Case Report

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Serum procalcitonin as a tumor marker in lung adenocarcinoma with ovarian metastasis: a case report

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Introduction and importance: Primary lung cancer is the leading cause of mortality worldwide. The major sites of lung cancer metastasis are the bones, liver, brain, lung, and adrenal glands. However, secondary localizations in the genital tract are extremely rare.

Case presentation: The authors report the case of a 36-year-old woman who consulted for a right scapular swelling evolving for 4 months associated with a chronic cough. Clinical examination showed a hard fixed right scapular mass with any inflammatory signs. The extension assessment followed by histological analysis concluded in a secondary ovarian location of a lung adenocarcinoma. A very high serum procalcitonin level unrelated to sepsis was detected in the patient along with a substantial hematological paraneoplastic disease. The patient died after 6 months of palliative chemotherapy.

Clinical discussion: Ovarian localization is found in only 0.4% of metastatic ovarian tumors, which is extremely low, the differentiation between primary and secondary ovarian adenocarcinoma is fundamental since the treatment and prognosis are very different. The serum procalcitonin can be elevated in lung adenocarcinoma.

Conclusion: This case report highlights the interest to encourage doctors to look for ovarian metastasis during the clinical course of lung cancer, and explain the elevation of serum procalcitonin during lung adenocarcinoma.

Key words: case report, immunotherapy, ovarian metastasis, serum procalcitonin, targeted therapies

Introduction

Cancer mortality has decreased for most cancer sites, the main exception being lung cancer in women[1], which justifies the need for screening for high-risk patients in combination with smoking cessation. Lung cancer is an aggressive subset with a high metastatic potential. The major sites of lung cancer metastasis are bones, liver, brain, lung, and adrenal glands. Ovarian metastasis of nonsmall cell lung cancer is seldom reported in the literature data[2,3], and the prognosis is generally quite poor. Furthermore, the differentiation between primary and secondary ovarian adenocarcinoma is fundamental since the treatment and prognosis are very different.

Herein, we report a case of a 36-year-old female patient with ovarian metastasis secondary to lung adenocarcinoma with a high serum procalcitonin level without a bacterial infection.

HIGHLIGHTS

- The differentiation between primary and secondary ovarian adenocarcinoma is fundamental since the treatment and prognosis are very different.
- The pillars of lung cancer prevention are smoking cessation combined with screening for high-risk patients.
- Elevated serum procalcitonin is associated with disease progression with short survival and a poor prognosis, and can be used as a predictive and prognostic marker in lung adenocarcinoma.
- The identification of molecular drivers in metastatic nonsmall cell lung cancer allows the transition from chemotherapy to personalized treatment using targeted therapies and immunotherapy.

This work has been reported in line with the Surgical CAse REport (SCARE) 2020 Guideline[4].

Case report

We present the case of a 36-year-old female patient, without any significant personal or family history. The patient is not a smoker, and has no notion of drugs or allergies. The disease began 4 months ago with the onset of a scapular swelling and a hacking cough. The patient sought a private doctor; she had a thoracic computed tomography (CT) scan with a biopsy and was then referred to our oncology center for further treatment. The clinical

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examination showed a performance status of two, a firm fixed right scapular mass. The thoracic CT scan revealed a mediastinal-hilar tumor process of the right lower lobe measuring 98 × 60 mm, with a cutaneous parietal mass of the anterior arch of the fourth right rib. A right scapular mass biopsy under CT guidance revealed carcinomatous proliferation (Fig. 1). The presence of TTF1 (thyroid transcription factor 1) +, Cytokeratin 7 +, and P40 - in poorly differentiated adenocarcinomas was confirmed by complementary immunohistochemistry (Fig. 2).

Fluoro-deoxy-carboglucose positron emission tomography imaging was used as part of the extension work-up, identifying a mediastinal-pulmonary tumor process of the right lower lobe, active right parietal and scapular thoracic tissue lesions, the right diaphragmatic pillar, and a large right presacral latero-uterine hypermetabolic mass of primary or secondary origin (Fig. 3).

