A PRIMARY PAPILLARY ADENOCARCINOMA OF THE LUNG

: A CASE REPORT OF A RARE LUNG NEOPLASM DIAGNOSED BY CYTOLOGICAL SMEAR AND MICROBIOPSY :

Čeganová L., Dvořáčková J.(1), Čegan M., Janásková T.(2), Kiša T. (2),
Nieslanik J., Šustíková J.

CGB Laboratory Inc., Ostrava, Czech Republic
(1) Institute Of Pathology, Faculty Hospital, Ostrava, Czech Republic
(2) Departement Of Tuberculosis And Respiratory Diseases, Vítkovice Hospital, Ostrava, Czech Republic

ABSTRACT

A case report of an unusual lung neoplasm that present less than 8 % of all lung neoplasms. Primary papillary adenocarcinoma of the lung is rare disease and may cause diagnostic difficulties both in cytology and histology without immunohistochemistry, especially by women.

63-year old woman with clinically presenting tumor of left pulmonary apex. Endoscopically visible dilatation of main carina and bronchostenosis in B1-2 left, suspect for malignancy. Cytological smears and microbiopsy were performed in two sequences. Histological sections were stained by haematoxylin-eosin and PAS method, cytological smears by May-Grünwald-Romanowski and PAS staining too.

In cytology smears (flush, lavage and brush) we find inflammatory irritated background with bunches of a malignant cells in a virtual papillary formations with sporadic psammoma bodies. First executed microbiopsy showed intravascular located plugs of a several malignant cells with psammoma bodies. Immunohistochemistry failed for a little material and there was concluded diagnosis of suspicion on metastatic infliction by papillary carcinoma (maybe thyroid or ovary). No clinical signs of tumor in this sites was find. Then a second draft of tissue was made. Cytological smears hold identical image of first opinion like. From second microbiopsy was made an immunohistochemical study. The tumor cells presented CK7 and TTF-1 positivity and CK20 and thyreoglobulin negativity provided irrefutable evidence for the diagnosis of primary lung cancer.

Primary papillary lung carcinoma is rare tumor. We suggest that in dealing with coexistence of ovarian and pulmonary tumors, only immunohistochemical study (CK7, CK20, TTF-1, thyreoglobulin) may be helpful in the differentiation of the primary origin.

MATERIAL AND METHODICS

63-year old non-smoking woman presenting with pathological fracture of a left thigh. Further diagnostic presents with stellate density (cca 40,0 mm in diameter) of the apicodorsal segment of the left lung with intrathoracic lymphadenopathy and metastases in axial skelet on CT imaging *(Fig 1a)*. Scintigraphy showed multiple osteolytic metastases in the skull, ridge *(Fig. 2b)*, pelvic bones and a left thigh bone too.

By bronchoscopy a transbronchial pulmonary microbiopsy and cytological smears (flush, lavage and brush) were made. Cytological smears were stained by *MGG Quick Stain (Bio-Optica, Milano)* and *PAS* methods. A material from the microbiopsy was classically processed by formol fixation and embedded in paraffin. Paraffin histological sections were stained by haematoxylin-eosin and PAS method.

In cytology smears we find an inflammatory irritated background with bunches of a high grade malignant cells in a virtual papillary formations *(Fig. 2a-c)* with sporadic psammoma bodies *(Fig 3)*. First executed microbiopsy showed intravascular located plugs of a several malignant cells with psammoma bodies *(Fig 4a-c)*. Immunohistochemistry failed for a little material and there was concluded diagnosis of suspicion on feasible metastatic infliction by papillary carcinoma (maybe thyroid or ovary).

All suspected sites was overlooked. No signs of tumor in this locations were registered. After consultation a second draft of microbiopsy and cytology was made. Histological sections indicate a presence of papillary formations of tumor cells, without a presence of a psammoma bodies. Immunohistochemical study shows positivity of cytokeratin 7 (monoclonal mouse, clone OV-TL 12/30, DAKO, dilution 1:100) *(Fig 5)* and TTF-1 (monoclonal mouse, clone 8G7G3/1, DAKO, dilution 1:100) *(Fig. 6)*. Staining for cytokeratin 20 (monoclonal mouse, clone Ks20.8, DAKO, dilution 1:100) and thyreoglobulin (polyclonal rabbit, DAKOm dilution 1:50) was completely negative. These results lead to diagnosis of primary papillary adenocarcinoma of the lung.

