

CASE REPORT

Abdominal wall metastases due to a squamous cell carcinoma of the lung: Case report and literature review

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Introduction: At the time of diagnosis, most patients with lung cancer are in an inoperable stage, with distant metastases. Most often, these patients have metastases to the brain, adrenal glands, liver, or bones. This article presents the case of a patient with non-small-cell lung cancer (NSCLC) metastases in the abdominal wall. **Case presentation:** A 67-year-old patient came to our service reporting the existence of a tumor 5 cm in diameter, located at the level of the abdominal wall, without other clinical symptoms. Surgical excision of the tumor was performed. The postoperative evolution was favorable, with the patient discharged on the third postoperative day. Histological examination of the resected specimen revealed metastasis of squamous cell carcinoma of the lung. **Conclusions:** The appearance of a tumor in the abdominal wall of patients with NSCLC may raise the suspicion of metastasis at this level.

Keywords: lung cancer, abdominal wall, metastases

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Introduction

Metastatic non-small-cell lung cancer (NSCLC) is the most common cause of cancer death. The prognosis of these patients is particularly unfavorable, the survival rate is very low, and quality of life is severely affected [1,2]. Smoking is the main risk factor for lung cancer. Of all histological types of lung cancer, NSCLC accounts for approximately 85% of cases [3].

At the time of diagnosis, approximately 55% of patients with NSCLC have distant metastases and are not surgically resectable. The long-term survival of these patients is particularly low: the 5-year survival rate in stage IVA disease is around 10%, and in stage IVB disease, it is less than 1% [4].

This manuscript presents the case of a patient whose symptoms were represented by the appearance of a tumor in the abdominal wall that turned out to be a metastasis of NSCLC. Initially, the patient showed no symptoms in the respiratory tract.

Case presentation

A 67-year-old patient, approximately 2 months before presentation to the doctor, noted the appearance of a tumor at the level of the abdominal wall, which progressively increased in size. At the time of presentation, the patient had a tumor at the level of the left abdominal flank with a diameter of around 5 cm. It was painless, firm, and relatively well-delimited by the surrounding tissues. At the time

of diagnosis, the patient had no other clinical symptoms that would raise suspicion of another condition. Contrast abdominal computed tomographic (CT) examination revealed no lesions in the abdominal viscera, only identifying the presence of tumor in the abdominal wall. Therefore, surgical excision of the tumor was proposed.

Before surgery, a chest X-ray was performed, showing an inhomogeneous lung opacity in the lower left hemithorax, around 7 cm in diameter. This opacity had irregular edges with spiculiform extensions. Considering the radiological examination, a chest CT examination with contrast was performed. It revealed a tumor in the left lower lung lobe of an inhomogeneous structure, with areas of necrosis and cavities, with a diameter of 75/96/85 mm. It extended from the left pulmonary hilum in the mediastinal pleura, causing obstruction of the left lower lobe bronchus, producing atelectasis of the left lower lung lobe. The CT also revealed multiple left and mediastinal hilar enlarged lymph nodes, many over 1 cm in diameter (Figure 1).

In the interdisciplinary oncological commission, given the suspicion of the existence of a tumor metastasis at the level of the abdominal wall, the first therapeutic option recommended was the excision of the tumor. The post-operative evolution of the patient was favorable, and they were discharged 3 days postoperatively.

Histological examination of the resected specimen revealed an abdominal wall tumor that was located deep within the soft tissues, also it reveals a skin fragment lined with intact keratinized stratified squamous epithelium. In the dermis, the existence of breaches and invasive tumor plaques was highlighted, consisting of a tumor prolifera-