A biopsy of the ovary and the endometrial lesions objectified an ovarian localization of adenocarcinoma (Figs. 4, 5, and 6) and simple endometrial hyperplasia without atypical retrospectively.

Quantitative immunohistochemical evaluation of PD-L1 is positive with a percentage of 55%. epidermal growth factor receptor, anaplastic lymphoma kinase (ALK), and ROS1 mutations are negative.Tumor marker CA125 is at 152 IU/ml. Laboratory examinations show a hematological paraneoplastic syndrome withhyperleukocytosis at 42750/mm^3 (predominance of neutrophils 36277/mm^3), CRP at 112 mg/l, serum procalcitonin at 1.9 ng/ml, negative blood culture.

Following the multidisciplinary consultation meeting, it was decided to treat the patient with palliative chemotherapy using weekly carboplatin AUC 2 (area under the curve) 3 days 1, 8, 15, q4w in combination with weekly paclitaxel 80 mg/m² days 1, 8, 15 q4w as first-line therapy for three cycles, followed by an assessment. The patient did not receive immunotherapy based on pembrolizumab due to the unavailability of the drug at the oncology center, as well as the high cost and nonreimbursement of the treatment by the health insurance.

After three cycles of palliative chemotherapy (3 months), the evolution was characterized by an alteration of the general state, a disturbance of the C-reactive protein (Table 1) associated with a linear increase of the serum procalcitonin (Table 2), a radiological progression of the mediastinal-pulmonary process with the appearance of mediastinal adenopathies and an increase of the right thoracic parietal mass, The patient received antibiotic therapy based on ceftriaxone 2 g for 15 days associated with Gentamycin 160 mg for 7 days, after which the patient was referred to the pneumology department for a bronchoalveolar lavage, which returned negative, with a cyto-bacteriological study showing no acid-fast bacilli.

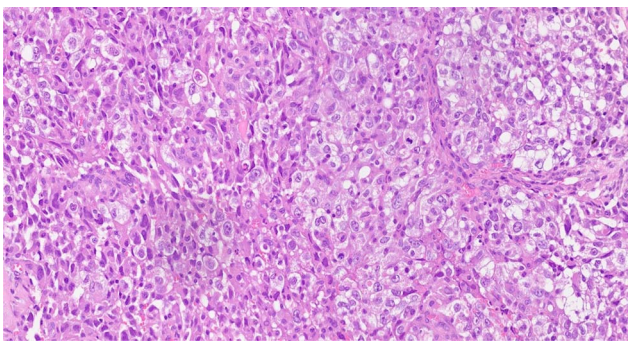


Figure 1. Carcinomatous proliferation with moderately eosinophilic or clear cytoplasm and irregular nuclei with highly atypical nucleoli (hematoxylin and eosin).

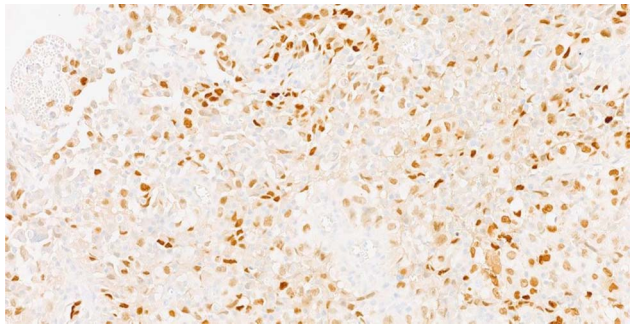


Figure 2. Right scapular mass biopsy showing TTF1 positive nuclear expression (adenocarcinoma).