The patient clinically staged T2N2M1, stadium IV, ECOG 1 and was indicate to paliative chemotherapy ever obtained 6 cycles of combined chemotherapy *(docetaxel+carboplatinum)* with clodronate. A control CT imaging and scintigraphy indicate a partial tumor regression without lymphadenopathy after first line of cure. In second line was begun monotherapy with gefinitibe (Tarceva). To this time no control stage-imaging are available.

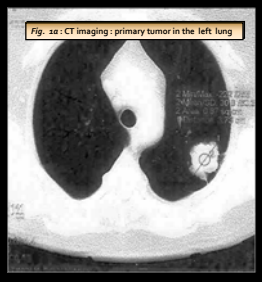
Fig. 1a : CT imaging : primary tumor in the left lung

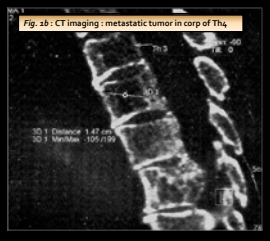
Fig. 1b : CT imaging : metastatic tumor in corp of Th4

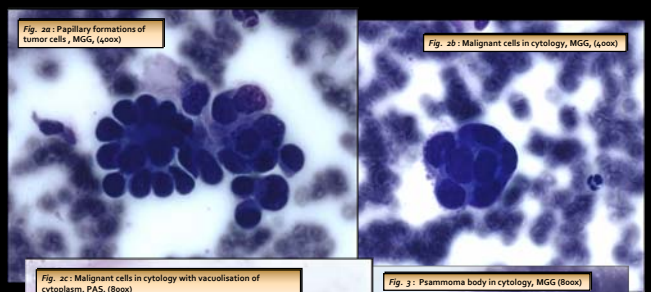
Fig. 2a : Papillary formations of tumor cells , MGG, (400x)

Fig. 2b : Malignant cells in cytology, MGG, (400x)


Fig. 2c : Malignant cells in cytology with vacuolisation of cytoplasm, PAS, (800x)

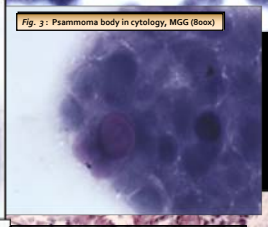
Fig. 3 : Psammoma body in cytology, MGG (800x)

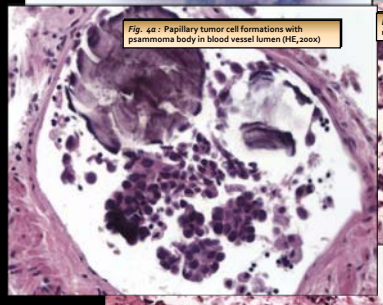
Fig. 4a : Papillary tumor cell formations with psammoma body in blood vessel lumen (HE, 200x)

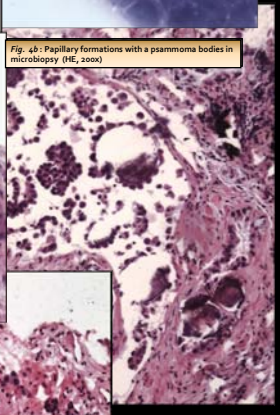
Fig. 4b : Papillary formations with a psammoma bodies in microbiopsy (HE, 200x)

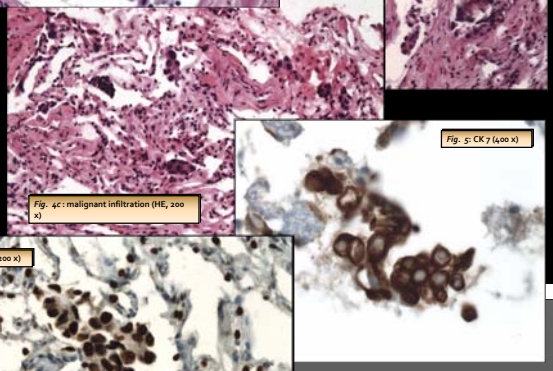
Fig. 4c : malignant infiltration (HE, 200 x)

