed on the chest X-ray. The X-ray picture showed bilateral, irregular shadows of various sizes interpreted as infiltrations in the course of Hodgkin's disease or tuberculous or fungal lesions. Hodgkin's lymphoma – nodular sclerosis type in stadium II – was diagnosed one year earlier on the basis of histopathological examination of the cervical lymph node.

The physical examination showed bilateral enlargement of cervical and axillary lymph nodes, 1.0–1.5 cm in size and chest- X-ray revealed a widened shadow of the upper mediastinum. The CT examination of the chest and abdomen disclosed the 4 x 7 x 6 cm tumour with heterogenous contrast enhancement, ranging from 26–37 to 45–64 HU, located in the anterior mediastinum – medially and left-laterally. No enlarged lymph nodes were found in the abdominal cavity. The patient was qualified for the ABVD (Doxorubicinum, Bleomycinum, Vinblastinum, Dacarbazidum) treatment. After two courses of chemotherapy the enlarged cervical and axillary nodes disappeared. After 3 courses computed tomography was carried out which showed the regression of the mediastinal lesion and the ABVD therapy was continued. During the 5th and 6th course the patient complained of severe nausea despite the antiemetics used. After a 2-month break PET and next CT examinations were performed, the results of which suggested the presence of residual active proliferative process in the

mediastinum. During the next months the patient underwent radiotherapy in 3 stages (12.520 cGy/g). After further three months the chest X-ray revealed infiltrations.

The thoracic CT examination was conducted using the 64-row LightSpeed VCT tomography with collimation 2.5 mm (the previous one with the 8-row tomograph and the same collimation). During the examination CT-guided thin needle biopsy was taken. The CT revealed the presence of several tumours surrounded by the halo zone of the ground glass density and 10–50 mm size located throughout the pulmonary parenchyma with the tendency to subpleural areas. The biopsy material confirmed the changes typical of Hodgkin's disease while thoracic and abdominal PET confirmed the neoplastic nature of pulmonary foci and excluded abdominal lesions.

The Stanford V therapy was introduced. After 22 days of treatment the patient developed epigastric pains, which were initially suspected of being associated with the use of steroids. The abdominal US examination and gastroscopy were performed. Catarrhal gastritis was detected. Despite the treatment used symptoms did not completely subside. During the chemotherapy instituted the patient lost weight, had dyspeptic symptoms and slightly increased jaundice with the total bilirubin level of 3.4 mg%. Since the ultrasound picture was not clear, the patient was referred to another thoracic and abdominal CT examination, which was performed using the native scanning method following two-phase post-contrast scanning (collimation 1.2 mm). The number of infiltration changes in the pulmonary parenchyma did not increase; however their diameter increased by about 10–15%. The density of tumours was about 22 HU before contrast administration. The picture of mediastinal structures did not change. The liver was significantly enlarged with features of cholestasis. The common bile duct was dilated to 27 mm and the gallbladder enlarged to 9 cm. Within the pancreatic head a tumorous lesion – 5 x 4.2 x 4.1 cm in diameter, was observed (pre-contrast density – 34 HU in the peripheral part and 26 HU in the centre). Numerous hypodense areas of this type and 2-cm diameter were also found in the pancreatic body and cauda; the Wirsung duct was dilated to 7 mm along its whole length and the organ enlarged. In the arterial phase the density of bigger lesions was about 35 HU (26 HU in the centre – features of necrosis) and of smaller ones 20–24 HU; in the parenchymal phase the foci showed non-homogenous density – about 25–40 HU.