The case was discussed in a multidisciplinary consultation meeting, the decision was to start the patient on a second line of chemotherapy based on Gemcitabine 1000 mg/m² 2 days 1, 8, q3w for three cycles then evaluation, The patient's condition worsened with an increase in procalcitonin to 100 ng/ml with a CRP of 298 mg/l, the patient received 2 g of imipenem associated with amikacin 15 mg/kg for 7 days without improvement, the patient died of cardio respiratory arrest.

Discussion

Lung cancer is a real public health problem worldwide, it is the leading cause of death in industrialized countries[5], The clinical signs are numerous and not very specific. Diagnosis is often delayed, hence the interest in finding a means of screening high-risk patients (smokers, ex-smokers).

Several randomized trials have found that the best effective screening method is still an annual low-dose chest CT scan[6]. According to the NLST trial, lung cancer-specific mortality was specifically down by 20%, while total mortality decreased by 6.7%[7]. Recent findings from the NELSON research revealed a 24% decrease in specific mortality after 10 years[7]. The combination of cancer screening and smoking cessation implies that management should be optimized, which justifies work on modifying smokers' behavior during screening and training health professionals in these techniques[8]. The limitations of screening are the high number of false positives, radiation, overdiagnosis, and the impairment of quality of life, and anxiety induced by screening[9].

Ovarian localization is found in only 0.4% of metastatic ovarian tumors, which is extremely low[10]. The mode of dissemination is lymphatic and hematological due to the rich vascularization of the ovaries. The distinction between primary and

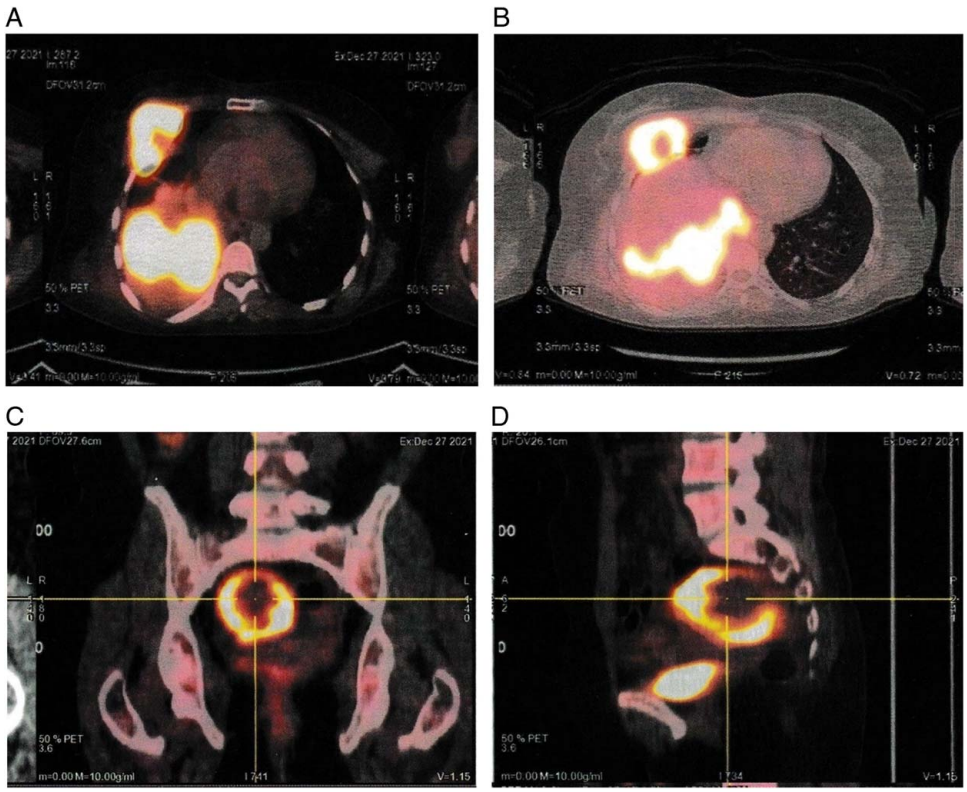


Figure 3. (A and B), Mediastino-pulmonary tumor process of the right lower lobe, active right parietal and scapular thoracic tissue lesions; (C and D), Large right presacral latero-uterine hypermetabolic mass of primary or secondary origin.

