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Multi-Metastatic Hepatoid Adenocarcinoma of the Lung: Report of Case

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Abstract

Hepatoid adenocarcinoma of the lung is a rare tumor with a poor prognosis. There are no specific treatment-recommendations for this cancer. We report a 59-year-old man, a former smoker, with this condition. He presented with a cough and computed tomography revealed a pulmonary nodule (50 × 47 × 48 mm) with a right pleural effusion, together with a cerebral right temporal-lobe lesion and a right adrenal lesion. The serum alpha-fetoprotein value was normal. Histological examination via bronchoscopic biopsy revealed an adenocarcinoma. Positive CK7, AE1/AE2, and TTF1 with granular cytoplasmic staining on immunohistochemical study confirmed the diagnosis of hepatoid adenocarcinoma of the lung, stage IV-B. The patient had received chemotherapies (carboplatin-pemetrexed, gemcitabine) and cerebral radiotherapy, but he died at eight months of the treatment as a result of tumor progression.

Keywords

Hepatoid Adenocarcinoma, Lung, Chemothérapy, Metastasis

1. Introduction

Hepatoid adenocarcinoma is a rare primary extrahepatic neoplasia, with morphological characteristics similar to those of hepatocellular carcinomas. Hepatoid adenocarcinoma usually occurs in the stomach, ovary, pancreas, and bladder. Pulmonary involvement represents 2.3% of hepatoid adenocarcinomas [1]. In Madagascar, to our current knowledge, no case of pulmonary hepatoid adeno-

carcinoma has yet been reported. We describe a case of multimetastatic hepatoid adenocarcinoma of the lung in a 59-year-old man who underwent chemotherapy and cerebral radiotherapy. The patient died of tumor progression eight months into his illness. Our objective was to describe the management and to discuss it through the literature.

2. Case Report

A 59-year-old man was consulted in July 2019 for a cough and repeated expectoration which appeared 4 months ago with worsening symptoms for 1 month. The patient was a former smoker at 17 rods a day for 20 years. Physical examination revealed decreased breath sounds and dullness at the base of the right lung. The chest CT scan revealed a tumor mass of the right upper lobe measuring (50 mm × 47 mm × 48 mm), a right pleural effusion of moderate abundance, and a right lateral mediastinal ganglio-tumor mass Figure 1. A bronchoscopy with needle biopsy was performed. Histological examination of the fragments of lung tissue was in favor of an adenocarcinoma. Tumor cells were positive for immunohistochemical stain CK7, AE1/AE3, and TTF1 with granular cytoplasmic staining Figure 2. AMACR, CK20, CK5/6, and P63 immunohistochemical stains were negative. The alfa fetoprotein level was 8 ng/ml. The abdominal-pelvic and cerebral CT scan showed a right adrenal lesion and a right parietal cerebral intra-parenchymal lesion Figure 3. The tumor was confirmed as primary hepatoid adenocarcinoma of the lung, stage IV-B. TNM eighth edition 2017: CT 4 N 2 M 1c: metastases were found in the mediastinal and hilar lymph nodes, the right adrenal gland, and cerebral which is asymptomatic. After a multidisciplinary consultation meeting, the patient was treated with carboplatin type chemotherapy AUC 5-pemetrexed 600 mg/m^2 every twenty-one days. The reassessment scan after four courses of chemotherapy revealed a progression in size of the lung and brain lesion, the appearance of a new lung lesion. In November 2019 the patient began to present headaches. Panencephalic radiotherapy of 10 grays in 10 fractions