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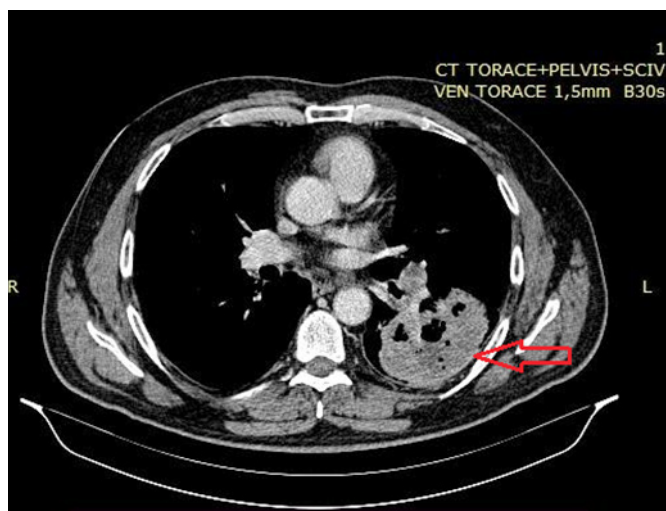


Fig. 1. Thoracic angio-CT, axial section.

tion of squamous cells with moderate cito-nuclear atypia and atypical mitotic figures. In the middle of some plaques, keratinization phenomena and foci of necrosis were observed. Immunohistochemical examination showed that the tumor cells were p40, CTK 5/6, and EMA positive. No perineural or lymphovascular invasion was found, and the lesion was excised within surgical safety limits. A metastasis of squamous cell carcinoma was found in the abdominal wall (Figure 2).

The genetic study of the resected specimen was negative for EGFR and ALK mutations, and the tumor proportion score for PD-L1 was higher than 1%. Given the squamous subtype and the metastatic stage of the disease, first-line systemic therapy was initiated. This consisted of pembrolizumab-type immunotherapy, at a standard dose of 200 mg, and chemotherapy Paclitaxel 200 mg/mp, in combination with carboplatin (area under curve = 6), with appropriate premedication, was administered at 21 days. No acute reactions or late toxicity were registered after administration. After 4 cycles, maintenance treatment was given, consisting of pembrolizumab up to 35 cycles. Additionally, the patient underwent adjuvant radiotherapy divided into 2 courses in the abdominal wall, the total dose being 42 Gy. At 1 year after surgery, the patient is in good general condition. The lung tumor is stationary according to imaging examinations, which have found no local tumor recurrence or appearance at the level of the abdominal wall or other distant metastases.

Discussions

Histologically, there are 3 predominant types of NSCLC (squamous cell carcinoma, adenocarcinoma, and large-cell carcinoma), but there are other less common types as well [5]. Patients with lung cancer are often diagnosed with distant metastases and thus considered inoperable at the time