secondary nature is based on clinical-biological and radiological features, which are confirmed by immunohistochemistry. TTF1, which is positive in 74% to 92%[11] of cases, is the predominant particular marker of primary origin. The association with cytokeratin 7(+) and cytokeratin 20(-) immunophenotyping is strongly suggestive of primary lung adenocarcinoma. The use of napsin A increases the sensitivity and specificity for identifying the primary pulmonary nature. Ovarian tumors rarely display TTF1 expression[12].

In 10% of lung cancer cases, paraneoplastic syndrome develops as a result of hormone or peptide release by the tumor or an immunological cross-reaction between the tumor and the host[13]. It can be the only revealing symptom of lung cancer[14]. Some syndromes such as hematological syndromes are often asymptomatic, and associated with a poor prognosis, they are manifested by leukocytosis, and its diagnosis requires exclusion of other causes of leukocytosis, mainly infections and hematological neoplasia, treatment of the tumor may also improve the hematological disorders[13].

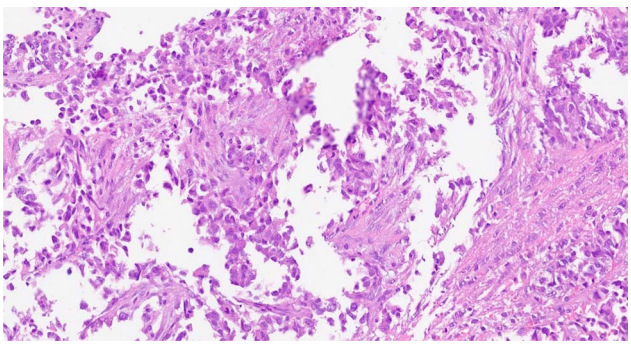


Figure 4. Ovarian parenchyma massively occupied by a carcinomatous proliferation arranged in mucinous patches with glands and cribriforms, Isolated 'kitten-ring' cell clusters.

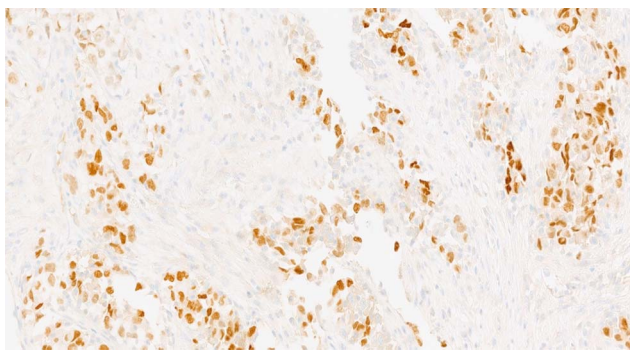


Figure 5. Ovarian metastasis of lung adenocarcinoma: strong positive expression of TTF1.

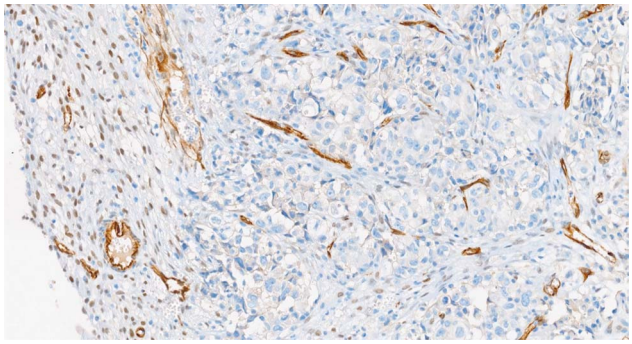


Figure 6. Ovarian metastasis of lung adenocarcinoma: negative expression of WT-1.

