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CASE REPORTS

Diagnostic Challenges in Atypical Pulmonary Carcinoid

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Abstract

Atypical pulmonary carcinoid is a very rare and aggressive neuroendocrine tumor with a very poor prognosis and a high incidence of metastasis. We report a case of atypical pulmonary carcinoid diagnosed by resected secondary parotid tumor. A 67-year-old man was extensively investigated almost one year for a suspicion of lung tumor that could not be biopsied during bronchoscopy due to peripheral location of the lesion. At the presentation to our service, the patient had multiple diffuse distant metastases, which raised diagnostic difficulties. The final diagnosis was made by histopatological and immunohistochemical exam from the secondary parotid cancer. The key of the diagnosis could be the attentive clinical examination. The preoperative diagnosis can be extremely difficult, needle aspirate or small biopsy being most of the times insufficient for diagnosis.

Keywords: neuroendocrine tumor, atypical pulmonary carcinoid, parotid metastasis

Rezumat

Carcinoidul pulmonar atipic este o tumoră neuroendocrină agresivă, foarte rară, cu prognostic prost şi incidență crescută a metastazelor. Prezentăm cazul unui pacient în vârstă de 67 ani cu carcinoid pulmonar atipic, diagnosticat prin rezecția unei determinări secundare parotidiene. Acest pacient a fost intens investigat timp de un an pentru tumoră pulmonară, ce nu a putut fi biopsată în timpul bronhoscopiei, din cauza localizării periferice a leziunii. La internarea în clinica noastră pacientul avea multiple metastaze, ce au ridicat dificultăți de diagnostic. Diagnosticul de certitudine a fost pus pe baza examenelor histopatologic şi imunohistochimic dintr-o mestastază parotidiană. Cheia diagnosticului într-un astfel de caz poate fi examenul obiectiv atent. Diagnosticul preoperator poate fi extrem de dificil, aspiratul sau biopsiile mici fiind de multe ori insuficiente pentru diagnostic.

Cuvinte-cheie: tumoră neuroendocrină, carcinoid pulmonar atipic, metastază parotidiană

INTRODUCTION

The spectrum of neuroendocrine tumors (NETs) of the lung is wide and heterogeneous, ranging from well-differentiated bronchial neuroendocrine tumors to highly malignant and poorly differentiated small cell lung cancer and large cell neuroendocrine carcinoma[1]. NETs of the lung share both morphologic and immunohistochemical characteristics with neuroendocrine tumors[2,3].

MATERIAL AND METHODS

We report a case of a 67-year-old man who presented to the Emergency Department of our hospital for palpitations, dyspnea at rest, productive cough, upper

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abdominal pain, weight loss, anxiety. He was a former smoker (36 pack-years). The patient had a medical history of type 2 diabetes mellitus and chronic viral hepatitis HBV. During the last year, he was extensively investigated for a suspicion of lung tumor. Thoracic and abdominal CT scan one year ago revealed infracarinal heterogenous mass infiltrating the right main bronchus, secondary lung, liver and bones tumors. Whole body bone scintigraphy showed secondary bone determinations and right femoral osteogenic lesion, possible primitive or secondary tumor. Surgical femoral resection for biopsy had no concluding result. Repeated CT scan 3 months later revealed pancreatic body lesion, infiltrating anterior peritoneum with expansion to Wirsung channel downstream. The possibility of infiltrative tumor of the pancreas has been raised. The patient has undergone transgastric pancreatic biopsy, without atypical lesions. Total colonoscopy showed no lesions. Bronchoscopy indicated distorted right lower lobar bronchus, with altered mucosa. The distally location of the lesion made impossible the biopsy. Bronchoalveolar aspirate had mucilaginous aspect, negative Ziehl-Nielsen stain, numerous red blood cells, eosinophils and macrophages, microbial flora, without atypical cells.

