

Hepatoid adenocarcinoma of the lung accompanied with multiple systemic metastases

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To the Editor: Hepatoid adenocarcinoma of the lung (HAL) is a rare malignant tumor, which can be defined as alpha-fetoprotein (AFP)-producing primary lung cancer. Most hepatoid adenocarcinomas (HAC) have high AFP expression. HAL lacks effective treatment and has poor prognosis, but early diagnosis and timely treatment can improve long-term survival rate.

A 63-year-old male patient with no special past medical history or history of hepatitis, presented lumbar soreness, and pain without obvious causes, accompanied by a sensation of skin tear. The pain showed diffuse and wandering location, was intense every afternoon and improved by self-administration of ibuprofen. One month later, the patient found 6 to 7 solitary subcutaneous nodules in the lumbar, back, abdomen, and forechest region, slightly protruding from the body surface with a diameter of about 1 to 2 cm. The nodules could be propelled, with no fusion, rigidity, no fluctuation, partial tenderness, and no local redness and swelling, ulceration or itching. Routine blood test demonstrated that white blood cells $11.07 \times 10^9/L$, neutrophils 70.5%, hemoglobin 95 g/L, and platelet $436 \times 10^9/L$. Liver and kidney function examination revealed that alanine aminotransferase 68 U/L, total bilirubin 7.8 $\mu\text{mol/L}$, creatinine 87 $\mu\text{mol/L}$, and lactate dehydrogenase 359 U/L. Tumor marker detection presented that carcinoembryonic antigen >100 ng/mL, carbohydrate antigen (CA) 19-9 41.9 U/mL, CA 72-4 >300 U/mL, and cyfra21-1 31.8 ng/mL.

The patient underwent resection of multiple lumbar and dorsal skin masses under local anesthesia. Consultation in the Department of Pathology in Ruijin Hospital suggested poorly differentiated adenocarcinoma by skin biopsy [Figure 1]. The patient was transferred to our hospital, and positron emission tomography/computed tomography showed a soft-tissue mass in the apex of the left lung, a

nodule in the right upper lobe near the pleura, and increased metabolism, which was suspected as lung cancer. Systemic multiple lymph node enlargement, soft-tissue masses, multiple subcutaneous nodules, and increased metabolism were also found, which were considered as metastatic lesions. The patient died of multiple organ failure due to distant metastases in February 2018. The overall survival was 4 months after initial diagnosis.

HAC is a special extrahepatic adenocarcinoma with both adenoid and hepatocyte-like differentiated structures, usually occurring in tumors of the digestive tract. HAC of the stomach is the most common type, accounting for 63% of HAC.^[1] Ishikura *et al*^[2] first described HAL in 1990 and its characteristics are highly similar to hepatocellular carcinoma (HCC). Haninger *et al*^[3] modified Ishikura diagnostic criteria for HAL in 2014. The expression of AFP is not necessary for the diagnosis. Haninger diagnostic criteria fully recognize the presence of HAL without AFP expression and define it as AFP-negative HAL. Common treatments for patients with HAL include surgical resection, chemotherapy, and radiotherapy. Patients with diagnosed stage I-II HAL has longer survival after radical resection. Early diagnosis and timely surgery are helpful to improve the overall survival rate.^[4] Patients at stage III-IV usually do not have surgical indications and are suggested to try radiotherapy and chemotherapy. Similar to other types of non-small cell lung cancer, clinical stage is the most important prognostic factor for HAL. Most patients with advanced HAL have poor prognosis, may accompanied with multiple metastases including the rib, vertebra, adrenal gland, brain, liver, and tonsil.^[5] Only a few patients present long-term disease-free survival.

In conclusion, HAL is a rare and special tumor, frequently occurring in elderly male patients with a long-term smoking history. High serum AFP level is only an important indicator of HAL, but not a necessary factor for its diagnosis. The diagnosis of HAL is based on the

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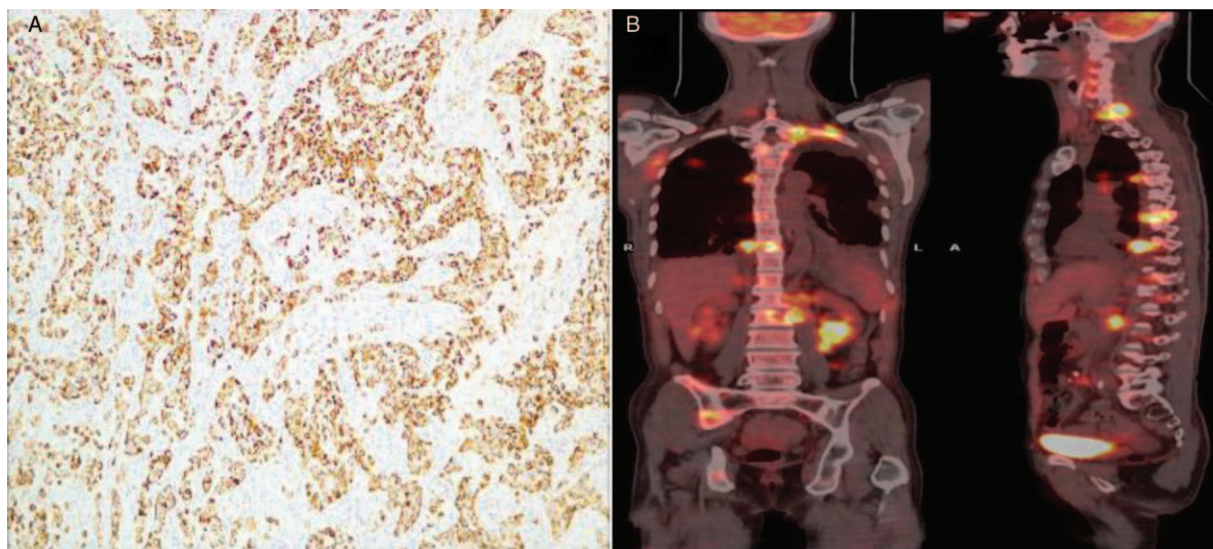


Figure 1: PET/CT and pathological findings of the patient. (A) Immunohistochemical staining of lumbar masses shows HCC-like changes (original magnification $\times 100$). (B) Whole-body PET/CT shows a soft-tissue mass in the apex of the left lung, a nodule in the right upper lobe near the pleura and increased metabolism; systemic multiple lymph node enlargement, soft-tissue masses, multiple subcutaneous nodules, and increased metabolism. PET/CT: Positron emission tomography/computed tomography; HCC: Hepatocellular carcinoma.

morphological characteristics of HCC in lesions of the lung tissue. Further long-term and large-sample studies are suggested to gain a better understanding of its immunophenotypes, genetic changes, molecular pathology, and diagnosis and treatment methods.

Declaration of patient consent

The authors certify that they have obtained the appropriate patient consent form. In the form, the patient's family provided his consent for images and other clinical information to be reported in the journal. The patient's family understand that the patient's name and initials will not be published and that due efforts will be made to conceal her identity.

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Conflicts of interest

None.

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