Extremely numerous nodular lesions located mainly cortically were also observed in the kidneys. The nodule size was 5–30 mm, pre-contrast density 32–35 HU – 35–45 in the arterial phase and 55–75 HU in the parenchymal phase. Moreover, a 10-mm nodule was detected in the medial part of the right gland. In general, the second examination showed markedly progressed organ lesions during the course of Hodgkin's disease. The ESHAP (Etopisidum, Metylprednizolon, Cisplatinum, Cytarabinum) therapy was decided. After the therapy the patient developed the acute tumour degradation syndrome with renal failure which required two haemodialyses. Moreover, transient liver dysfunction occurred (pre-ESHAP hyperbilirubinemia resulted from the compression of the bile ducts by abdominal tumours) accompanied by hearing and sight damage. The patient required numerous transfusions of erythrocytes and platelets. During post-therapy aplasia the presence of antigens was found in blood, first – *Candida krusei*, then *Aspergillus*. Fungizone was used, the general condition substantially improved, body temperature normalized, the amount of blood *Aspergillus* antigens decreased. Moreover, the *Pseudomonas aeruginosa* urine infection developed, which was treated with suitable antibiotics.

The next CT examination was carried out due to changed character of pulmonary infiltrations. The pulmonary nodular lesions decreased by about 25%, the biggest focus showed features of necrosis. The liver was still enlarged, however the cholestasis was less severe and the common bile duct was 16 mm wide. The number and size of nodules in the pancreas and its general dimensions markedly decreased – the biggest lesion in the pancreatic head was 34 x 31 x 27 mm; its pre-contrast

density – 32 HU peripherally and 14 HU medially, in the arterial and parenchymal phases: 92 and 17, 64 and 36 HU, respectively. The renal lesions substantially regressed. In the corticomedullary phase, fine hypodense foci were still visible – density 55–80, size up to 10 mm. In the parenchymal phase only some 60 HU changes were observed.

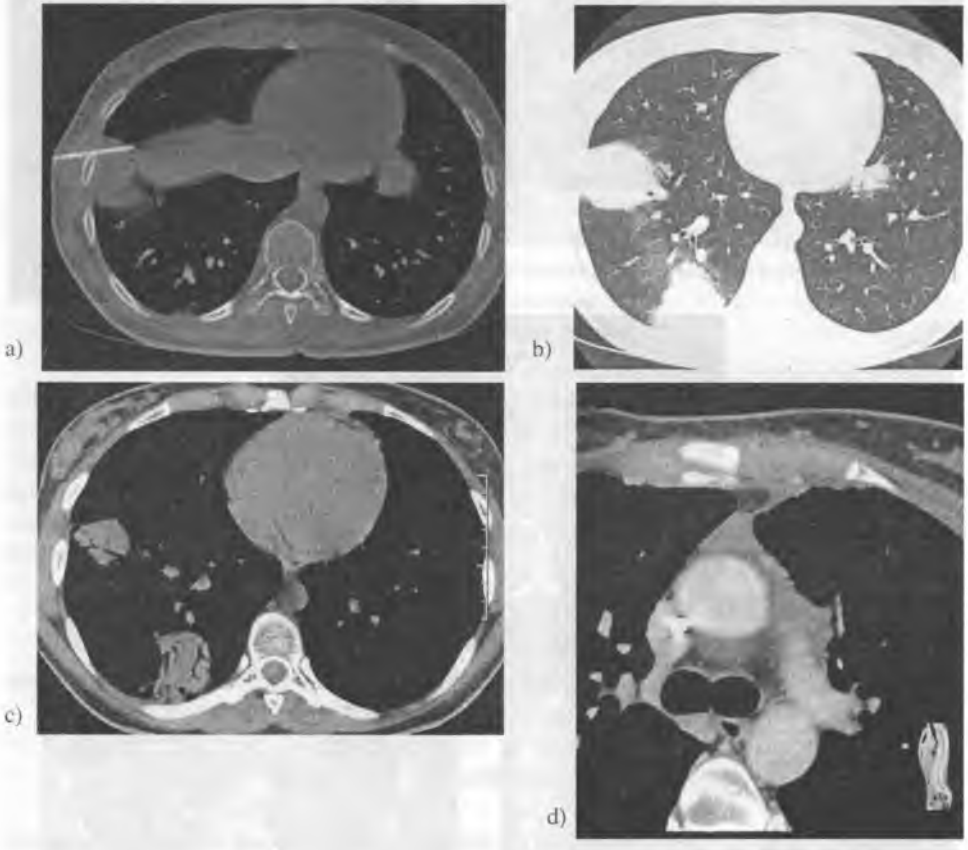

Fig. 1. CT examination with fine needle biopsy (a). CT axial view visualizes tumours in the pulmonary parenchyma surrounded by the ground glass zones (b). In the central part an air bronchogram is found (c). Residual infiltrative changes in the mediastinum (d)