Serum procalcitonin is a precursor to calcitonin that is secreted in very small quantities by the C-cells of the thyroid gland and the pulmonary neuroendocrine cells. It is an ideal specific and sensitive biological marker of bacterial infection[15], and it also makes it possible to differentiate paraneoplastic fevers from infectious complications in cancer patients[16]. The mean procalcitonin level is higher in advanced cancer stages compared to early stages (0.190 ng/ml versus 0.127 ng/ml, $P=0.004$)[17]. a study found an increased level of serum procalcitonin compared with healthy subjects by 29% in patients with lung adenocarcinoma[18]. This rise can be explained by the tumor microenvironment which favours the production of pro inflammatory factors (TNF alpha, IL-6 and IL-1) especially in hypoxic conditions, which increases the level of procalcitonin, and promote metastatic dissemination[19]. A small retrospective study of 51 patients (including 29 lung adenocarcinomas) showed that high procalcitonin levels were associated with a poor prognosis[19].

The identification of molecular drivers in metastatic nonsmall cell lung cancer allows the transition from chemotherapy to personalized treatment using targeted therapies and immunotherapy. In the absence of molecular drivers and PD-L1 expression, platinum salt chemotherapy combined with a third-generation drug is the standard treatment[20,21]. However, the presence of a PD-L1 signal on the tumor cell membrane greater than 50% has supported the use of immunotherapy as a first-line treatment due to the significantly improved progression-free survival and overall survival[22]. The combination of immune checkpoint inhibitors and chemotherapy is an effective option regardless of PD-L1 status.

The search for oncogenic addictions has become a routine examination in advanced stages, epidermal growth factor receptor mutation (especially exon 19 deletion and exon 21 mutation) is a predictive factor for response to tyrosine kinase inhibitors (TKIs), osimertinib (3rd generation TKI) is the preferred option, 1st and 2nd generation tyrosine kinase inhibitors

Table 1

The evolution of CRP kinetics over time.

