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CASE REPORT

Hepatoid Adenocarcinoma of the Lung: A Case Report and Literature Review

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Introduction

Hepatoid adenocarcinoma of the lung is a rare form of malignancy defined as an alpha-fetoprotein (AFP)-producing primary lung carcinoma with specific morphological features resembling hepatocellular carcinoma (HCC). Hepatoid lung adenocarcinomas are extremely rare. Due to the rarity of the tumor, any new case contributes to the clarification of its complete clinico-morphological description, biological behavior, and prognosis. It occurs in a multitude of organs: most frequently in the stomach, but also rarely in other areas, including the lung, kidney, female reproductive tract, pancreas, and gallbladder. We present a case of stage IV primary lung cancer with highly elevated AFP levels and morphological and immunohistochemical characteristics for hepatoid adenocarcinoma of the lung.

Case Report

A 52-year-old man with a 20 pack-year history of smoking presented with 5-month history of dyspnea, left-sided chest pain, and weight loss. The patient was asthenic with decreased physical activities. The computed tomography scan revealed an 11.8×12×8-cm tumor formation in the superior lobe of the left lung invading the vascular structures of the homolateral mediastinum, encasing the trachea, esophagus, and multiple left lung nodules (Fig. 1).

However, no other sites of metastasis were found on abdominal–pelvic CT, MRI of the brain, double-helical liver CT, testicular ultrasound, and bone scan.

A biopsy of the left lung mass revealed a tumor with solid, trabecular, and papillary structure. The tumor cells were large, polygonal, with abundant eosinophilic cytoplasm, and with the presence of intracytoplasmic lumens. The cells resembled hepatocytes and had large, nucleolated and centrally located nuclei (Figs. 2 and 3). On the cytoplasmic membrane of the cells and around the intracytoplasmic lumens, periodic acid-Schiff was positive, and hyaline globules were found sporadically. Immunohistochemical stains showed the tumor cells to be strongly positive for CK20 and focally positive for AFP and CD10. In contrast, stains for CK7, TTF-1, PLAP, CK5, CK6, and CD30 were all negative. Hepatocyte-1, which is an antigen that is presumed to be hepatocyte specific, was weakly positive. The expression of HNF-4α was exclusive in hepatoid foci with AFP production. Laboratory findings on admission showed normal PSA 0.38 ng/ml, and BHCG was 1.2 mUI/ml. Subsequently, serum AFP was noted to be elevated to 5,000 ng/mL, and a diagnosis of hepatoid adenocarcinoma of the lung was made. The patient received apalliative chemotherapy based on vinorelbine and cisplatin; after two cycles, we have noticed clinical and radiological stabilization. The patient received six cycles in all and remained disease stable until 2 months after the end of the chemotherapy.

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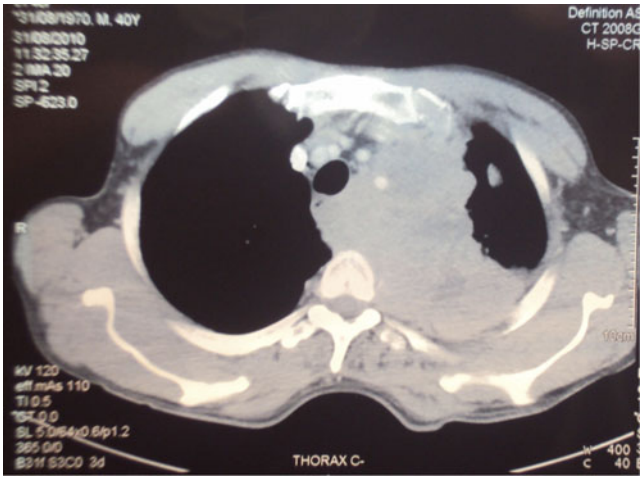

Fig. 1 CT scan of tumor mass in the superior lobe of the left lung

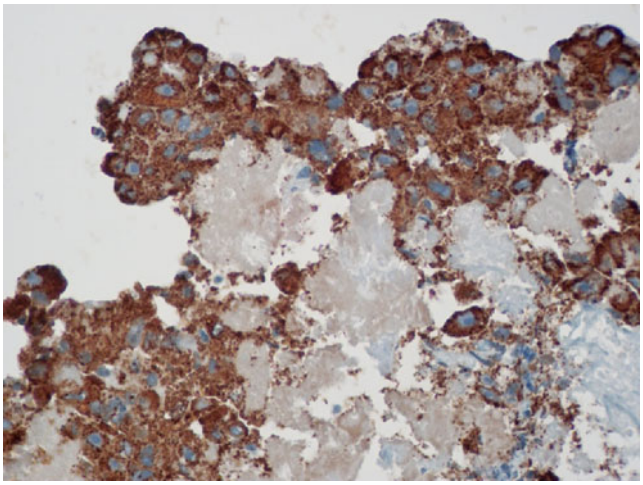

Fig. 3 Immunolabelling positive for antihepatocyte (×400)

Discussion

Hepatoid adenocarcinoma was first described by Ishikura et al. as an AFP-producing tubular or papillary adenocarcinoma with a sheet-like or trabecular proliferation of neoplastic cells [1, 2] and the presence of cells with abundant, eosinophilic cytoplasm and centrally located nuclei in sheet-like or trabecular portions, resembling those of hepatocellular carcinoma cells.

