CASE REPORT

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Disseminated typical bronchial carcinoid tumor

Diseminovani tipični karcinoidni tumor bronha

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Abstract

Introduction. Bronchial carcinoids belong to a rare type of lung tumors. If they do not expose outstanding neuroendocrine activity, they develop without clearly visible symptoms. They are often detected during a routine examination. According to their clinical pathological features, they are divided into typical and atypical tumors. Typical bronchial carcinoids metastasize to distant organs very rarely. Localized forms are effectively treated by surgery. The methods of conservative treatment should be applied in other cases. **Case report.** We presented a 65-year-old patient with carcinoid lung tumor detected by a routine examination. Additional analysis (chest X-ray, computed tomography of the chest, ultrasound of the abdomen, skeletal scintigraphy, bronhoscopy, histopathological analysis of the bioptate of bronchial tumor, as well as bronchial brushing cytology and immunohistochemical staining performed with markers specific for neuroendocrine tumor) proved a morphologically typical lung carcinoid with dissemination to the liver and skeletal system, which is very rarely found in typical carcinoids. **Conclusion.** The presented case with carcinoid used to be showed morphological and pathohistological characteristics of typical bronchial carcinoid. With its metastasis to the liver and skeletal system it demonstrated unusual clinical course that used to be considered as rare phenomenon. Due to its frequent asymptomatic course and varied manifestation, bronchial carcinoid could be considered as a diagnostic challenge requiring a multidisciplinary approach.

Key words:
carcinoid tumor; lung neoplasms; diagnosis; neoplasm metastasis; liver; skeleton; diagnosis, differential; immunohistochemistry.

Apstrakt

Uvod. Karcinoidi bronha spadaju u retke tumore pluća. Ukoliko nemaju izraženu neuroendokrinu aktivnost, karcinoidi bronha protiču bez jasno uočljivih simptoma. Često se otkrivaju tokom rutinskih ispitivanja. Prema kliničko morfološkim karakteristikama karcinoidi bronha dele se na tipične i atipične. Tipični karcinoidi bronha izuzetno retko daju udaljene metastaze. Lokalizovani oblici se efikasno leče hirurški, a u ostalim slučajevima primenjuju se metode konzervativnog lečenja. **Prikaz bolesnika.** Prikazali smo bolesnike starog 65 godina, kod koga je karcinoid pluća uočen tokom rutinskih ispitivanja. Dodatnim analizama (radiografija pluća, kompjuterizovana tomografija grudnog koša, ultrazvuk abdomena, scintigrafija skeleta, bronhoskopija, patohistološka analiza bioptata bronhijalnog tumora i citologija bronhijlanog brisa, kao i imunohistohemijsko bojenje markerima specifičnim za neuroendokrini tumor) dokazano je da se radilo o morfološki tipičnom karcinodu pluća, sa diseminacijom u jetru i koštani sistem, što se izuzetno retko sreće kod tipičnih karcinoida. **Zaključak.** Prikazani slučaj tumora bronha prema citomorfološkim i patohistološkim karakteristikama odgovarao je tipičnom karcinoidu. Imunohistohemijskim analizama potvrđeno je neuroendokrino poreklo tumora. Ovaj tumor je pokazao izražen metastatski potencijal sa metastazama u jetru i koštani sistem, što se sreće u vrlo malom procentu tipičnih karcinoida. Zbog čestog asimptomatskog toka, kao i neobičnih i raznolikih manifestacija, karcinoidi bronha mogu predstavljati dijagnostički izazov čije rešenje zahteva multidisciplinarni pristup.

Ključne reči:
karcinoid; pluća, neoplazme; dijagnoza; neoplazme, metastaze; jetra; kostur; dijagnoza, diferencijalna; imunohistohemija.

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Introduction

A bronchial carcinoid tumor is a rare neoplasm accounting for 2% of all lung tumors. It belongs to a group of neuroendocrine tumors and arises from cells of the bronchial epithelium. These tumors were earlier classified as benign neoplasms [1–4].