Fig. 5: CK 7 (400 x)

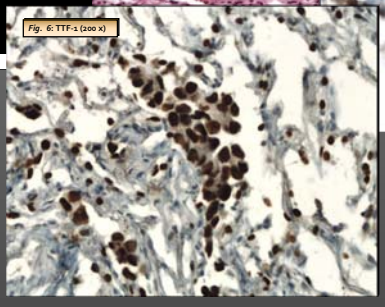
Fig. 6: TTF-1 (200 x)

DISCUSSION

Papillary adenocarcinoma of the lung occured in cca 7,0 % of all lung malignancies and dominantly in female non-smokers patients *(Jan)*. In the past there was confusion as to wheter papillary adenocarcinoma of the lung is a specific histologic entity or simply a variant of bronchioloalveolar carcinoma. Today it is looked upon a distinct clinicopathological entity with considerably worse prognosis than bronchioloalveolar carcinoma *(Silver)*. Clinicopathologically the dominant papillary structures are positive predictors of the response to gefinitib *(Kim)*.

In most cases of papillary adenocarcinoma, areas of adenocarcinoma or bronchioloalveolar carcinoma can be identified, true papillary adenocarcinoma is diagnosed when more than 75 % of the neoplasm mass contained papillary structures supported by fibrovascular cores with complicated secondary and tertiary branches *(Silver)* Pure forms they need to be distinguished from other types of tumors (eg.: ovary or thyroid carcinoma).

Papillary adenocarcinoma of the lung is composed of papillary tufts containig fibrovascular core. Psammoma bodies can also be seen (almost in 42 %) *(Silver, Parwani)*. The papillae are lined by large, atypical cells with enlarged hyperchromatic nuclei, prominent nucleoli and frequent mitotic figures. The lining cells in papillary adenocarcinomamay be cuboidal to columnar, mucinous or non-mucinous. Some evidence suggests a micropapillary pattern of adenocarcinoma, in which papillary tufts lack a central fibrovsacular core, may be prognostically unfavourable for an early metastasizing *(Duncan,Travis)*. Micropapillary patterns can be seen in papillary carcinomas too *(Cagle)*.

Differential diagnosis is very important because pure papillary adenocarcinomas of the lung can show histopathological features similar to those seen in the ovary or thyroid gland. Thus , a detailed clinical history is of importance *(Chen. Moran, Silver)*

i. The tumor may mimic a papillary thyroid carcinoma – thyreoglobulin stain should help in the differential diagnosis

ii. Separation from metastatic papillary carcinoma of ovarian origin requires a detailed clinical history, pelvic examination and radiologic studies to allow adequate identification of the latter. A problem may arrived when papillary adenocarcinoma of the lung is metastasing to ovary. The immunohistochemical study by TTF-1, CA125, CEA and CK 7 staining is helpfull in diagnostic *(Chen , Householder)*.

iii. Distinction from bronchioloalveolar carcinoma with papillary growth pattern can be very difficult, particularly on micrfobiopsy material. True papillary adenocarcinoma is characterized by marked cytologic atypia, with high mitotic rate and tumor necrosis, unlike bronchioloalveolar carcinoma, which is characterized by very low-grade, well differentiated cytologic features *(Ohori)*.

CONCLUSION:

Papillary adenocarcinoma of the lung is a rare distinct clinicopathological entity with considerably worse prognosis than bronchioloalveolar carcinoma and may be diagnosed when more than 75 % of tumor masses contained a papillary structures. Diagnostics from cytology and microbiopsy can be difficult and in first line to exclude a metastatic disease (ovary or thyroid) is necessary. In dealing with coexistence of ovarian, thyroid and pulmonary tumors, only immunohistochemical study (CK7, CK20, TTF-1, thyreoglobulin) may be helpful in the differentiation of the primary origin.

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CGB laboratory Inc.
Czech Republic
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