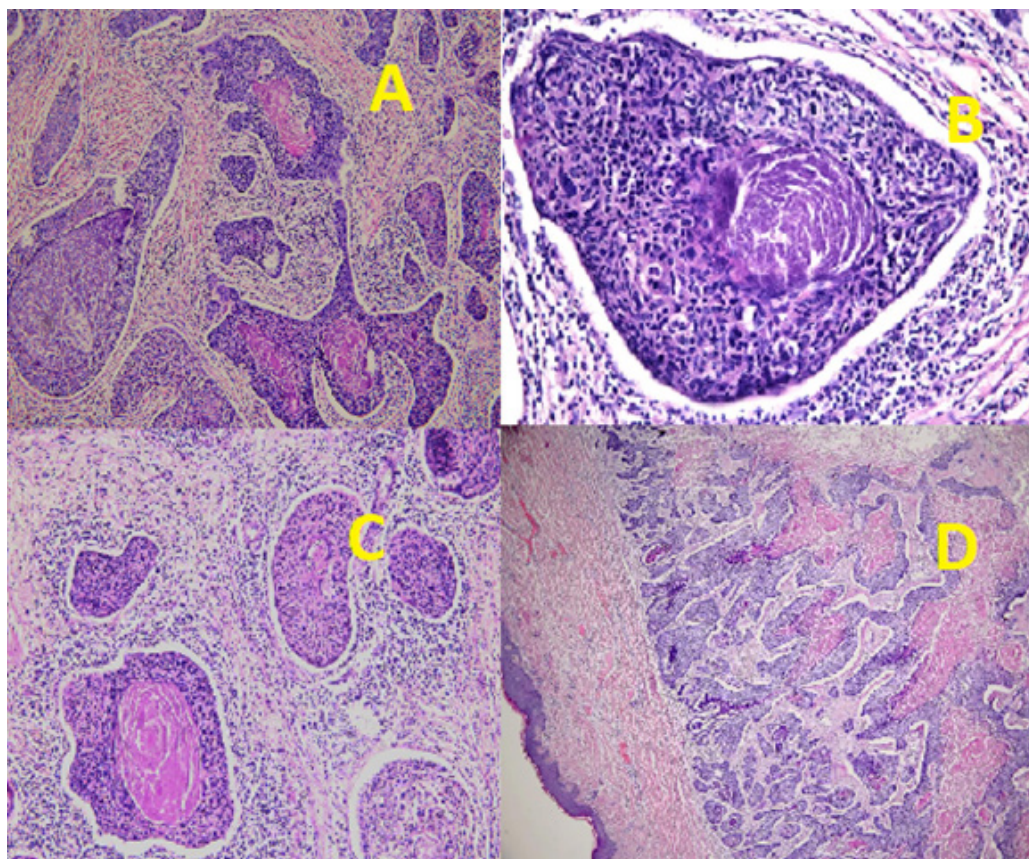


Fig. 2. A (Ob 4x, skin fragment infiltrated by tumor plaques with squamous differentiation and keratinization in the center of the plaques), B (Ob 10x, infiltrative tumor plaques composed of cells with squamous differentiation, with keratinization or necrosis in the center of the plaques with lymphoid inflammatory infiltrate), C (Ob 20x, solid tumor plaques, some with central keratinization composed of atypical tumor cells, pleomorphic, with squamous differentiation), D (Ob 40x, tumor plaque with cytonuclear atypia, necrosis in the center of the tumor plaque).

of diagnosis. Lung cancer most commonly metastasizes to the brain, bones, adrenal glands, or liver [6]. At the time of diagnosis, 20–40% of patients with NSCLC have distant metastases [7]. Interestingly, no published cases in the English literature attest to the possibility of NSCLC metastases in the abdominal wall as in our case. Metastases occur most frequently in young patients, more frequently in women, and especially in small-cell lung cancer (SCLC) [8].

Studies have shown that, depending on the histological type of lung cancer, a higher probability exists of metastases in certain organs. For example, in SCLC, metastases most commonly occur in the brain and liver. At the time of diagnosis, 17% of patients with SCLC have liver metastases, whereas only 4% of patients with NSCLC have liver metastases [9]. Additionally, at the time of diagnosis, patients with NSCLC are less likely to have distant metastases compared to patients with SCLC [10].

The diagnosis of the histological type of lung cancer is particularly important in clinical practice, in terms of both therapeutic attitude and prognosis. Therefore, immunohistochemical examinations are important in establishing a correct histological diagnosis. Lung cancer metastases usually retain the histological features of the primary tumor. TTF-1 is a specific marker for thyroid carcinomas and pulmonary adenocarcinomas but also occurs in neuroendocrine carcinomas [11,12]. Another immunohistochemical marker used in the histological diagnosis of lung cancers is napsin A, which is particularly useful in differentiating pulmonary adenocarcinomas from squamous cell carcinomas. Napsin A may also be positive in clear-cell renal cell carcinoma, clear-cell ovarian carcinoma, and endometrial carcinoma [13,14]. Cytokeratin 5, p40, and p63 are positive in squamous cell carcinomas. However, cytokeratin 5 is also positive in thymomas, mesotheliomas, salivary gland carcinomas, and urothelial carcinomas [15,16]. Cytokeratins 7 and 20 are useful in differentiating lung, breast, and ovarian tumors from colon, prostate, and kidney cancers [17].

In the last 15 years, the oncological treatment of lung cancer has made great progress in both its principles and results. The greatest benefit has been the introduction of immunotherapy in patients with metastatic lung cancer. Tumor cells have specific antigens on their surface, which can be targets for specific molecules, ultimately leading to the destruction of tumor cells [18,19].