The physical examination on admission revealed a blood pressure of 130/90 mmHg, irregular heart rate of 143 bpm, bronchial rales, dyspnea at rest, firm hepatomegaly, cachexia, SpO_2 87% while breathing ambient air and a 2 cm mass adherent to the deep tissue in the right parotid area. Blood tests showed normal hemogram values, high amylase (222 IU/L), cholestasis syndrome (total bilirubin 1.8 mg/dL, direct bilirubin 1.1 mg/dL, alcaline phosphatase 370 IU/L, gamma-glutamyl-transferase 750 IU/L), mild hepatic cytolysis; positive anti-HBs antibodies, positive inflammatory tests, tumor markers (alpha-fetoprotein, CA-125, CA 15-3, PSA, free-PSA) in normal limits with exception of mild elevated levels of CA 19-9 (70 U/mL) and calcitonin (33.2 pg/mL).

Abdominal ultrasonography revealed multiple irregular hypoechoic nodules throughout the liver, up to 27.5x23 mm (Figure 1a,b), a retroperitoneal mass of 86x53x39 mm, with hypoechoic inhomogeneous structure, ill-defined margins, probably arising from pancreas (Figure 1c), mild splenomegaly. Thyroid ultrasound showed multiple hypoechoic nodules, up to 7.6 x 7.2 mm, with irregular margins. Right parotid ultrasound revealed a well-delineated hypoechoic nodule, 16/9.2

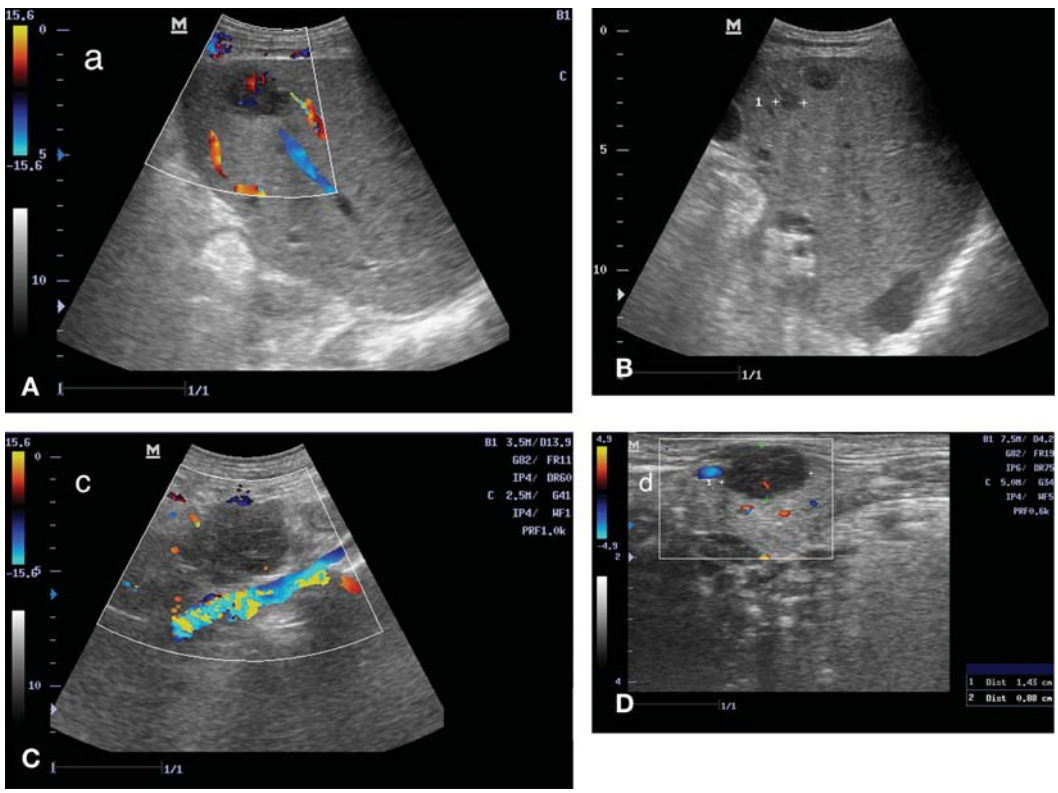

Figure 1. Imaging studies: A. Abdominal ultrasonography revealed irregular hypoechoic nodule in the right lobe of the liver, 27.5x23 mm diameter, with positive color Doppler signal. B. Multiple irregular hypoechoic nodules throughout the liver. C. A retroperitoneal mass of 86 x 53 x 39 mm, with hypoechoic inhomogeneous structure, ill-defined margins, arising from pancreas, adjacent to the inferior vena cava. D. Right parotid ultrasound revealed a well-delineated hypoechoic nodule, 16/9.2 mm, with visible color Doppler flow.