According to the modern conceptions, bronchial carcinoid tumor is considered as malignant neoplasm with neuroendocrine differentiation. It shows low degree of malignancy and its biological nature cannot be precisely assessed only on the basis of its morphological appearance [1, 5–7].

These tumors grow endobronchially in the form of polypoid mass with a smooth surface while at the intersection show a characteristic yellow-brown color with calcification often being present. They often arise in the right lung. In about 68% of cases, they manifest as centrally localized spheral formations sized 0.3–7.5 cm in diameter while in about 30% of all cases they appear as peripheral changes in the form of clearly limited, non-encapsulated nodules [4].

They are classified as central and peripheral, based on their location in lung. Symptoms can vary depending on the location of a tumor. In central tumors symptoms as recurrent pneumonia (41%), cough (35%), hemoptysis (23%) most often occur, while peripheral tumors show significantly fewer symptoms and often develop without any symptoms [4, 8, 9]. Due to this fact, they often develop as undetected and may be revealed during a routine examination [10, 11].

Typical carcinoids are composed of characteristic, uniform population of polygonal cells with fine eosinophil granulocyte cytoplasm and centrally located dark-coloured nucleus. There are rare mitotic figures, no more than two in ten visual fields. The cell can grow as mosaic structures placed around blood vessels, building trabecular and adenopapilar structures with often-present calcifications and amyloid deposits.

Through special, immunohistochemical staining, high positive reaction for chromogranin, synaptophysin and neuron-specific enolase (NSE) is registered which also confirms the carcinoid diagnosis [1, 3, 10, 11].

Unlike typical carcinoids, atypical carcinoids are characterized by nuclear pleomorphism and hyperchromasia, higher degree of cell disorganization, necrosis, as well as by more intensive mitotic activity. Because of their histological characteristics derives greater metastatic potential of atypical carcinoids. In accordance with the above presented facts, there is a difference between clinical courses in these two types of carcinoids. Typical carcinoids rarely develop distant metastases, therefore they have more favorable prognosis. In about 15% of all cases, they metastasize to regional lymph nodes while the metastases to distant organs are very rare and can be registered in about 2% of all patients. A 5-year survival rate for typical carcinoids is 87–100% of all cases. Unlike them, atypical carcinoids in 10% of all cases develop distant metastases while 5-year survival rates in this type of carcinoid approach 35–69% [11–14].

Carcinoids may also arise from other organs. They are often detected at various levels of gastrointestinal tract, yet most commonly in appendix, ileum and rectum. Appendix carcinoids are usually benign and may cause appendicitis. In addition to the above cited characteristics, these tumors can have outstanding neuroendocrine component in cases where, due to the serotonin excess, they exhibit carcinoid syndrome whose main manifestations are present as facial redness, nausea, diarrhea and hypotension [4].

In terms of therapeutic methods, surgical treatment [15] is most effective. In some cases, chemotherapy for non-small cell lung tumors may be applied.

Case report

A 65-year-old man was admitted to the Military Medical Academy (MMA), Belgrade, for medical examination in order to clarify the etiology of infiltrative changes in the lungs and liver, which were accidentally detected during examination, because the patient complained of vague symptoms of discomfort in the area of rib cage and thoracic spine.

The changes in the liver with morphologic features of metastases were detected at initial ultrasound of the abdomen.

Chest X-ray (radiography) showed a change in the left lung, which might be interpreted as tuberculous nodule, nonspecific inflammation, or tumor change.

On the day of admission to our clinic, the patient reported pain in the area of rib cage and thoracic spine. Objective examination below the rib cage revealed an increase of liver size by 3 cm. Physical report on other systems and organs was normal.

Blood and biochemical test results were within the reference ranges.

Control chest X-ray confirmed the existence of an oval shadow 3 × 4 cm in diameter, localized parahilary to the left – on the lower pole of the hilar region (Figure 1).

