Chemical Anaplasia in Atypical Debut of Non-small Cell Lung Cancer with Inguinal and Obturator Lymph Node Metastases

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Non-small cell lung cancer (NSCLC) represents almost 80-85% of lung cancer cases. It is the most frequent malignancy after skin cancer. The therapeutic options for stage IV of disease consider histology, molecular characteristics, age, performance status, comorbidities, and not in the lust, patient's option. This paper presents the case of a male patient, 73 years old, smoker, presented and treated in May 2016 in the Sf. Ap. Andrei Emergency Clinical Hospital Galati. The first sign of disease was inguinal and obturator right lymph node metastases whose histopathological test revealed metastases from malignant melanoma. Immunohistochemical tests (IHC) indicated undifferentiated carcinoma with lung as starting point, (Ck7 (+), TTF1 (+)). Thorax, abdominal and pelvic computed tomography (CT) imaging not evidenced space replacement processes in lung, but with mediastinal, right obturator and inguinal adenopathy. From personal pathological history we retain basocellular carcinoma in lumbar region, treated with surgery in 2009. It was initiated palliative chemotherapy and radiotherapy with remission of obturator and inguinal adenopathy, and at 9 months from diagnosis the Positron Emission Tomography (PET-CT) evidenced primary lung tumor situated in right superior lobe (RSL). At the present, patient is alive performing palliative chemotherapy. This case presented diagnostic and treatment issues, being a challenge for multidisciplinary team. We are mentioning the paucity of literature data regarding cases of primary tumors situated upper diaphragm which metastases in inguinal lymph nodes.

Key words: inguinal lymph node metastases, lung cancer, treatment

Non-small cell lung cancer (NSCLC) represents almost 80-85% of lung cancer cases. It is the most frequent malignancy after skin cancer [1]. The therapeutic options for stage IV of disease consider histology, molecular characteristics, age, performance status, comorbidities, and not in the lust, patient's option [1]. In specialty literature are scarce data regarding cases of primary tumors situated upper diaphragm which metastases in inguinal lymph nodes.

NSCLC usually metastases, into mediastinal lymph nodes, liver, brain and adrenals [2,3] and NCLC metastases in other parts of the body are very rare, metastases in inguinal lymph nodes as NSCLC first sign being extremely rare. Metastases in inguinal lymph nodes, frequently, have origin in rectum, anus, genitals or urinary bladder.

Experimental part

We are presenting the case of a male patient, 73 years old, smoker, presented and treated in May 2016 in the Sf. Ap. Andrei Emergency Clinical Hospital Galati. From personal pathological history we retain basocellular carcinoma in lumbar region, treated with surgery in 2009, high blood pressure, stroke sequelae, right hemiparesis, prostate benign hyperplasia scapular cellular pigment nev, also treated with surgery in 2009.

In May 2016, the patient is hospitalized in Surgery Clinic of Sf. Ap. Andrei Emergency Clinical Hospital Galati with right inguinal adenopathy discovered 3 weeks prior hospitalized for which was performed biopsy. The performance status, IP=2. The histopathological (HP) tests of right inguinal lymph node revealed massive lymph node metastases from malignant melanoma. Clinically, patient manifested right inguinal-femoral massive adenopathy, fixed in profound plane, ulcerated, thin-skinned, functional impotence at right inferior member, right pelvic member lymphedema. Second line antalgic treatment was initiated.

In June 2016 the Computed Tomography (CT) scan, native and intravenous contrast (i.v.) contrast for evaluation was performed. Adenopathy in Barety lodge 23/15mm, right hilar adenopathy 23/18 mm, left hilar adenopathy 22/16 mm, inter-carinal, no space replacement processes in lung were revealed. Also liver increased in dimensions, homogenous prostate increased in volume, free Douglas were evidenced. Psoas muscle increased in volume in right part, with imprecise contour and iodophilic, right obturator adenopathy of 56/23mm, right inguinal round mass with 24 mm diameter, with fluid content and peripheral iodophilic ring were evidenced (fig. 1).

For this patient was recommended the Immuno-histochemical (IHC) test that revealed lymph node

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metastases from undifferentiated carcinoma (with Ck7 (+), TTF1 (+)), with lung origin; S100 (-), VIM (-), Melam A (-), MNF 116(+) difuz, Ki67 (+) ~10-15%, Ck7 (+), Ck20 (-), TTF1 (+).

