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ACUTE INFLAMMATORY ABDOMEN: AN ATYPICAL PRESENTATION OF PULMONARY SQUAMOUS CARCINOMA

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Abstract: **Objective:** To report a case, as well as investigation of propaedeutic, surgical and complementary approaches applied to the management of abdominal pain and atypical findings in a patient diagnosed with pulmonary squamous cell carcinoma. **Case report:** A patient from the emergency department of `` Hospital Universitário Alzira Velano`` complains of severe abdominal pain. The anamnesis collected shows severe abdominal pain that started in the mesogastric and posterior region, migrating to the right hypochondrium, right flank and right iliac fossa. History and exams suggestive of appendicitis, indicated the realization of tomography in which it reports an expansive lesion in the upper third of the right hemithorax, with imprecise limits and spiculated contours. In the abdomen, intraperitoneal abscess and free fluid in the cavity were found. Thus, an exploratory laparotomy was designated, in which the presence of intestinal adhesions was observed, accompanied by whitish secretion suggestive of lymph throughout the explored cavity. The lymph node sample and duodenal lesion located in the first portion were biopsied. Bronchoscopy was also performed, which confirmed the presence of a friable, vegetating, whitish endobronchial lesion measuring approximately 5 cm in the posterior segment of the right upper lobe. After these findings, immunohistochemistry was performed to diagnose the lesion in which pulmonary squamous cell carcinoma was found. **Conclusion:** Even with a multidisciplinary approach to the patient, it was difficult to define the diagnosis, precluding early treatment before the progression of the carcinoma.

Keywords: acute abdomen, pulmonary squamous cell carcinoma, radiological findings.

INTRODUCTION

Lung cancer is the malignant tumor with the highest mortality rate among men and, in women, it is second only to breast cancer. Only 20% of cases are detected in the early stages and, often, the diagnosis is late, when the disease is in advanced stages, preventing curative treatment. [1] The expected 5-year overall survival for most patients with advanced disease is minimal. [4]

Lung tumors are classified into small cell carcinoma and non-small cell carcinoma. This last group is responsible for about 80% to 85% of cases of lung cancer and comprises squamous cell or squamous cell carcinoma, adenocarcinoma and undifferentiated large cell carcinoma. [4] The aggressiveness of the tumor varies according to the histological type. [1]

The main risk factor is smoking, demonstrating that nicotine induces cell cycle progression, angiogenesis and metastasis during cancer. There is induction of cellular apoptosis possibly by increased expression of the HSP90 protein that is present in lung cancer. [4]

The immunohistochemical study in lung tumors is essential for the diagnostic definition, demonstrating cytokeratin expression in squamous carcinomas, while this reaction is focal and less intense in pulmonary adenocarcinoma. Carcinoembryogenic antigen (CEA) is a frequent marker in almost all types of lung cancer, but more pronounced in adenocarcinomas. These results suggest that a diagnostic method for undifferentiated lung carcinomas would be the cytokeratin/CEA profile. [2]

The report to be described is configured as a peculiar malignancy, as it is an uncommon lung squamous carcinoma for the patient's age group and negative history of smoking. In addition, the atypical manifestation of acute abdomen and absence of respiratory symptoms are highlighted.

CASE REPORT

Patient A.O.L, male, 22 years old, in good general condition, was admitted to the emergency room of the Hospital Universitário Alzira Velano with a complaint of severe abdominal pain for 2 days. Pain starting in the mesogastrium and posterior region, migrating to the right flank, hypochondrium and iliac fossa; continuous and intensified pain on deep palpation of the abdomen. Absence of pain on sudden decompression in the four quadrants. He reported severe weight loss, hyporexia and two episodes of bilious vomiting on the day of admission. He had no fever or urinary symptoms. There was no surgical history or previous hospital admissions. He denied comorbidities and allergies. He denied smoking and exposure to toxic agents. History of death of the maternal grandfather due to leukemia and the paternal grandfather also died of cancer, but he was unable to inform the focus of the tumor.

Initially, the hypothesis of acute appendicitis was raised, as it is a pathology typically located in the right iliac fossa and is common in the patient's age group.

Laboratory tests on admission included: Red blood cells: 4.45 million/mm^3; Hemoglobin: 12.30 g/dl; Hematocrit: 36.70%; Leukocytes: 24810/mm^3; 91% segmented, 2% rods and 3% lymphocytes; Platelets: 295000/mm^3. PCR: 10.7. Total bilirubin: 3.20 mg/dl; Direct bilirubin: 1.60 mg/dl; Indirect bilirubin: 1.60 mg/dl; AST: 54 U/L; GT range: 145 U/L; Lactic dehydrogenase: 807 U/L.

Chest X-ray showed hypotransparency in the pulmonary hilum, with multiple diffuse nodular images.

The total abdomen ultrasound showed echographic signs suggestive of an inflammatory/infectious process in the right iliac fossa and the presence of free fluid in the

cavity, but inconclusive.