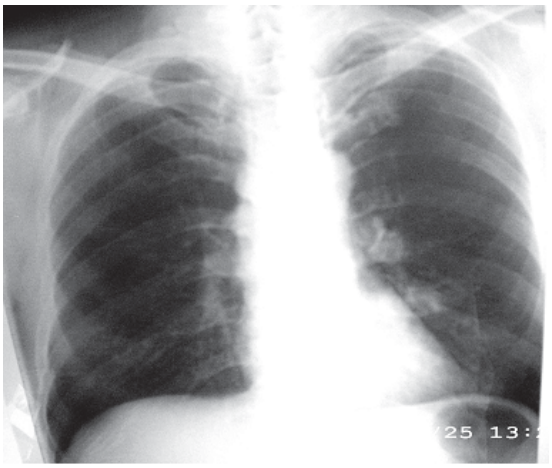

Fig. 1 – Left chest X-ray in the projection of the lower pole of hilar region showing an oval-shaped shaded area of 3 cm × 4 cm.

Computed tomography (CT) scan of the left chest, under the main bronchus, between the hilum and posterobasal segment revealed a solid, oval tumor formation 3 × 4 cm in

diameter (Figure 2). Cross section through the upper abdomen demonstrated a large number of changes in both lobes of the liver that according to their morphological features corresponded to metastatic deposits (Figure 3).

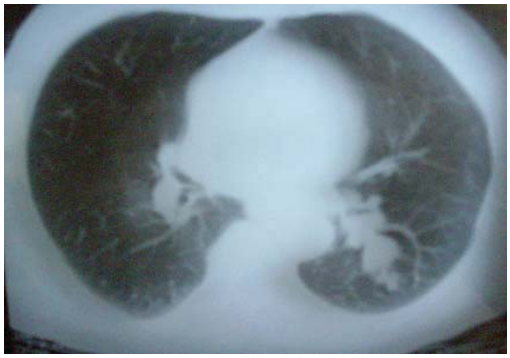

Fig. 2 – Chest computed tomography (CT) scan showing left, a solid, oval tumor formation of 3 × 4 cm, below the main bronchus, between the hilum and the posterobasal segment.

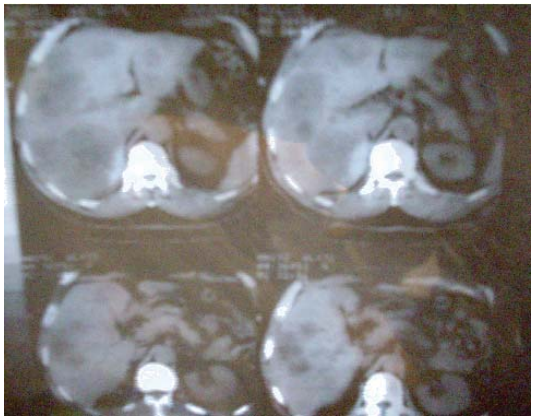

Fig. 3 – In sectional views through the upper abdomen, there are a large number of lesions in both liver lobes, which could, according to their morphological characteristics, represent metastatic deposits.

Ultrasound scan of the abdomen revealed an enlarged liver with several round, solid, diffusely placed lesions. The greatest lesion was 8 cm in diameter with signs of central necrosis (Figure 4). Skeletal scintigraphy showed an increased accumulation of radiotracer in the ribs and in the sternum (Figure 5).

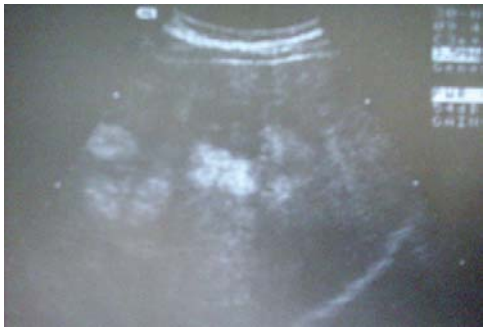

Fig. 4 – Ultrasound examination of the abdomen revealed the enlarged liver with a number of round, solid, diffusely distributed changes (the greatest change was as large as 8 cm, with signs of central necrosis).

Next, bronchoscopy revealed obturation of bronchi LB9 and LB10 by smooth, pink and round tumor change (Figure 6).