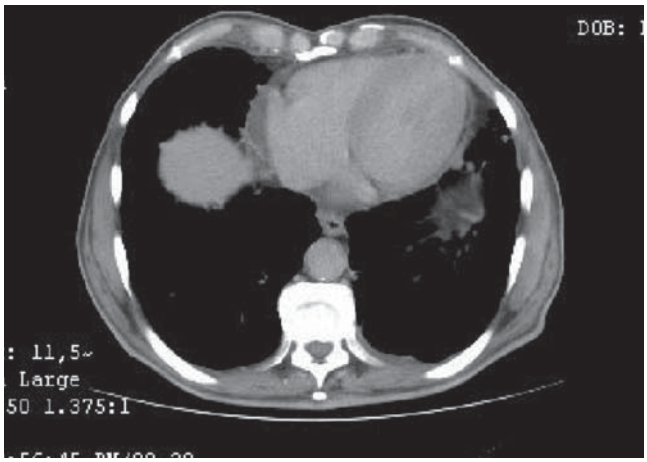

Figure 2. Thoracic CT scan: Tumoral masses in both lungs.

mm, with visible color Doppler flow (Figure 1d). Transthoracic echocardiography showed normal aspect. ECG at rest: atrial fibrillation with ventricular rate of 143 bpm. Thoracic, abdominal, head and neck CT scan identified multiple tumors in the lungs (Figure 2), liver, pancreas, mediastinal lymph nodes, bones, thyroid and parotid glands, probably with starting point in the lungs; without brain lesions.

The fact that despite the severity of multiple organ lesions the patient was in a relatively good condition raised the suspicion of a neuroendocrine neoplasia. The parotid tumor was resected. Histopathological examination of the specimen revealed a nodular lesion located within parotid gland and covered by its capsule.

RESULTS

Microscopic appearance of the tumor was a proliferation composed of medium size cells, with uniform, rather monomorphic, round shaped, with aveolar and compact pattern (Figure 3a). The cytoplasm was moderate eosinophilic with some clear features and the nuclei showed finely granular chromatin. The mitotic activity was low, around 4 mitoses / 2 mm^2 and no necrosis was identified. The tumor infiltrated the salivary gland parenchyma. Immunohistochemistry showed chromogranin (Figure 3b), synaptophysin and TTF-1 (Figure 3c) with diffuse strong reaction in tumor cells. Ki67 index was around 25% (Figure 3d). Only rare tumor cells were positive for S100. Ck7, Ck20, actin, vimentin and CEA were absent.

The diagnosis was neuroendocrine tumor of intermediate differentiation grade, consistent within clini-