Compared to the previous condition, new pulmonary lesions resembling the post-radiation areas were found in the vicinity of the mediastinum and fluid in the pericardial sac was detected, which was likely to be related to past therapy.

After further 10-day treatment with beta-blockers added the echocardiography showed reduced amount of fluid in the pericardial sac. For about one week after the discharge from the Department of Haematooncology the patient was treated with Orungal; once the *Aspergillus* antigenemia subsided, the treatment was discontinued. The patient stayed at home for 2 weeks and then presented with epigastric pains. The chest X-ray showed progression of the infiltration – supraphrenic on the right side and above the upper pole of the left hilus. The abdominal US examination demonstrated two hypoechogenic pancreatic foci, about 17 and 19 mm in diameter, located in the body, on the border of the pancreatic body and cauda. No enlarged abdominal lymph nodes or cholestasis were observed. At present, the patient undergoes the second ESHAP therapy with the cisplatinum dose reduced by 50%.

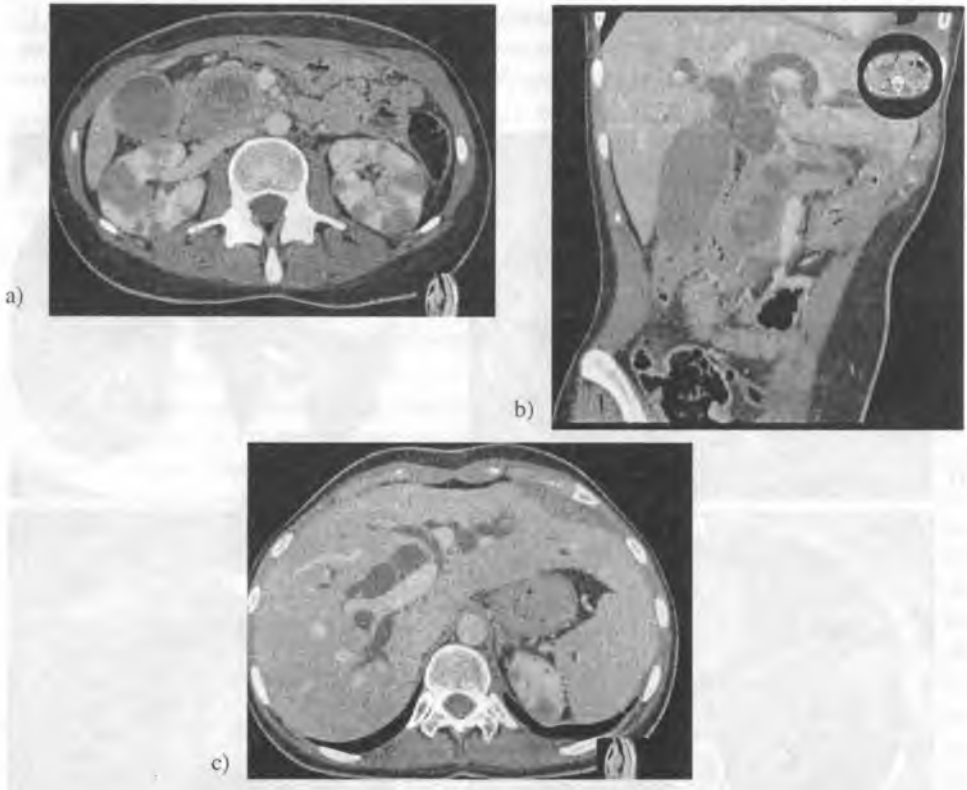

Fig. 2. The axial (a, b) and oblique (b) views show a big, non-homogenous tumour in the pancreatic head and marked dilatation of extra- and intra-hepatic bile ducts