Therefore, a CT scan of the chest and abdomen was requested, showing the presence of an intraperitoneal abscess in the abdomen, a moderate amount of free fluid in the abdominal cavity and distention of the intestinal loops with fecal content, notably in the right colon. (Image 1). In the chest, he found an expansive lesion in the upper third of the right hemithorax, with imprecise limits and spiculated contours, measuring approximately 6.7 x 4.1 cm, in addition to mediastinal lymphadenopathy. (Image 2)

Due to the clinical picture and the abdominal tomographic findings, exploratory laparotomy was indicated. Intraoperatively, a large amount of diffuse white liquid was observed in the cavity (suggestive of lymph), generalized lymphadenomegaly and an inflammatory process in the retroperitoneum, posterior to the first portion of the duodenum. A sample of lymph nodes was collected from the retroperitoneal region and also from the lesion in the first duodenal portion, subsequently sent for pathological anatomy that concluded inflammation, but no cellular atypia suggestive of neoplasia.

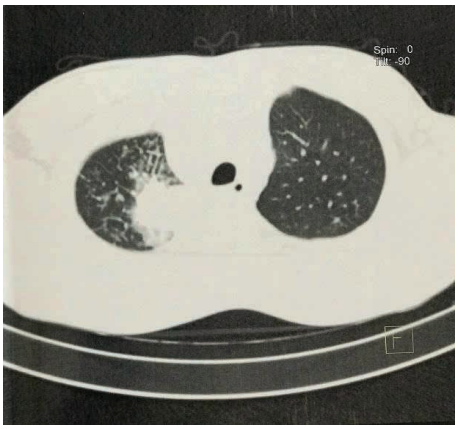

Image 1: Chest CT findings showing the presence of a lesion in the upper third of the right hemithorax.

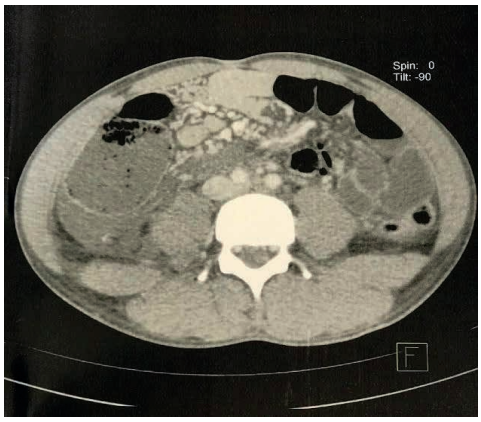

Image 2: Abdominal CT findings showing the presence of free fluid in the Morrison space (hepatorenal).

The patient had a good postoperative clinical evolution and bronchoscopy was requested, while the results of the histological exams collected during surgery were awaited.

The bronchoscopy performed confirmed the presence of a friable, vegetating, whitish endobronchial lesion measuring approximately 5 cm in the posterior segment of the right upper lobe. Findings referring to a malignant neoplasm of small cells with frequent plasmacytoids, suggestive of a lymphoproliferative process.

Immunohistochemistry revealed a hypercellular neoplasm, composed of ovoid cells with irregular, hypercolored nuclei, high nucleus-cytoplasm ratio and diffuse cell arrangement. The expression of antibodies in the study was positive only for cytokeratin, being a finding of epithelioid neoplasia, favoring poorly differentiated carcinoma. The possibilities of germ cell tumor and lymphoid neoplasia were ruled out due to SALL4 negativity. In addition, the non-expression of synaptophysin and chromogranin A antibodies does not favor the diagnosis of neuroendocrine carcinoma.

DISCUSSION AND RESULTS

Lung cancer is currently the most diagnosed

type of tumor in the world, in addition to being related to the highest mortality of patients worldwide. It is more frequent between 40 and 70 years of age, with a peak incidence between 50 and 60 years of age. Only 2% of cases affect individuals before 40 years of age. The main symptoms are cough, weight loss, chest pain and dyspnoea that persist for several months. [3]

The main risk factor is smoking, which is proportional to the frequency of cancer and the number of packs/years consumed. The risk increases 60 times among patients who are heavy smokers (two packs a day for 20 years) compared to non-smokers. Women are more susceptible to tobacco carcinogens. Other predisposing factors for cancer are exposure to industrial toxics such as asbestos, arsenic, chromium, uranium, nickel, vinyl chloride. Radiation and air pollution, mainly radon gas, are also contributors by inducing cell mutations. [3]

Lung cancer in non-smokers is approximately 10% to 15% in Western countries, more common in women and most are adenocarcinoma. Tumors in non-smokers are likely related to KRAS and TP53 mutations. [3]