In July 2016, Oncology Committee decided palliative chemotherapy (CMT) and palliative radiotherapy (EBRT). Chemotherapy with Cisplatin 100mg/m² was performed. Post-chemotherapy patient manifested grade 1 digestive toxicity.

Genetic molecular tests were performed but did not detect activating mutation in EGFR gene. Also ALK test showed immunoreactions ALK negative in tumoral cells (external control positive). Tumoral proliferation / infiltration with epithelioid and fusiform cell ALK negative.

Because the clinical picture was dominated by walk disorders, inguinal pain syndrome, EBRT on target volume right inguinal and iliac lymph nodes was initiated. Total dose, TD=50Gy/25fractions; dose/fraction=200cGy was administrated.

After two months the patient has performed another CT by his own initiative which revealed mediastinal adenopathy decrease with 2-3 mm, lung bilateral micronodular images, with maximum diameter of 5.5 mm, in left inferior lobe. Right obturator lymph node adenopathy was in dimensional regression (from 56/23 mm at 38/17 mm), without right inguinal lymph node adenopathy (fig. 2).

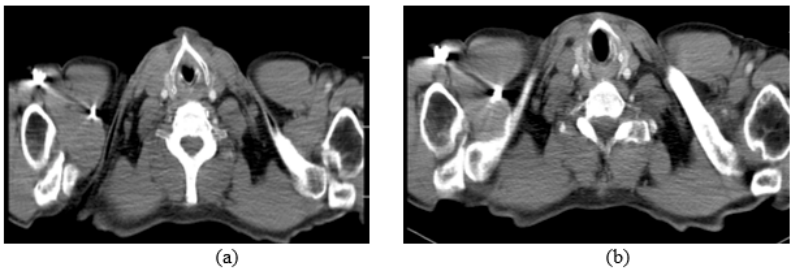
Palliative chemotherapy with Cisplatin 100mg + Vinorelbine 90 mg, (days 1, 8, 15) in August-November 2016 period was continued.

In December 2016 patient presented in Emergency Unit of Sf. Ap. Andrei Emergency Clinical Hospital Galati with asthenia, fatigability, secondary anemia, without fever. Hematological presented: leukocytes=870/mm^3, neutrophils= 240/mm^3, hemoglobin = 8.3g/dL, hematocrit =23.7%. Patient refused hospitalization and received treatment with granulocytes increase factors, corticotherapy, rebalancing with erythrocyte transfusion (CER), proton pump inhibitors (PPI), and antimycotic therapy.

The patient has successfully crossed over leucopenia episode and metronomic monotherapy CMT with Navelbine 30 mg, 3 days / week, days 1, 3, 5 was performed until February 2017, with good compliance and IP = 2, without digestive and hematological toxicity.

At 9 months from diagnosis, the ^{18}F FDG Positron Emission Tomography (PET-CT) whole body evidenced nodular area with *opaque glass* aspect, including bronchial lumens, of 22/16 mm, situated in anterior segment of right superior lobe, in contact with horizontal scissure, without high metabolic activity. Some other lung bilateral micronodular images, with maximum diameter of 5.5 mm, in left inferior lobe, with no significant changes respect previous CT. Right hilar lung adenopathy, active metabolic, (standardized uptake values, SUV=2.83) of 11/8 mm diameter. In conclusion, PET-CT scan revealed primary lung tumor situated in superior right lobe (RSL), without high metabolic activity; also PET-CT indicated right hilar lymph node and right adrenal secondary lesions, metabolic active (fig. 3).

Starting from March 2017 the patient has done metronomic monotherapy with Navelbine 30 mg, 3 days / week, days 1, 3, 5, good compliance to the treatment without symptomatology.



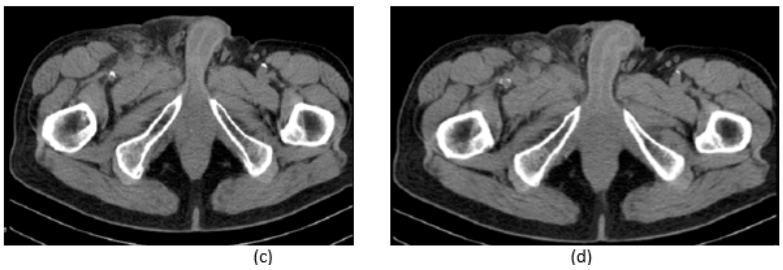
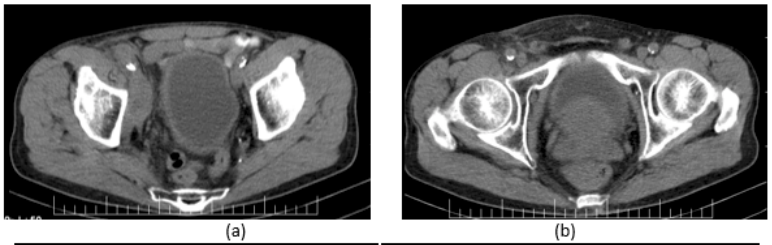