DISCUSSION

Hodgkin's disease accounts for 17% of all malignant lymphomas and 0.6% of all malignant neoplasms (6). Its primary extranodal form occurs in 15–30% of cases and is rarer than in non-Hodgkin's lymphomas (60%) (2). The frequency of involvement of individual organs is as follows: the spleen (30–40%), bone marrow (5–32%), bones (5–20%), nasopharyngeal cavity (20%), liver (6–20%), other organs < 14%. The changes in the infiltrated organs in the case presented above are extremely rare – the incidence of pulmonary lesions is assessed as 5.9–11.6% and of pancreatic ones – 0.3–2.2% (1).

CT features of kidney lymphomas. The kidney involvement in non-Hodgkin's disease is quite common, even 30–60% according to autopsy data; the diagnoses in imaging examinations are rare – 3–8% of CT conducted to evaluate the disease staging. The majority of cases reported in the literature concern non-Hodgkin's lymphomas, however CT images of Hodgkin's and non-Hodgkin's lymphomas are similar. The lymphomatous lesions in kidneys may occur as single tumours (10–20%) or multiple uni- and bilateral foci (60%) (8). Moreover, some rare forms are described, e.g. features of haematoma, kidney necrosis, non-homogenous parenchymal densities or cysts.

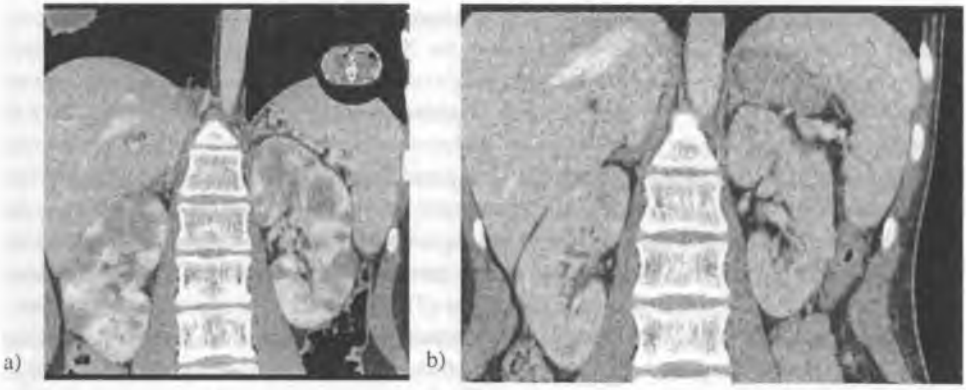

Fig. 3. The CT image in coronal projection of numerous renal tumours in the parenchymal phase before (a) and after treatment (b)

Typical cases show numerous tumours, 1–3 cm in size; after intravenous contrast administration, minimal enhancement is observed and the lesion manifests itself in the form of hypodense area in comparison with healthy parenchymal renal tissue; typical homogenous foci, heterogenous foci or cysts are visible demonstrating the tumour necrosis in patients after chemotherapy. In about 50% of patients the kidney lesions accompany nodal involvement. In our case, the picture of renal changes was similar; preserved normal renal excretory function despite severe nodular lesions and short time of their development (several weeks) are worth stressing.