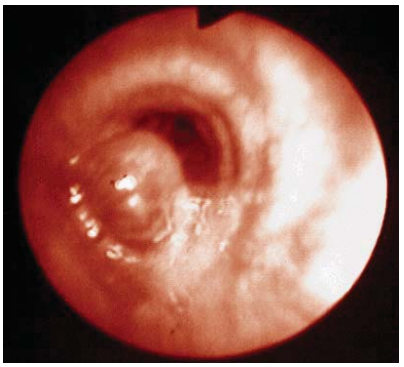

Fig. 6 – Endoscopic finding: an obturation of the bronchi LB9 and LB 10 with a smooth, pinkish, round tumor change.

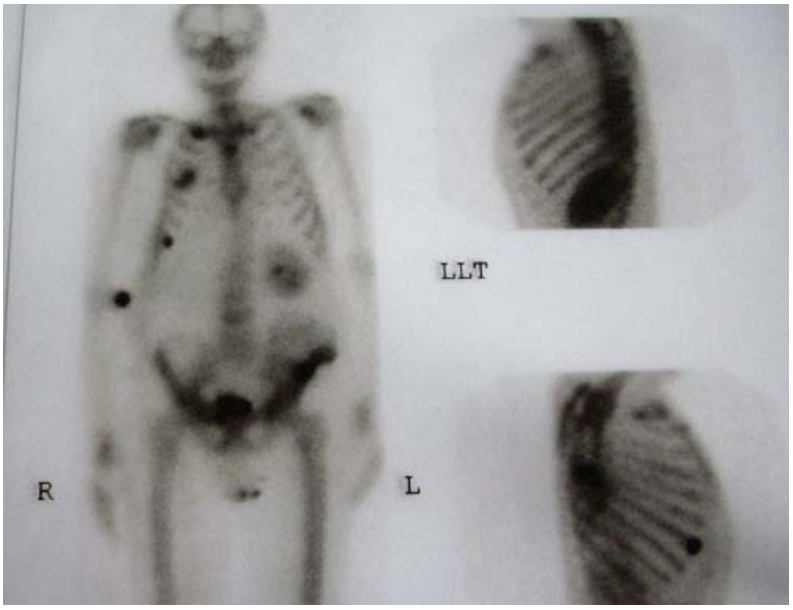

Fig. 5 – Sceletal scintigraphy discovered intensified radiotracer collections in the ribs and the sternal bone.

Histopathological analysis of bronchial tumor change bioptate showed stringy proliferation of uniform, neoplastic cells with nuclei without mitotic figures and visible nucleoli (Figures 7 a and b). Cytological analysis of smear of bronchial brushings detected monomorphic cells with round or oval nuclei, fine chromatin structure, without visible nucleoli and mitotic figures. The nuclei were centrally or eccentrically located in light, basophilic cytoplasm moderate in abundance (Figures 8 a and b). The test results indicated a carcinoid tumor.