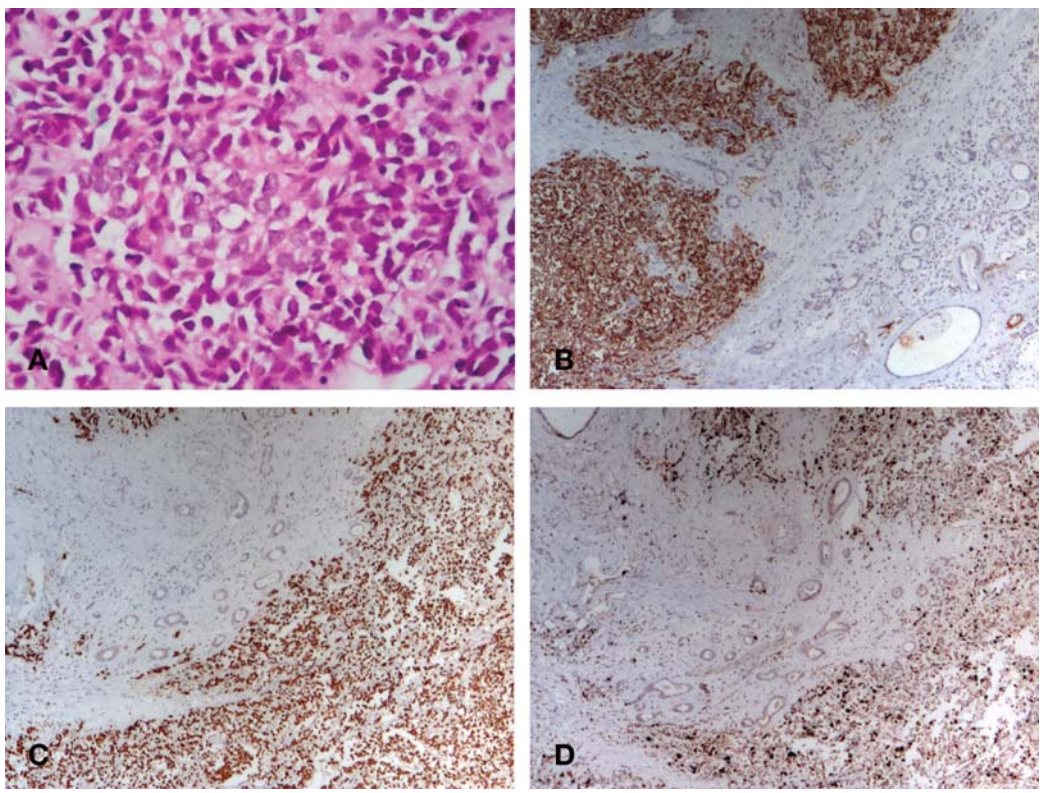

Figure 3. A. Microscopic appearance showed a compact proliferation of medium size cells, round shaped, with moderate eosinophilic or clear cytoplasm and finely granular nuclear chromatin (Hematoxylin and eosin staining, magnification x 20). B. Chromogranin expression (Immunohistochemistry, magnification x 10) C. TTF-1 expression (Immunohistochemistry, magnification x 10) D. Ki67 index around 25% of tumor cells (Immunohistochemistry, magnification x 10).

cal context with a metastasis of an atypical pulmonary carcinoid.

DISCUSSION

The incidence of pulmonary NETs is low, although reported to have increased over the last years, mainly due to improved methods and diagnostic protocols[1]. NETs of the lungs comprise 20%-25% of all invasive lung malignancies[1,2]. Atypical carcinoids represent 0.1%-0.2% of primitive pulmonary tumors[1,3]. 40%-50% of them have lymphatic metastases and 20%-25% have distant metastases at the time of diagnosis[3]. Because of its tendency for metastasis, multiple imaging methods could be useful[4]. Metastatic NETs of the parotid were rarely reported[5]. Immunohistochemically, chromogranin, synaptophysin, thyroid transcription factor 1 (TTF-1) and the proliferation index by Ki-67 staining are necessary for positive diagnosis[1,2,6,7]. Small biopsies couldn't make an easy differential diagnosis between typical and atypical carcinoid[8].

This case shows a lung tumor and diffuses distant metastases, which raised diagnostic difficulties. The primitive lung tumor was located peripherally and biopsy could not be done during bronchoscopy. The results of initial pancreas and bone biopsies were negative because the needle aspirate or small biopsies are sometimes insufficient for histopathological diagnosis. The patient did not have any sign of carcinoid syndrome, hypoglycemia, diarrhea or hypertensive crisis. Glandular involvement was suspected in the context of atrial fibrillation without valve disease. Ultrasound examination raised the suspicion of neuroendocrine neoplasia, due to multiple tumors in liver, pancreas, thyroid and parotid glands, confirmed by CT scan. The histopathological diagnosis was finally done after the resection of the superficial parotid tumor.

CONCLUSIONS

Atypical pulmonary carcinoid is a very rare and aggressive neuroendocrine tumor with a very poor prognosis and a high incidence of metastases. The exact incidence of atypical carcinoid is not known. The preoperative diagnosis can be extremely difficult, needle aspirate or small biopsy being most of the times insufficient for diagnosis.

Acknowledgement: no financial support for this work.
Conflicts of interest: none declared.

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