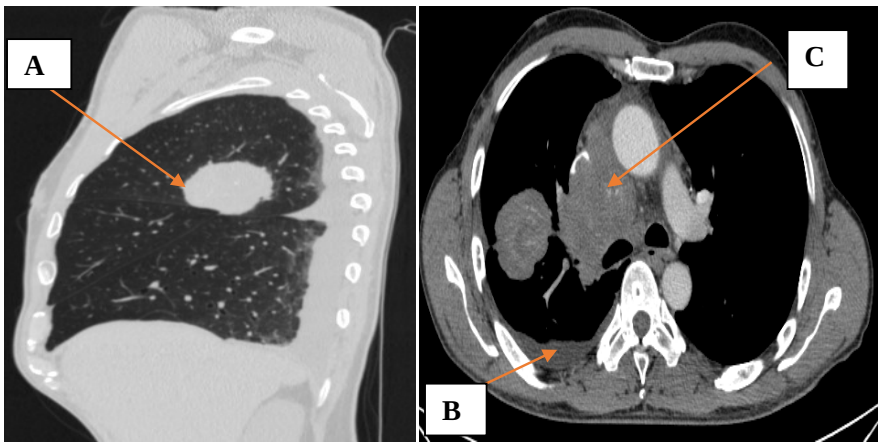

Figure 1. Chest scan. (A) Right upper lobe tumor mass of 50 mm × 47 mm × 48 mm. (B) Right pleural effusion. (C) Right lateral mediastinal lymph node mass.

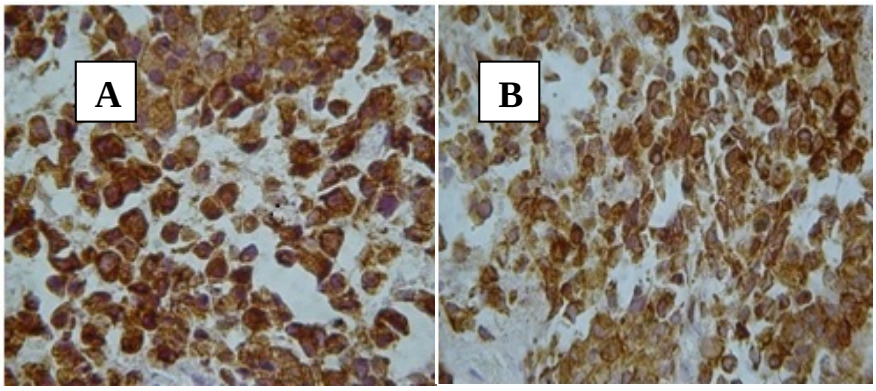

Figure 2. Examen immunohistochimique. (A) The tumor cells were positive for CK7, magnification × 400. (B) The tumor cells were positive for TTF1, magnification × 400.

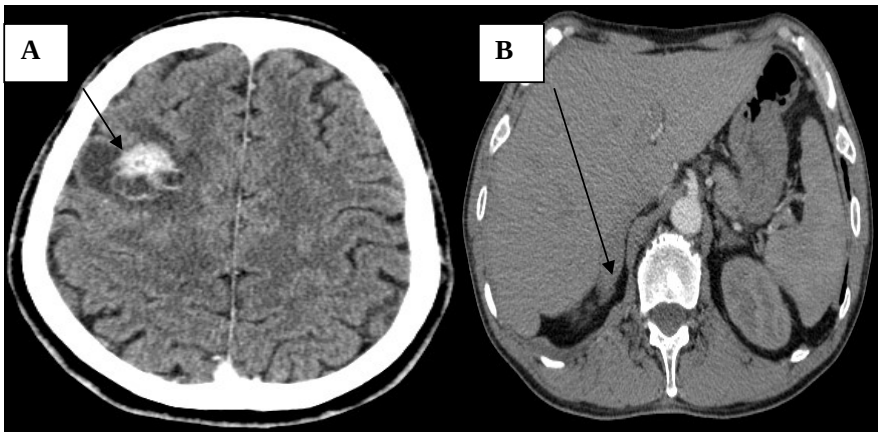

Figure 3. (A) Brain CT-scan, right parietal intra-parenchymal lesion. (B) Abdomino-pelvic scan, right adrenal lesion.

was performed, followed by three courses of chemotherapy such as gemcitabine 1000 mg/m^2 on D1, D8, and D15 every twenty-eight days. Pulmonary progression and appearance of peritoneal carcinomatosis were revealed by reassessment of the thoraco-abdomino-pelvic CT scan after these 3 treatments. The patient died of multiple organ failure.