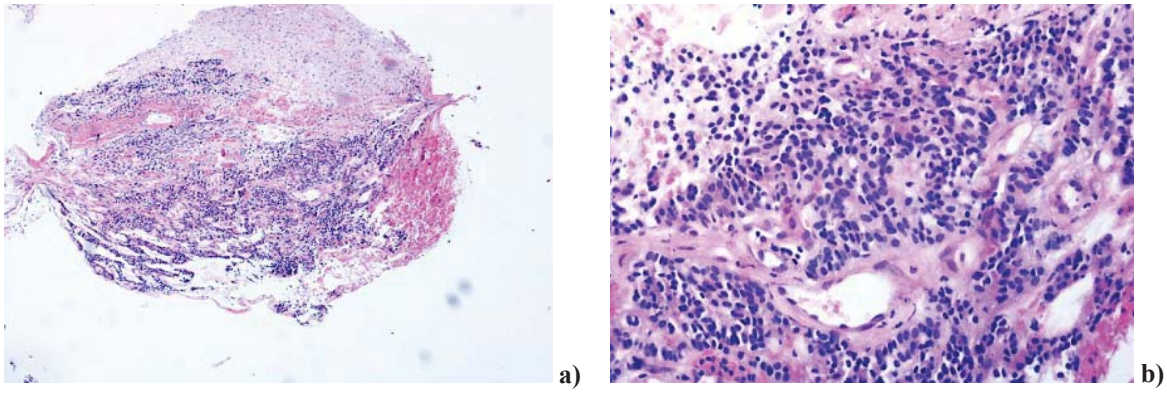

Fig. 7 – Histopathological analysis of the tumor change bioptate: a) stringy proliferation of uniform, neoplastic cells [hematoxylin and eosin (HE), ×200]; b) nuclei without mitotic figures and visible nuclei (HE, ×400).

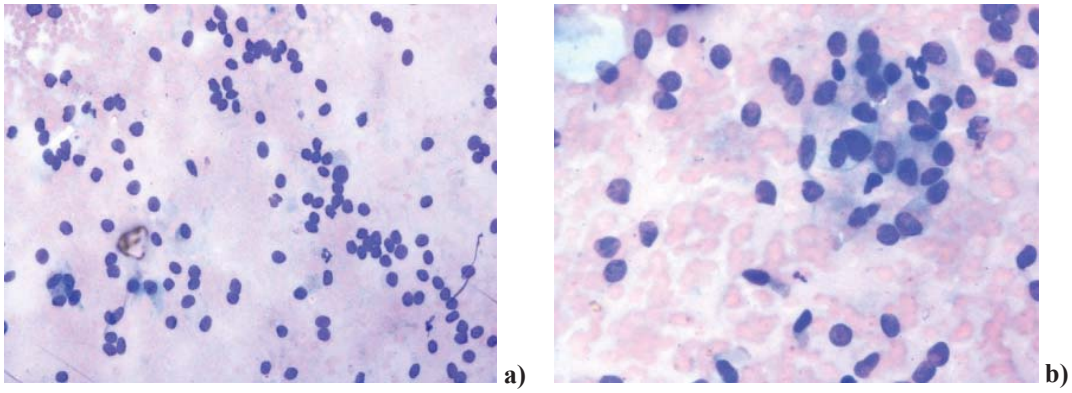

Fig. 8 – Citology analysis of a bronchus swab: a) monomorphic cells with round or oval nuclei of fine chromatin structure, without visible nucleoli and mytotic figures [May-Grünwald-Giemsa (MGG), ×200]; b) nuclei are centrally or eccentrically located in light basophilic and moderate quantity cytoplasms (MGG, ×400).

Immunohistochemical staining performed with markers specific for neuroendocrine tumor demonstrated diffuse a high positivity of tumor cells for chromogranin, neuron specific enolase (NSE), synaptophysin and focal membrane positivity of CD57, which was considered as additional confirmation that it was a carcinoid tumor (Figures 9 a–d).

Cytological analysis of material obtained by a needle biopsy of the liver change showed numerous disperged, separate and grouped tumor cells with fine chromatin structured nuclei, shown as "salt and pepper", without mitotic figures and nucleoli. The parts of capillary loops filled with tumor cells were also found. The obtained results indicated metastatic changes of the bronchial carcinoid (Figures 10 a–d).

Discussion

Bronchial carcinoids are rare neuroendocrine lung neoplasms that are divided into typical and atypical carcinoids according to their pathological and clinical characteristics.

Typical bronchial carcinoids in relation to atypical ones are characterized by increased frequency, milder clinical course and low malignant potential [8, 15, 16].

Typical carcinoids usually appear in the right lung, as solitary endobronchial proliferation localized in the larger airways to the level of the lobar bronchi. They are rarely present as peripheral pulmonary tumors. Most frequently, they metastasize to regional lymph nodes while the occurrence of distant metastases is extremely rare [17].

In our review, bronchial carcinoid showed no typical respiratory symptoms and through additional testing we discovered several unusual features.

The patient was a man aged 65 years, although this type of tumor is more often found in women of 50 years of age [4].