Fig. 1. CT scan June 2016. (a) and (b) mediastinal under 1cm diameter obturator right adenopathies; (c) and (d) right obturator adenopathy of 38/20mm,right inguinal round mass with 56/23 mm diameter, with fluid content and peripheral iodophilic ring.



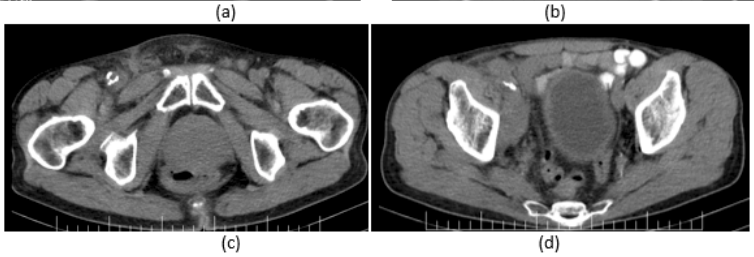
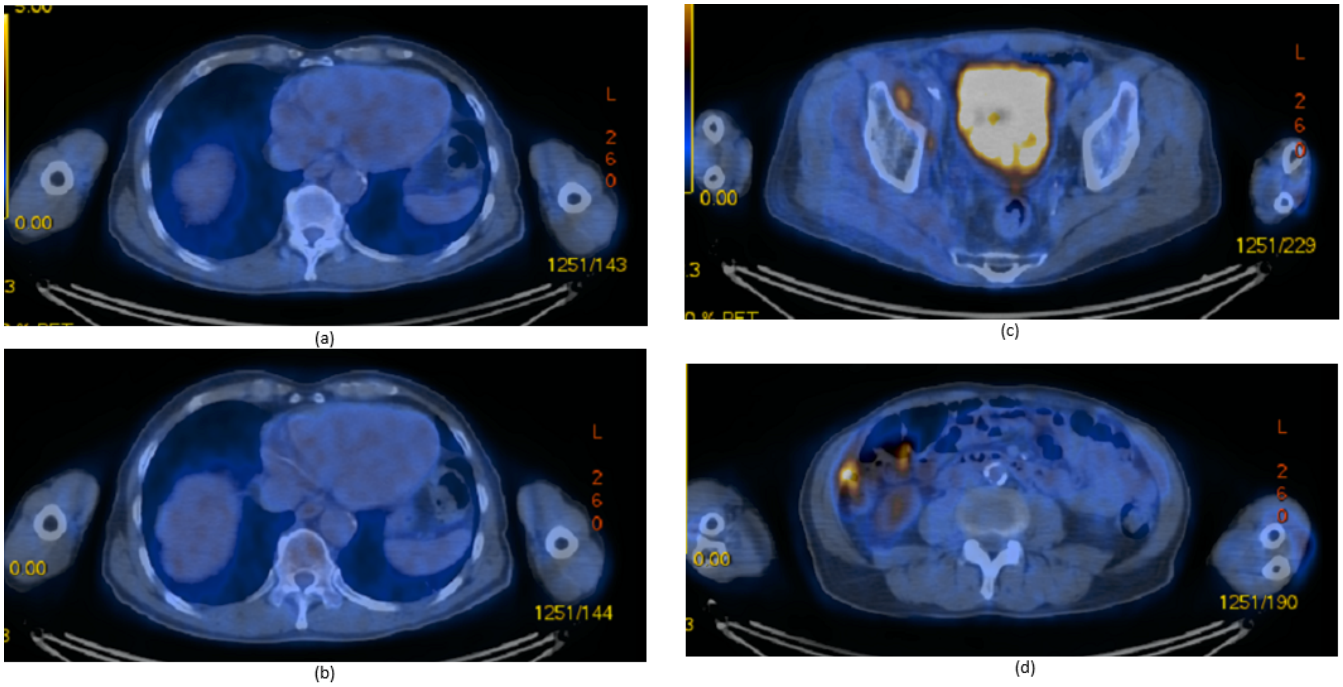


Fig. 2. CT scan August 2016 (a, b, c, d). Right obturator lymph node adenopathy was in dimensional regression



(a) (c) (b) (d)

Fig. 3. PET-CT scan. Primary lung tumor situated in superior right lobe (LSD), without high metabolic activity (a, b); right hilar lymph node and right adrenal secondary lesions, metabolic active (c,d)

In May 2017 at the last reevaluation the patient presented a good condition, without subjective claims, with complete remission of inguinal and obturator secondary lesions.

