METACHRONOUS LUNG CANCER - CASE PRESENTATION

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METACHRONOUS LUNG CANCER - CASE PRESENTATION (Abstract): Multiple primary tumors can be synchronous when detected simultaneously or metachronous when detected after a variable time interval. We present the case of a 62-year-old female patient with a history of keratinized squamous cell carcinoma of the cervix, stage T₃bNₓMₓ, operated, and treated by chemotherapy and radiation therapy which develops after three years a large cell neuroendocrine carcinoma of the lung detected by imaging. Of major importance in the selection of the optimal therapeutic approach was the accurate determination of the histologic type of the metachronous tumor by microscopy and immunohistochemical techniques. The discrete respiratory symptoms and the absence of lung imaging screening accounted for tumor development to an inoperable stage, thus emphasizing the importance of close monitoring of the oncologic patient, thus greatly increasing their chances of survival. Keywords: METACHRONOUS CANCER, LUNG CANCER, CERVICAL CANCER.

Multiple primary tumors in a patient are characterized as synchronous, when detected simultaneously, or metachronous, when there is a variable time interval between the detection of the first tumor and the detection of a second or even a third tumor. These are the more common as those surviving a form of malignancy live longer (1). The exact causes of the development of other primitive tumors in some oncologic patients are unknown, but radiotherapy and chemotherapy used to treat the first cancer are believed to be predisposing factors.

A recent study (1), using data from the Rhode Island Cancer Registry covering a period of about 20 years, showed a steady upward trend of cancers diagnosed as a second primary tumor from 11.5% to 20.3% in men and 12.8% to 20.7% in women. Of all metachronous cancers, the lung, colorectal, breast and prostate ones account for 54.3% of cases, the average time to diagnosis being 6.5 years in men and 4.8 years in women.

In the literature, multiple primary lung tumors are often described (2-5), but lung cancers metachronous to other organ cancer are less frequent (6).

CASE PRESENTATION

We present the case of a 62-year-old female patient who presented at the Pulmonary Rehabilitation Clinic of the Iasi Rehabilitation Hospital for episodes of inspira-
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tory dyspnea, mucus coughing and fatigue, with onset 3 months earlier. The patient was not a smoker, did not drink alcohol, and was not exposed to respiratory hazards.

In her medical history there was a cervical cancer diagnosed in stage T3bN0M0 three years earlier, treated multisequentially: pre-operative radiotherapy and cisplatin chemotherapy, surgery (radical hysterectomy type C1 and pelvic lymphadenectomy level 2) with favorable postoperative course, followed by postoperative radiation therapy. Pathological examination of the surgically removed specimen established the histopathological type of the cervical tumor - keratinized squamous cell carcinoma.

Physical examination at the time of presentation revealed no significant changes except for some wheezes over the anterior left hemithorax and grade I obesity (BMI = 31 kg/m²). Laboratory tests revealed a nonspecific inflammatory syndrome (ESR = 54 mm/1h, CRP = 2.82 mg/dl), mixed dyslipidemia (total cholesterol = 225 mg/dl, HDL-cholesterol = 33.43 mg/dl), and impaired fasting glucose (114.1 mg/dl), while ventilatory function tests were within normal range.

Given the patient's symptoms and history, thyroid and abdominal-pelvic ultrasonounds were recommended; these showed normal issues without nodular organ lesions or lymphadenopathy. Instead, pulmonary X-ray, the first one performed after genital cancer was surgically removed, showed an ovalary opacity of 7/5 cm, relatively well-defined, located in the left para- and suprahilar areas (fig. 1), which required a chest computed tomography (native and with intravenous contrast).

![Fig. 1. Chest X-ray](image)
(left – lateral view, right – anterior-posterior view; white arrow – tumoral mass)

The resulting images helped to characterize more precisely the expansive mass as solid, inhomogenous, with areas of necrosis, located in the left upper lobe, with no cleavage plane with the aortic arch and left pulmonary artery (fig. 2). Also, there were no mediastinal lymphadenopathies and pleuropericardial effusion.

In this clinical and imaging context, a late secondary lesion of cervical cancer
was suspected, and the determination of serum squamous cell carcinoma antigen (SCCA) was recommended to guide the diagnosis but the result was within normal range (SCC = 0.2 µg /L). The patient was referred to the Iasi Oncology Clinic and Thoracic Surgery Clinic, with a diagnosis of probable left upper lobe lung primary cancer.

Surgery with curative intent was limited only to taking multiple biopsies from different tumor areas as intraoperatively the lung tumor proved to be adjacent to the large vessels of the left pulmonary hilum, surrounding and discretely compressing them.

![Chest computed tomography](image)

**Fig. 2.** Chest computed tomography
(left – native, right – intravenous contrast; white arrow – tumoral mass)

Microscopic examination (hematoxylin-eosin, van Gieson) of the collected tumor fragments showed an undifferentiated carcinoma. For an accurate characterization of the tumor multiple immunohistochemical markers were tested (tab.1), the final diagnosis being pulmonary large cell neuroendocrine carcinoma.

<table>
<thead>
<tr>
<th>Immunohistochemical markers</th>
<th>Result</th>
</tr>
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<tbody>
<tr>
<td>CK7</td>
<td>Zonal positive distribution</td>
</tr>
<tr>
<td>CK 5</td>
<td>Positive in very rare cells</td>
</tr>
<tr>
<td>TTF-1</td>
<td>Poorly positive zonal distribution</td>
</tr>
<tr>
<td>p63</td>
<td>Negative</td>
</tr>
<tr>
<td>Synaptophysin</td>
<td>Focally positive</td>
</tr>
<tr>
<td>CD56</td>
<td>Zonal positive distribution</td>
</tr>
</tbody>
</table>

The oncologist initiated primary chemotherapy with carboplatin 600 mg and paclitaxel 300 mg, with good immediate clinical tolerance.

**DISCUSSION**

This case brings up a relatively rare
The condition of the oncologic patient who is monitored for locoregional recurrence or metastatic spread, but after clinical recovery, the likelihood of new primary tumors is overlooked. However, statistics show that approximately 20% of cancer survivors develop one or more metachronous cancers (1), requiring a careful, lifelong follow up of these patients.

The patient was diagnosed with lung cancer late and the prognosis was worsened mainly due to the discrete alarm symptoms and also by the absence, for a long time (three years) of a screening chest X-ray.

Of major importance after the discovery of the metachronous lung cancer process was the accurate histological typing of the new tumor in view of optimal selection of therapeutic approach. Initially, serum SCCA was determined, this tumoral antigen being well related with the clinical course of squamous cell cervical cancer (the first tumor in our patient) in terms of recurrent or progressive disease or presence of residual tumor after treatment (7). The very small seric levels suggested that a diagnosis of late pulmonary metastasis of the cervical carcinoma was unlikely. Immunohistochemical techniques, supported by data in the literature (8), were useful in determining the neuroendocrine nature of the second primary lung cancer, poorly differentiated and large cell - type, unfortunately associated with a poor response to chemotherapy (9); also, its perivascular location was contraindication to surgical resection of the tumoral mass.

In conclusion, given the fact that the time interval for the development of metachronous primary tumors in an oncologic patient is unpredictable, but usually takes years, the opportunity for screening and early diagnosis, mainly by imaging monitoring, has not to be neglected, the chances of survival of these patients being thus improved.

REFERENCES