In 2004, the WHO reclassified primary lung tumors mainly because poorly differentiated squamous cell carcinomas are often confused with small cell carcinomas. The distinction between them, classically via immunohistochemistry, is essential because it directs the therapeutic approach since in small cell carcinoma, the response to chemotherapy is around 50%, while in non-small cell carcinomas, the rate may not exceed 15 %. It is also worth noting that the diagnosis must also consider the patient's clinical history and radiological findings, as this information helps to separate the types of lung injury. Abnormal expression of the nuclear marker p63 is present in poorly differentiated squamous cell carcinomas. [5]

Squamous cell carcinoma is highly associated with tobacco exposure and demonstrates more TP53 mutations than other lung carcinomas. Overexpression of the p53 protein is present in 60% to 90% of *in situ* carcinomas. This type of tumor can also induce hypercalcemia due to the synthesis of parathyroid hormone and prostaglandin E. [3] It presents some type of cellular differentiation that suggests the diagnosis, such as intercellular bridges, well-differentiated squamous cells and even horny pearls. Normally, the chromatin has a vesicular pattern and often has clear nucleoli. [5] The lesion seems to be related to smoking and the toxic substances present in cigarettes, which cause hyperplasia of basal cells with metaplasia evolving to dysplasia and, progressively, the accumulation of mutations generates carcinoma *in situ* and tissue invasion. [3]

Lung tumors are rarely resectable when discovered. Non-small cell carcinoma is usually treated, when possible, surgically or with chemotherapy. [5] It is known that there is an exacerbated expression of the HSP90 protein, a marker of poor prognosis in lung cancer. This protein modulates lung growth and metastasis, affecting the proliferation, migration and invasion of isolated tumor cells, in addition to stimulating angiogenesis. Therefore, combined therapy with HSP90 inhibitors and radiation may improve therapeutic response. The HSP90 inhibitor induces cell death in the lung, which is why it is under study, but survival in this type of therapy remains undetermined. [4]

The lung is the site most affected by metastases, whether by lymphatic, hematogenous or contiguity, these in the case of mediastinal lymphomas and esophageal carcinomas. The pattern of metastatic growth is variable, with multiple scattered nodules being common in all lobes, most located in

the periphery. Other patterns include solitary nodule, endobronchial, pleural, pneumonic consolidation, and a mixture of these. [3]

In the report described, the diagnostic study started after an atypical case of acute abdomen with inconclusive intraoperative findings. Subsequently, the patient was submitted to bronchoscopy, the specimen being examined and sent for pathological anatomy, under diagnostic suspicions of tuberculosis and lymphoma.

The investigation continued with serologies for AFB, HIV 1 and 2 which showed negative results, as well as absence of bacterial growth in the abdominal fluid culture. Bronchoscopy revealed an endobronchial lesion with findings of small cell malignancy, revealing frequent plasmacytoids, suggestive of a lymphoproliferative process, and immunohistochemistry was indicated for diagnostic elucidation. This defined epithelioid neoplasia favoring poorly differentiated carcinoma due to expression of cytokeratin only.

The diagnostic hypothesis after the multidisciplinary investigation of the case was lung squamous cell carcinoma with evolution to infected chyloperitoneum. Therefore, the patient was referred to the oncology reference service in the region.

CONCLUSION

Although the inflammatory acute abdomen, caused by appendicitis, is common in the right iliac fossa, it is necessary to pay attention to the differential diagnoses in this region. As demonstrated in this case, a mediastinal tumor reflected pain in the right iliac fossa, due to probable metastasis and induction of peritonitis, simulating the picture of acute appendicitis.

Correlating the case in question with the medical literature, it is possible to verify the lack of specificity of symptoms, the gender affected, atypical age group, absence of respiratory symptoms or paraneoplastic syndrome such as hypercalcemia, common in squamous cell carcinoma. However, it is worth mentioning that the type of neoplasm mainly affects long-term smokers, individuals with exposure to toxic agents, radiation and mutations in the KRAS gene. Furthermore, it is an extremely rare tumor in young people. [3]

Among the complementary diagnostic resources, it is worth mentioning the importance of computed tomography for the investigation of thoracic and abdominal pathologies, showing abnormalities and masses [5], as an expansive lesion was evidenced in the right hemithorax, with imprecise limits, spiculated contours and suspicious adjacent lymph nodes. Based on the report of such examination, neoplasia was suspected. In addition, the presence of free fluid in the abdominal cavity and the formation of an abscess observed on tomography guided the surgical approach and the collection of tissue samples.

Bronchoscopy with biopsy was important to confirm the diagnosis, as it confirmed the presence of plasmacytoid neoplastic cells in the apex of the right lung.

It is necessary to highlight the importance of forwarding the atypical findings found during the surgical procedure for anatomopathological analysis. In this case, these findings were a lesion in the first portion of the duodenum, suspicious mesenteric lymph nodes and atypical ascitic fluid.

In view of the location of the supposedly neoplastic mass at the apex of the lung, immunohistochemistry becomes essential for the diagnosis of pulmonary squamous cell carcinoma. However, it is noteworthy that the patient did not present any symptoms of the respiratory system.

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