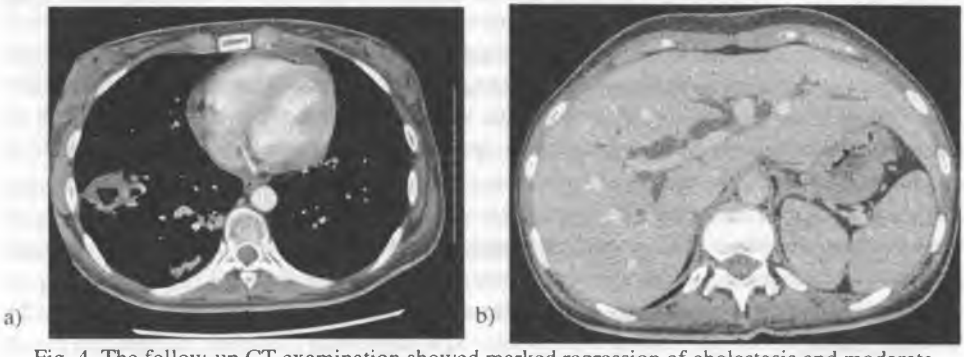

Fig. 4. The follow-up CT examination showed marked regression of cholestasis and moderate reduction of foci in the lungs (a, b)

The picture of a single lymphomatous tumour may be more difficult to interpret. The structure is similar to that in multiple lesions – usually homogenous with slight contrast enhancement. The tumour size may reach even 15 cm. In such cases, the differentiation between primary lymphomatous infiltration, some forms of kidney carcinoma and benign tumours is more difficult; in general, however, the kidney foci are secondary to nodal lesions. Less difficult to diagnose are lymphomatous infiltrations in the form of big tumours involving kidney vessels and penetrating its parenchyma due to their spread from the retroperitoneal space; such lesions occur in about 25–30% of cases (8).

CT image of pancreatic lymphomas. The lymphoma, mainly non-Hodgkin's, B-cell subtype, involves secondarily the pancreas in about 30% of patients with disseminated disease. The pancreatic lymphoma picture is most often visible as homogenous tissue tumours with slight

enhancement following intravenous contrast administration. The primary involvement of pancreatic parenchyma may be difficult to differentiate from the lymphoma involving peripancreatic lymph nodes. Two different CT pictures were described, single or multiple tumours and diffused enlargement of the gland caused by the infiltrating tumour (7). Marked enlargement of the pancreas may be caused by the diffused tumour as well as tumour-induced pancreatitis or pancreatitis connected with tumour disintegration following chemotherapy, the pancreas is usually homogenous and relatively hypodense on native CT scanning. The peripancreatic vessels may be involved, however the obstruction of the pancreatic duct is not common (in contrast with massive tumours), which is the feature differentiating it from adenocarcinoma. The presence of lymphadenopathy below the level of kidney veins also speaks in favour of lymphoma (5). The authors found the literature reports describing single, similar cases with analogous symptoms: weight loss, pale stools with painless jaundice, yet they concerned non-Hodgkin's lymphomas (3, 9). In our case numerous tumours up to 5 cm in size which deformed the organ contours. The biggest tumour located in the pancreatic head caused the features of cholestasis.

Lymphoma of the lungs. The thoracic location is common in Hodgkin's disease although involvement of pulmonary parenchyma is relatively rare (5.9%–11.9% of cases; 4.3% bilaterally) and is usually accompanied by hilar or mediastinal lymphadenopathy. Primarily the disease is located in hili and spreads to the pulmonary parenchyma. A predilection to upper lobe involvement is observed. In general, chest CT is used in lymphoma patients to assess their response to therapy, evaluation of recurrences, to monitor the patients before and after bone marrow transplantations and to diagnose some complications, e.g. pneumonia, metastases and post-radiation lesions (1). Lymphomatous infiltrations in the pancreas, lungs and kidneys found in our patient are extremely rare. The authors did not come across any cases of such coexisting lesions complicated with obstructive jaundice in Hodgkin's disease patients without nodal involvement. The CT picture of the focal changes described is not characteristic and may occur during the spread of other neoplastic processes. Our case, however, shows that in young patients Hodgkin's lymphoma should be taken into account when metastatic renal or pancreatic lesions have been detected and patients with the diagnosis of Hodgkin's disease regular follow-ups at abdominal parenchymal organs ought to be conducted even during therapy.