3. Disscussion

Primary pulmonary hepatoid adenocarcinoma is a rare malignant epithelial neoplasia of the lung. The terminology "hepatoid" refers to an ectopic tumor similar to the liver. On histological examination, it presents in terms of morphology and immunohistology the characteristics of a hepatocellular carcinoma [2]. In 1990, the first case of pulmonary localization was described by Ishikura *et al.* [3]. The first diagnostic criteria for hepatoid lung carcinoma were as an acinar or papillary adenocarcinoma producing AFP and a component of the carcinoma that resembles hepatocarcinoma [3].

In 2014, Haninger *et al.* [4] changed the diagnostic criteria to include tumors that also contain components of typical acinar or papillary adenocarcinoma,

signet ring cells, or neuroendocrine carcinoma. AFP expression was not considered diagnostically mandatory as long as other hepatic differentiation markers are expressed. Immunohistochemically, EpCAM markers including napsin A, monoclonal CEA, HEA125 and MOC31 and multiple cytokeratins such as CK5/6, CK7, CK19 and CK20 were expressed only by hepatoid lung carcinoma [4]. Male patients over the age of 50 and heavy smokers were most frequently affected [5].

Clinically, the signs and symptoms of hepatoid lung carcinoma are nonspecific and resemble lung adenocarcinoma, manifesting with symptoms such as chest pain, back pain, shooting pain in the shoulder, cough, sputum, hemoptysis, and dyspnea [3] [5]. Chest X-ray reveals a lung mass, usually the upper lobe. On CT, hepatoid carcinoma usually presents as smooth or irregular masses near the pleural margin with mild to moderate and heterogeneous enhancement. The large average size of 7 cm varies from 1 - 20 cm. In our case, the lesion was in the upper lobe, which is consistent with previous data [6]. On PET scan images, how strong fluorodeoxyglucose accumulation in the hepatoid carcinoma [7]. In our case, the serum alpha-fetoprotein value was normal however, a high serum alpha-fetoprotein was a marker of poor prognosis [8].

Due to the rarity of hepatoid lung carcinoma, no standard treatment is currently available. Surgery followed by adjuvant therapy has been suggested for hepatoid lung carcinoma diagnosed at an early stage [6].

For advanced-stage patients, efforts continue to try regimens of radiotherapy, chemotherapy, and especially targeted therapies [9]. The prognosis for patients with unresectable hepatoid pulmonary adenocarcinoma is generally poor. Liang ZZ *et al.* included and analyzed 78 patients diagnosed with HAL from 2001 to 2016 whose median survival time was 5 months, among which stage III-IV was 4 months [10]. Muroyama Y *et al.* [11] reported a case of a 66-year-old man with a stage IV T4N3M1b tumor with solitary brain metastasis. The patient had undergone excision of the cerebral lesion followed by adjuvant radiotherapy. The use of S-1 (tegadur/gimeracil/oteracil) has made it possible to obtain a long-term survival of more than 19 months after the failure of standard carboplatin-paclitaxel chemotherapies in the first line, pemetrexed in the second line of S-1 in the third line. For our patient, standard chemotherapy such as carboplatin-pemetrexed and gemcitabine did not show a significant improvement in survival. Our patient died 8 months from the onset of the disease. Encouraging data have recently been reported by Chen LL *et al.* regarding the use of chemotherapies and a PD-1 inhibitor, sintilimab in unresectable HAL. These treatments resulted in overall survival of 52 months [12].

4. Conclusion

Although rare, pulmonary hepatoid adenocarcinoma should be considered in elderly smokers with pulmonary masses secreting or not AFP. Immunohistochemistry is necessary for diagnostic confirmation. The stage of the disease at

the time of diagnosis is the most important prognostic factor. The use of chemotherapy, whether or not associated with targeted therapies or immunotherapies, could improve the survival of patients in the advanced stage.

Conflicts of Interest

The authors declare no conflicts of interest.

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