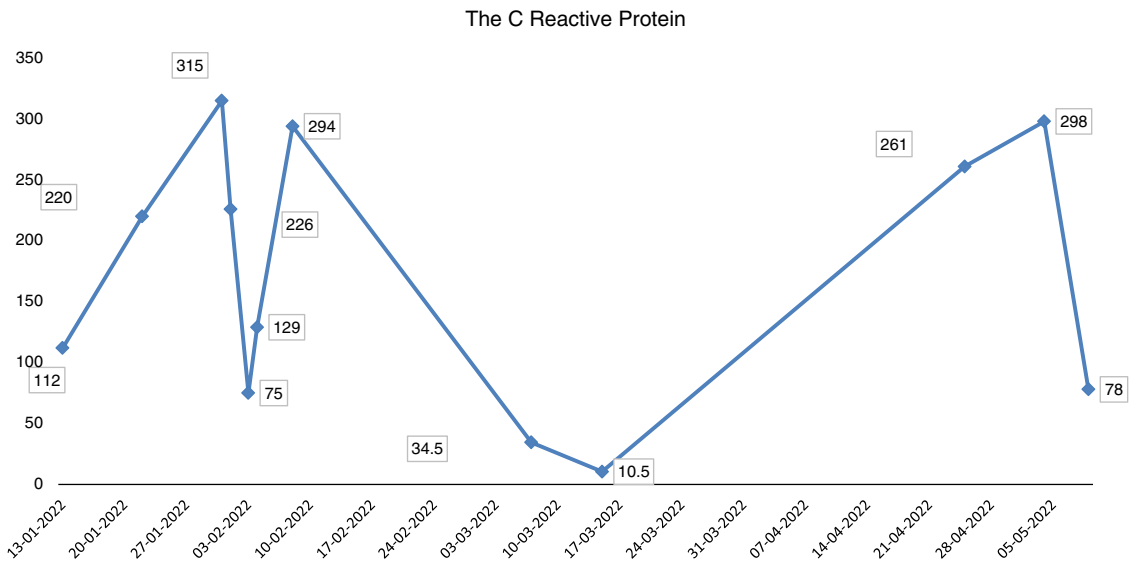
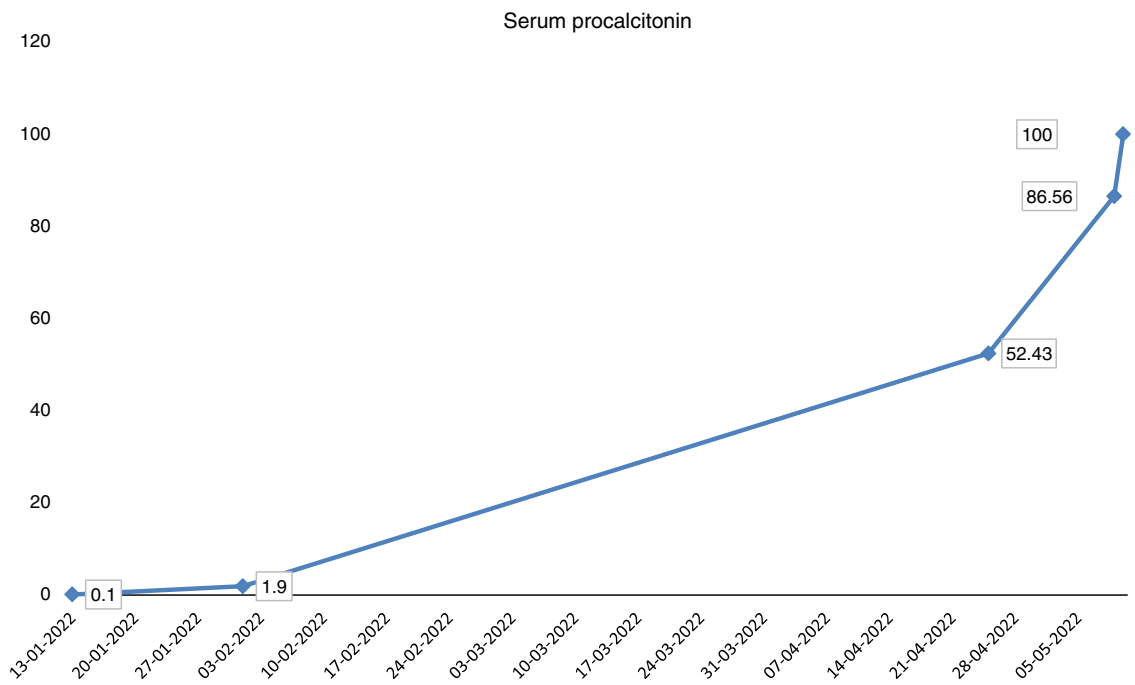


Table 2

The evolution of serum procalcitonin kinetics over time.



are valid choices[11], ALK translocation is a therapeutic target for 1st, 2nd, and 3rd generation ALK inhibitors[23], ROS1 gene fusion is predictive of response to ROS1 inhibitors including crizotinib, ceritinib, and entrectinib.

Conclusion

Elevated serum procalcitonin is associated with disease progression with short survival and poor prognosis, and can be used as a predictive and prognostic marker in lung adenocarcinoma pending confirmation by randomized studies.

Ethical approval

None.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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None declared.

Author contribution

Dr O.M.: written the article; P.A.J.O.: revision of the manuscript; Dr Z.A.: data collection and analysis; Dr J.L.: data collection and analysis; P.E.A.H.: interpretation of pathological data, and confirm the histological diagnosis; P.A.S.: revision and approval of the manuscript. All the authors reviewed and accepted the final version.

Conflicts of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

Research registration unique identifying number (UIN)

Our paper is a case report; no registration was done for it.

Guarantor

Mouhsine Omari.

Provenance and peer-review

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