Despite the progress made in the treatment of these cases, as well as the understanding of the mechanisms of metastasis in lung cancer patients, the survival rate of untreated patients is a maximum of 1 year [20]. Therefore, treatment is essential for their prognosis. In patients with single metastases in the brain, liver, or adrenal gland, surgery to resect the metastases may be a therapeutic option in conditions where complete removal of the lung tumor can be performed in the chest. However, in clinical practice, very few patients can lend themselves to such a therapeutic attitude, so oncology treatment is crucial.

First- and second-line treatment for patients with metastatic lung cancer uses the inhibition of driver genes and systemic chemotherapy [21,22]. Systemic chemotherapy for these patients is performed with conventional chemotherapeutic agents, inhibitors of tumor angiogenesis, and inhibitors of tumor metastasis. The most commonly used systemic chemotherapy agents in patients with advanced NSCLC are platinum derivatives [23]. If the therapeutic attitude of these patients is clear in the first 2 lines of treatment, starting with the third line of treatment, the therapeutic options are limited. Recently, positive results have been obtained using thyroid kinase receptor inhibitors [24,25].

One of the biggest advances in the last decade for patients with metastatic NSCLC is the combination of immunotherapy with platinum derivatives in systemic chemotherapy. The introduction of immunotherapy to clinical practice for these patients was based on the discovery of the clinical significance of PD-L1 gene mutations in patients with NSCLC. Pembrolizumab therapy has been effective in patients with a PD-L tumor proportion score greater than 1% [26]. This is why pembrolizumab treatment was introduced for our patient.

Radiation therapy is also available for local control of the disease, especially in patients with NSCLC [27]. Of all the ways to treat lung cancer, radiation therapy is the only method that can be applied regardless of the patient's clinical status, especially in advanced stages of the disease. Thus, over 70% of patients with NSCLC will at some point benefit from radiation therapy [28,29]. Newer studies have shown that increased radiation doses in patients with metastatic NSCLC are associated with slowing of the local course of the tumor [30]. Studies have also shown that in patients with stage IV NSCLC, the combination of palliative radiotherapy with systemic chemotherapy and immunotherapy can lead to increased survival rate [31]. This is why we combined radiotherapy with systemic therapy in our case.

The particularity of this case is in the appearance of a metastasis in the abdominal wall in a patient with NSCLC, as the first manifestation of the disease, the patient being completely asymptomatic regarding the respiratory system. Additionally, no published studies in the English literature to date have attested to the occurrence of metastases in the abdominal wall in patients with NSCLC.

Conclusions

The appearance of a tumor in the abdominal wall in patients with NSCLC may raise the suspicion of a metastasis at this level.

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Informed consent

The patient signed an informed consent for the publication of this manuscript.

Conflict of interest

The authors declare no competing interests.

Authors' contribution

I.C.F. (Conceptualization, Methodology, Writing – original draft), I.I.C. (Project administration), A.G. (Formal Analysis), B.A.S. (Data curation), D.M. (Visualization), A.I.B. (Resources), C.D.G. (Validation), I.H. (Writing – review & editing)