Hepatoid carcinoma contains a tubular adenocarcinoma that seems to develop "hepatoid features," but the relation between the tubular adenocarcinomatous and the hepatoid components remains unclear. AFP is an important diagnostic tumor marker for hepatocellular carcinomas, vitelline sac tumors as well as tumors developing from the primitive foregut [4] but none in the lung [5].

Reportedly, AFP-producing tumors other than liver cancer comprise malignant tumors, such as gastric cancer, other digestive tract tumors [6, 7], pancreatic cancer, as well as non-seminomatous cellular tumor [6] and ovarian cancer, but there have been relatively few reported cases of lung cancer. Following the first reports of AFP-producing primary carcinomas of the lung presented by Ysunami R et al. in 1981 [2], HLA was classified as a new distinctive entity [1, 9]. The origin of the tumor is not fully clarified [6, 7].

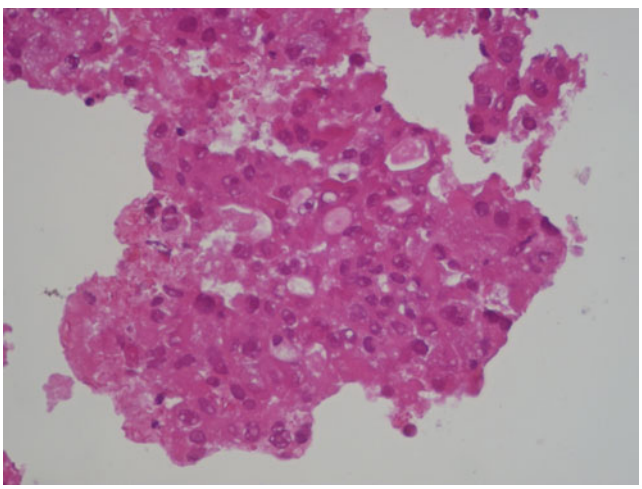

Fig. 2 Tumor cell proliferation in poorly limited cytoplasm and anisocaryotiques nuclei containing prominent nucleoli (HE, ×400)

The diagnosis of HAL is based on findings of hepatoid histopathology in lung tissue and high levels of AFP in the absence of liver disease. The elevated AFP levels correlate with disease activity and often decline after surgical resection of the primary tumor. Since HAL can also spread to the liver, differentiating metastatic HCC from metastatic HAL can be quite difficult. Immunohistochemical stains may be helpful in this regard. While all forms of hepatoid adenocarcinomas are usually positive for AFP, CK8, CK18, and polyclonal CEA, only HCC is positive for HepPar1 and CK7 [12]. Clinically, the cases of HAL described in the literature appear to have several common features: male predominance, large tumor size at presentation (average 9 cm), and poor prognosis. Even in malignant lung tumor, it is necessary to monitor the serum AFP levels when AFP-producing tumor or hepatoid adenocarcinoma is suspected clinically.

The prognosis correlates with the stage at presentation, which is most often advanced, as was the case in our patient [13]. Prognosis in HLA is little known because of the small number of cases that have been described and followed up.

Nowadays, the reasons for the poor prognosis are not clearly understood. One possibility is that hepatoid adenocarcinoma produces AAT (alpha-1 antitrypsin) and/or ACT (alpha-1 antichymotripsin) as well as AFP. AAT and ACT have immunosuppressive and protease-inhibitory properties that enhance invasiveness [14, 15]. Also, AFP has a suppressive effect on lymphocyte transformation. Furthermore, these tumors are known to be resistant to chemo-

therapy [14]. If complete surgical resection is performed, prognosis may be improved in select cases. Therefore, early recognition, staging, and timely intervention are key.

The survival in similar hepatoid adenocarcinoma of the stomach is more clarified and varies from several days to 1.5 year after the operation [8, 10, 11]. These tumors are highly aggressive and at the time of their diagnosis diffuse metastases are also present [3, 8].

Conclusion

We have reported a case of hepatoid adenocarcinoma of the lung, a rare entity, with well-defined clinicopathological features. Due to the advanced stage of disease in our patient, he was not a candidate for surgery but instead received palliative chemotherapy consisting of vinorelbine and cisplatin.

Hepatoid adenocarcinoma of the lung is usually associated to recognized poor prognosis, in which the administration of novel palliative systemic chemotherapy may have had major impact on survival.

Conflicts of interest RB and MM contributed equally to this work. All authors approved the final work. The authors declare no conflicting interests.

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