Chemical anaplasia

Blastomic or tumoral increase is a pathological process, characterized by morphological and physiological atypical increase of tissues, as a manifestation of organism's regulatory functions disordered. One of the tumor's particularities is atypical character, meaning all of biological proprieties that make the difference between tumoral tissue and all the others tissues; the base of atypical character of tumors is tissue anaplasia. Blastic tissue is characterized by a morphological, chemical, physic-chemical and energetic anaplasia.

Chemical anaplasia consists in changing of chemical composition of tumoral cells, with increasing of water quantity in cell. The increasing of tissue is directed correlated with increasing quantity of water and quantity of mineral substances is decreasing.

In any tissue, water quantity decreases with diminishing of growing energy.

Blatic tissues contains great amount of potassium salts, which conditions colloid's imbibition, and have relatively small quantities of calcium salts. With increasing of blastic development, also increase K/Ca coefficient.

In tumoral cells we can often see fat infiltration and increasing of unsaturated fat acids concentration and lipoids quantity, especially, cholesterol, is increased. Also, increase glycogenic contain of tumor, lactic acid accumulation is explained by glucose metabolism disorder.

With increasing of mass of cellular nuclei if blastic tissues, increase also concentration of nucleotide and nucleic acids whose breaking have the results of pentose's accumulation. Tumoral tissue is also characterized by protein metabolism disordered. The intensity of tumor growth is direct proportional with malignancy grade and the chemical modifications are more intense.

Results and discussions

Non-small cell lung cancer (NSCLC) represents almost 80-85% of lung cancer cases and therapeutic options, for IV stage of disease, take into consideration histology, molecular characteristics, age, performance status, comorbidities and, not in last, patient's option [1]. In cases of IP ≥ 2, CMT increase survival and quality of life [1]. Based Platinum CMT represents the preferred therapeutic option for elderly patients with IP =0-1. Monotherapy is indicated for elderly patients with multiple associated illnesses, from whom, probability of adverse reactions occurring post CMT in well known. Although the lung cancer usually metastases in brain, liver, adrenals, kidney and bones, secondary lesion originated in lung, are also found in skin, spleen, lungs and spermatic duct [2, 3].

There are very rare cases in which inguinal and obturator lymph node metastases represent the first sign of a lung primary tumor. Kocak et al. report a case of lung carcinoma with the only evidence of disease inguinal lymph node metastases [4]. There are sites of lymph node in which lung cancer disseminates. Late diagnosis of the disease is an unfavorable prognostic factor.

In this case the histology was undifferentiated carcinoma but Ki 67was low, approximately 10%. The prognostic value of Ki-67 for survival remains controversial, although there are a large number of studies performed in lung cancer patients [5].

The number (or fraction) of proliferative cells relates only to the growth fraction (and the Ki-67 labelling index) but not to the time needed for the completion of an intermitotic cycle. So, the estimation of the growth fraction offers information only about the state but not about the rate of proliferation; consequently, an additional marker would be useful to evaluate [5]. There are numerous studies which meta-analyzed the performing on early-stage resected NSCLC suggesting that high Ki-67 values are correlated with a shorter recurrence-free survival (RFS) after lung tumor resection [6https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5099507/], a shorter disease-free survival (DFS) [7, 8], and poor prognosis [9https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5099507/]. Also,

metastases in inguinal regions mark an advanced stage of disease (stage IV) and poor prognosis [2]. However, the five-year survival rate for stage IV lung cancer is only 5% regardless of multimodal treatment (radiotherapy or/and chemotherapy) received [10, 11].

Conclusions

This paper presents an atypical case, of lung cancer whose first sing was inguinal and obturator lymph node metastases. This article presents the diagnostic and treatment issues, which were challenging for the multidisciplinary team of hospital.

We are mentioning the paucity of literature data regarding cases of primary tumors situated upper diaphragm which metastases in inguinal lymph nodes.

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