References

- Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. *CA Cancer J Clin* 2009;59:225-249
- Jacobsen J, Pirl WF, Billings JA, Lynch TJ. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med.* 2010;363(8):733-742
- Molina JR, Yang P, Cassivi SD, Schild SE, Adjei AA. Non-small cell lung cancer: epidemiology, risk factors, treatment, and survivorship. *Mayo Clin Proc.* 2008;83(5):584-594. doi: 10.4065/83.5.584
- Simeone JC, Nordstrom BL, Patel K, Klein AB. Treatment patterns and overall survival in metastatic non-small-cell lung cancer in a real-world, US setting. *Future Oncol* 2019;15(30):3491-3502. doi: 10.2217/fon-2019-0348
- Bi N, Yang M, Zhang L, Chen X, Ji W, Ou G, Lin D, Wang L. Cyclooxygenase-2 genetic variants are associated with survival in unresectable locally advanced non-small cell lung cancer. *Clin Cancer Res.* 2010 Apr 15;16(8):2383-2390. doi: 10.1158/1078-0432.CCR-09-2793
- Riihimäki M, Hemminki A, Fallah M, Thomsen H, Sundquist K, Sundquist J, Hemminki K. Metastatic sites and survival in lung cancer. *Lung Cancer* 2014;86(1):78-84. doi: 10.1016/j.lungcan.2014.07.020
- Quint LE, Tummala S, Brisson LJ, Francis IR, Krupnick AS, Kazerooni EA, Iannettoni MD, Whyte RI, Orringer MB. Distribution of distant metastases from newly diagnosed non-small cell lung cancer. *Ann Thorac Surg.* 1996;62(1):246-250. doi: 10.1016/0003-4975(96)00220-2
- Socinski MA, Morris DE, Masters GA, Lilenbaum R. American College of Chest Physicians. Chemotherapeutic management of stage IV non-small cell lung cancer. *Chest.* 2003 Jan;123(1 Suppl):226S-243S. doi: 10.1378/chest.123.1_suppl.226s
- Kagohashi K, Satoh H, Ishikawa H, Ohtsuka M, Sekizawa K. Liver metastasis at the time of initial diagnosis of lung cancer. *Med Oncol.* 2003;20(1):25-28. doi: 10.1385/MO:20:1:25
- Sawyer TE, Bonner JA, Gould PM, Deschamps C, Lange CM, Li H. Patients with stage I non-small cell lung carcinoma at postoperative risk for local recurrence, distant metastasis, and death: implications related to the design of clinical trials. *Int J Radiat Oncol Biol Phys.* 1999;45(2):315-321. doi: 10.1016/s0360-3016(99)00189-3
- Vidarsdottir H, Tran L, Nodin B, Jirström K, Planck M, Mattsson JSM, Botling J, Micke P, Jönsson P, Brunnström H. Comparison of Three Different TTF-1 Clones in Resected Primary Lung Cancer and Epithelial Pulmonary Metastases. *Am J Clin Pathol.* 2018;150(6):533-544. doi: 10.1093/ajcp/aqy083
- Gremel G, Bergman J, Djureinovic D, Edqvist PH, Maindad V, Bharambe BM, Khan WAZA, Navani S, Elebro J, Jirström K, Hellberg D, Uhlén M, Micke P, Pontén F. A systematic analysis of commonly used antibodies in cancer diagnostics. *Histopathology.* 2014;64(2):293-305. doi: 10.1111/his.12255
- Turner BM, Cagle PT, Sainz IM, Fukuoka J, Shen SS, Jagirdar J. Napsin A, a new marker for lung adenocarcinoma, is complementary and more sensitive and specific than thyroid transcription factor 1 in the differential diagnosis of primary pulmonary carcinoma: evaluation of 1674 cases by tissue microarray. *Arch Pathol Lab Med.* 2012;136(2):163-171. doi: 10.5858/arpa.2011-0320-OA
- Xu B, Abourbih S, Sircar K, Kassouf W, Aprokian A, Tanguay S, Brimo F. Diagnostic and prognostic role of immunohistochemical expression of napsin-A aspartic peptidase in clear cell and papillary renal cell carcinoma: a study including 233 primary and metastatic cases. *Appl Immunohistochem Mol Morphol.* 2014;22(3):206-212. doi: 10.1097/PAI.0b013e31828ef24e
- Kaufmann O, Fietze E, Mengs J, Dietel M. Value of p63 and cytokeratin 5/6 as immunohistochemical markers for the differential diagnosis of poorly differentiated and undifferentiated carcinomas. *Am J Clin Pathol.* 2001;116(6):823-830. doi: 10.1309/21TW-2NDG-JRK4-PFJX