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SUMMARY

The extranodal forms of lymphomas are most frequently secondary and particular organs are more often involved by direct spread through node infiltrations than through blood. The extranodal lesions are more common in non-Hodgkin's lymphomas; when present in Hodgkin's disease they mostly involve the spleen, bone marrow, bones, nasopharyngeal cavity and liver. The authors present an extremely rare picture of lesions detected by 64-slice computed tomography in a 22-year-old female patient with Hodgkin's disease, nodular sclerosis type. Initially, the patient had the lesions in the mediastinum and cervical and axillary nodes; after a year of treatment multifocal infiltrations developed in the lungs. The parenchymal lesions had partially visible air bronchogram, some were surrounded by the ground glass zone. During chemotherapy multiple pancreatic nodular lesions developed with the features of cholestasis and jaundice as well as numerous bilateral tumours in the kidneys. On CT scans conducted using two-phase method the pancreas was enlarged, tumours were 1–5 cm in size, hypodense and showed slight non-homogenous contrast enhancement in the parenchymal phase. The 1–3 cm hypodense tumours of the kidneys were slightly enhanced in the parenchymal phase mainly on the periphery. The peripheral lyph nodes, abdominal and mediastinal nodes were not enlarged. After the ESHAP treatment the follow-up CT examination showed marked regression of renal lesions and moderate reduction of foci in the lungs and pancreas; the CT scan revealed the features of tumour. The paper also presents a review of the literature concerning the lesions in the pulmonary parenchyma, kidneys and pancreas found in Hodgkin's disease and non-Hodgkin's lymphoma.

Mnogie zmiany ogniskowe płuc, trzustki i nerek u młodej pacjentki z ziarnicą rozpoznane w wielorzędowej tomografii komputerowej – opis przypadku i przegląd piśmiennictwa

Lokalizacje pozawęzłowe chłoniaków zwykle występują jako postać wtórna, a zajęcie poszczególnych narządów występuje częściej drogą bezpośredniego szerzenia poprzez nacieki węzłowe niż drogą krwiopochodną. Zmiany pozawęzłowe częściej występują w chłoniakach nieziarniczych, a jeśli pojawiają się w ziarnicy, to dotyczą: śledziony, szpiku, kości, jamy nosowo-gardłowej i wątroby. Autorzy przedstawiają bardzo rzadki obraz zmian stwierdzonych w 64-rzędowej tomografii komputerowej u 22-letniej pacjentki z ziarnicą typu *nodular sclerosis*, u której pierwotnie wystąpiły zmiany w śródpiersiu oraz węzłach szyjnych i pachowych, a po roku leczenia pojawiły się wieloogniskowe zmiany naciekowe w płucach. Zmiany miąższowe miały częściowo widoczny bronchogram powietrzny, a niektóre otoczone były strefą *ground glass*. W trakcie zastosowanej chemioterapii pojawiły się mnogie zmiany guzkowe trzustki z objawami cholestazy i żółtaczką oraz obustronne liczne guzki w nerkach. W badaniach CT wykonanych techniką dwufazową trzustka była powiększona, a guzki miały wielkość od 1 do 5 cm, były hipodensyjne i ulegały bardzo nieznacznemu niejednorodnemu wzmocnieniu kontrastowemu w fazie miąższowej. Hipodensyjne guzki nerek wielkości 1–3 cm nieznacznie wzmacniały się w fazie miąższowej badania, głównie w części obwodowej . Nie stwierdzono towarzyszącego powiększenia węzłów chłonnych obwodowych, jamy brzusznej ani śródpiersia. Po zastosowaniu leczenia wg schematu ESHAP stwierdzono w kontrolnym badaniu CT znaczną regresję zmian w nerkach oraz umiarkowane zmniejszenie się ognisk w płucach i trzustce, w obrazie KT ujawniły się cechy rozpadu guzów. W pracy przedstawiono także przegląd piśmiennictwa dotyczącego występowania zmian w miąższu płuc, nerkach i trzustce w ziarnicy i chłoniakach nieziarniczych.