Radiographic and endoscopic examination methods indicated the presence of tumor of the lungs, with present metastatic changes in the liver and bones.

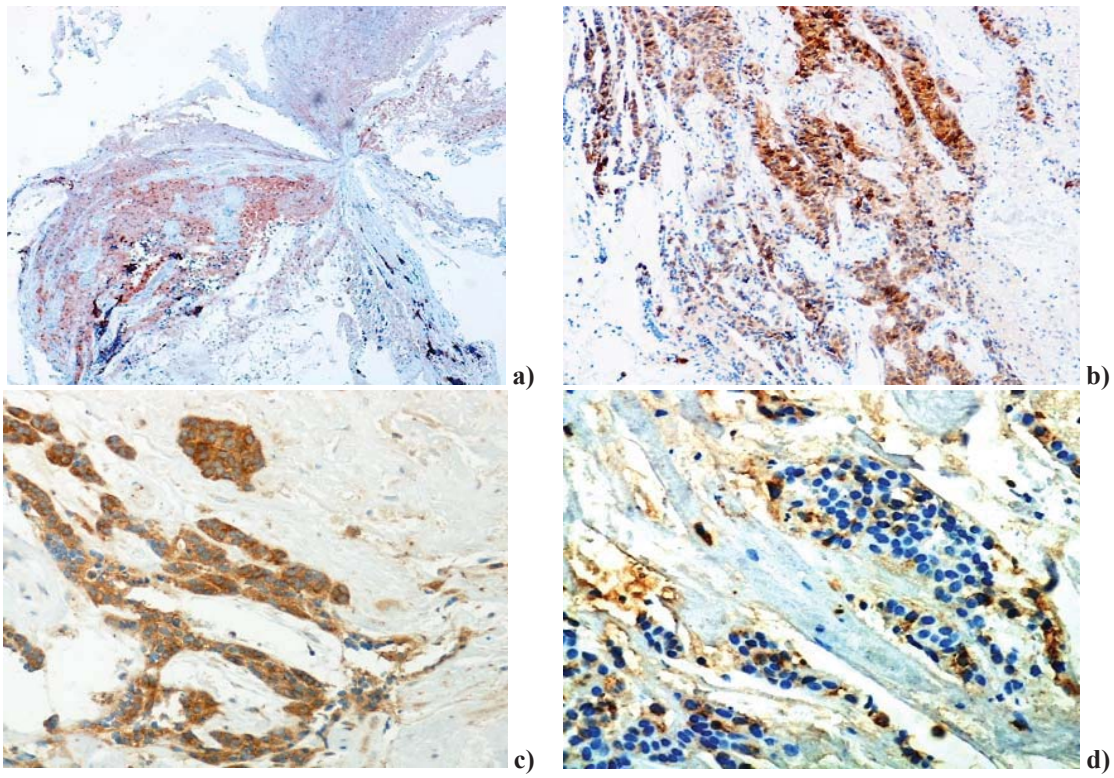

Fig. 9 – Immunohistochemical staining for neuroendocrinal tumor specific markers revealed tumor cells high positive to: a) chromogranin A (×200); b) high positivity of tumor cells for neuron specific enolase (NSE) (×400); c) high positivity of tumor cells to synaptophysin (×400); d) focal membranous positivity of Cd 57(×400).