- Hoang LL, Tacha D, Bremer RE, Haas TS, Cheng L. Uroplakin II (UPII), GATA3, and p40 are Highly Sensitive Markers for the Differential Diagnosis of Invasive Urothelial Carcinoma. *Appl Immunohistochem Mol Morphol.* 2015;23(10):711-716. doi: 10.1097/PAI.0000000000000143
- Chu P, Wu E, Weiss LM. Cytokeratin 7 and cytokeratin 20 expression in epithelial neoplasms: a survey of 435 cases. *Mod Pathol.* 2000;13(9):962-72. doi: 10.1038/modpathol.3880175
- Smith RA, Manassaram-Baptiste D, Brooks D., Doroshenko M., Fedewa S., Saslow D., Brawley OW, Wender R. Cancer screening in the United States, 2015: A review of current American Cancer Society guidelines and current issues in cancer screening. *CA Cancer J Clin* 2015;65(1):30-54. doi: 10.3322/caac.21261
- Wang X, Adjei AA. Lung cancer and metastasis: new opportunities and challenges. *Cancer Metastasis Rev* 2015;34(2):169-171. doi: 10.1007/s10555-015-9562-4
- Wao H, Mashkar R, Kumar A, Miladinovic B, Djulbegovic B. Survival of patients with non-small cell lung cancer without treatment: a systematic review and meta-analysis. *Syst Rev* 2013;2:10. doi: 10.1186/2046-4053-2-10.
- Lu J, Zhong H, Chu T, Zhang X, Li R, Sun J, Zhong R, Yang Y, Alam MS, Lou Y, Xu J, Zhang Y, Wu J, Li X, Zhao X, Li K, Lu L, Han B. Role of anlotinib-induced CCL2 decrease in anti-angiogenesis and response prediction for nonsmall cell lung cancer therapy. *Eur Respir J* . 2019;53(3):1801562. doi: 10.1183/13993003.01562-2018
- Ettinger DS, Wood DE, Aisner DL, et al. Non-Small Cell Lung Cancer, Version 5.2017, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Cancer Netw* 2017 Apr;15(4):504-535
- Hanna N, Johnson D, Temin S, Baker S Jr, Brahmer J, Ellis PM, Giaccone G, Hesketh PJ, Jaiyesimi I, Leigh NB, Riely GJ, Schiller JH, Schneider BJ, Smith TJ, Tashbar J, Biermann WA, Masters G. Systemic Therapy for Stage IV Non-Small-Cell Lung Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol.* 2017 Oct 20;35(30):3484-3515. doi: 10.1200/JCO.2017.74.6065
- Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. *CA Cancer J Clin.* 2021;71(1):7-33. doi: 10.3322/caac.21654
- Xiang M, Yang X, Ren S, Du H, Geng L, Yuan L, Wen Y, Lin B, Li J, Zhang Y, Feng G, Du X. Anlotinib Combined with S-1 in Third- or Later-Line Stage IV Non-Small Cell Lung Cancer Treatment: A Phase II Clinical Trial. *Oncologist.* 2021;26(12):e2130-e2135. doi: 10.1002/onco.13950
- Postow MA, Callahan MK, Wolchok JD. Immune Checkpoint Blockade in Cancer Therapy. *J Clin Oncol.* 2015;33(17):1974-82. doi: 10.1200/JCO.2014.59.4358
- Aupérin A, Le Péchoux C, Rolland E, Curran WJ, Furuse K, Fournel P, Belderbos J, Clamon G, Ulutin HC, Paulus R, Yamanaka T, Bozonnet MC, Uitterhoeve A, Wang X, Stewart L, Arriagada R, Burdett S, Pignon JP. Meta-analysis of concomitant versus sequential radiochemotherapy in locally advanced non-small-cell lung cancer. *J Clin Oncol.* 2010;28(13):2181-2190. doi: 10.1200/JCO.2009.26.2543
- Vinod SK, Hau E. Radiotherapy treatment for lung cancer: Current status and future directions. *Respirology.* 2020;25 Suppl 2:61-71. doi: 10.1111/resp.13870
- Delaney GP, Barton MB. Evidence-based estimates of the demand for radiotherapy. *Clin Oncol (R Coll Radiol).* 2015;27(2):70-6. doi: 10.1016/j.clon.2014.10.005
- Brown S, Banfill K, Aznar MC, Whitehurst P, Faivre Finn C. The evolving role of radiotherapy in non-small cell lung cancer. *Br J Radiol.* 2019;92(1104):20190524. doi: 10.1259/bjr.20190524
- Ashworth A, Rodrigues G, Boldt G, Palma D. Is there an oligometastatic state in non-small cell lung cancer? A systematic review of the literature. *Lung Cancer.* 2013;82(2):197-203. doi: 10.1016/j.lungcan.2013.07.026