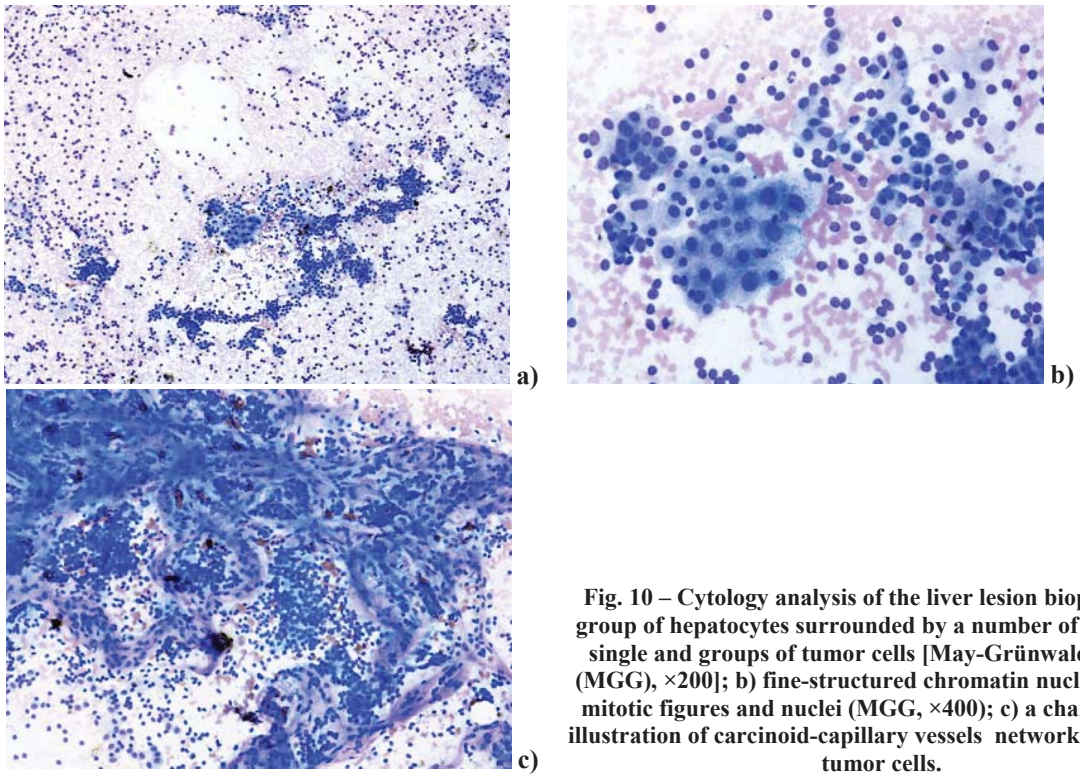

Fig. 10 – Cytology analysis of the liver lesion bioptate: a) a group of hepatocytes surrounded by a number of dispersed single and groups of tumor cells [May-Grünwald-Giemsa (MGG), ×200]; b) fine-structured chromatin nuclei, without mitotic figures and nuclei (MGG, ×400); c) a characteristic illustration of carcinoid-capillary vessels network, filled with tumor cells.

Cytological and histopathological findings suggested a picture of typical carcinoid. It was composed of dispersed cells and bands, trabeculae, papillae and rosettes of uniform, small neoplastic cells with round nuclei and "salt-and-pepper" chromatin without visible nucleoli and mitotic figures.

In liver metastatic change a typical picture of the network of blood vessels with neoplastic cells adhering to its wall was found. With the use of immunocytochemical staining for chromogranin A, NSE, synaptophysin and CD57 the differentiation of neuroendocrine tumor was confirmed.

Despite monomorphism of tumor cells without atypia and mitosis, which classifies the tumor as "low-grade" neuroendocrine neoplasm, it was a disseminated type of typical bronchial carcinoid with metastases in the liver and bones.

However, the appearance of multiple metastases of typical bronchial carcinoid, as described in our work, is very rare. A similar manifestation of this type of carcinoid was described in the work of Suemitsy et al. [18] reporting a case with typical bronchial carcinoid metastasized to the liver.

We presented a rare case of bronchial carcinoid that had cytological and patohistological morphologic features of typical carcinod, while according to its biological behavior and metastatic potential it corresponded to aggressive neoplasms of the lungs, which significantly deviated from the usual picture of typical bronchial carcinoid.

Conclusion

The reported case completely corresponded to a group of typical carcinoids, according to its morphological, cytological and pathohistological features. It differed from typical carcinoids in metastases to the liver and skeletal system that used to be considered extremely rare phenomenon. Due to its asymptomatic course and unusual and diverse manifestations, bronchial carcinoid could present a diagnostic challenge deserving multidisciplinary approach.

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