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Review article

Hepatoid adenocarcinoma of the lung: Review of a rare form of lung cancer

Kate Grossman [a, 1], Mary Beth Beasley [b], Sidney S. Braman [a, *]

[a] Division of Pulmonary, Critical Care and Sleep Medicine, Icahn School of Medicine at Mount Sinai, 1 Gustave L. Levy Place, New York, NY 10029-6574, USA
[b] Department of Pathology, Icahn School of Medicine at Mount Sinai, 1 Gustave L. Levy Place, New York, NY 10029-6574, USA

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ABSTRACT

Rationale: Hepatoid adenocarcinoma (HAC) is a rare malignant lung tumor that histologically resembles typical hepatocellular carcinoma (HCC) when it is metastatic to the lung. To date, this clinical entity has not been highlighted in the pulmonary literature.
Objective: We present a review of all known cases of HAC, including the relevant clinical and histopathological features important for pulmonologists.
Measurements and main results: The purpose of this report is to present a new case of HAC, with typical clinical and histologic features of this malignancy, and to summarize findings of previously reported cases. A systematic literature search of the electronic database PUBMED was conducted to identify all cases of hepatoid adenocarcinoma reported in the English literature, between January 1980 and June 2015. HAC and HCC can be distinguished by immunohistochemical staining. HAC usually presents as a large bulky solitary mass in the upper lobe; there is an exceedingly high prevalence in males and most patients with this tumor are smokers. Serum alpha-fetoprotein (AFP) in very high levels has been a distinguishing feature of this tumor. Nodal and distant metastases are common at initial presentation and, as a result, the prognosis is very poor. Resection and long-term survival, however, have been reported.
Conclusion: Hepatoid adenocarcinoma, first described as a gastric tumor, has also been described in the lung. It morphologically resembles and must be distinguished from metastatic HCC of the lung. While most tumors produce AFP, the case we present demonstrates that this should not be a criterion for diagnosis.

Contents

1. Introduction

Hepatoid adenocarcinoma (HAC) is a rare, aggressive tumor that most commonly arises from the stomach, but also has been reported to originate in the lung. A distinctive feature of this

Abbreviations: HAC, hepatoid adenocarcinoma; HCC, hepatocellular carcinoma; AFP, alpha-fetoprotein.

* Corresponding author. Icahn School of Medicine at Mount Sinai, 1 Gustav L. Levy Place, Box 1232, New York, NY 10029, USA.
E-mail address: sidney.braman@mssm.edu (S.S. Braman).
[1] Current address: 1601 E, Broadway Suite 240, Columbia, MO, 65203, USA.

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tumor is that it mimics typical hepatocellular carcinoma by light microscopy. Distinguishing HAC from metastatic hepatocellular carcinoma (HCC) requires immunohistochemical staining. HAC of the lung was first formally described by Ishikura [1] in 1990. At that time, two diagnostic criteria were proposed: histologic findings of a typical acinar or papillary adenocarcinoma; and, a component of the carcinoma that resembles hepatocellular carcinoma and produces alpha-fetoprotein (AFP). Since that time other cases have been reported [2–23] and, including our patient with HAC of the lung, the total number of cases is 28 (Table 1).

As cases of HAC have been published in Oncology, Pathology, and Gastroenterology journals, this aggressive primary lung malignancy, which appears to predominantly affect heavy smokers, has not been highlighted in the pulmonary literature. Pulmonary physicians are often the first to be involved in the diagnosis of lung tumors and, therefore, should be aware of main clinical features of this malignancy and the histopathological features that can secure this diagnosis and differentiate it from metastatic HCC.

The purpose of this review is to present a new case of HAC to demonstrate the typical clinical and histologic features of this malignancy and summarize findings of the 27 previously reported cases and our case. The tumor of this patient did not produce AFP, thus bringing into question whether this is a criterion for diagnosis.

2. Methods

We present a review of all known cases of HAC, including the relevant clinical and histopathological features important for pulmonologists, who may be the first physicians to diagnose these patients. A systematic literature search of the electronic database PUBMED was conducted to identify all cases of HAC reported in the English literature prior to June 2015. The search was conducted using search terms of “hepatoid adenocarcinoma lung”, hepatoid carcinoma lung” and “AFP producing tumor lung”. The literature search results and article selection were reviewed and verified by the authors to ensure their accuracy and appropriateness.

Table 1
HAC cases summarized.

Author	Age (years)	Gender	Location	Size (cm)	Smoker	AFP level (ng/uil)	Stage	Progression	Treatment
Arnould et al. [9]	36	Male	Left Upper Lobe	10	Yes	11,600	pT4 N2	Brain Metastasis	Chemo, Surg
Yasunami et al. [10]	67	Male	Left Upper Lobe	‘Fist-sized’	Not given	19,000	pT3 N2	Rib and vertebra metastases	XRT, Immuno tx (BCG)
Miyake et al. [11]	73	Male	Left Upper Lobe	5 × 6 × 5	Not given	1039	pT2b N2	Mediastinal, LN, brain metastases	Surg, XRT
Kim et al. [12]	49	Male	Left Upper Lobe	6	Not given	14,707	pT2b N1	Not reported	Surg
Iino et al. [13]	63	Male	Right Upper Lobe	2.8 × 2.5	Not given	N/A	cT1 N0 M0	No progression 5 mo after surgery	Surg
Genova [14]	71	Male	Left Upper Lobe	7.7 × 6.4	Not given	Not Assayed	pT3 N0	No progression at 24 months	Surg
Miyake et al. [15]	40	Male	Right Upper Lobe	8 × 9 × 7	Not given	3090	pT3M1b	Not applicable	Surg
Miyake et al. [15]	55	Male	Right Upper Lobe	5	Not given	2123	pT2a M1b	Not applicable	Surg
Yokoyama et al. [16]	69	Male	Right Lower Lobe	11 × 11 × 7	Not given	5050	pT3 M1b	Not applicable	N/A
Carlifante et al. [17]	82	Male	Left Lower Lobe	3.5	Yes	Not Assayed	cT2a N0 M0	No progression 7 yrs after surgery	Surg
Okunaka et al. [18]	49	Male	Right Upper Lobe	6 × 5 × 5	Not given	9300	eT3	No progression at 11 months	Surg
Nasu et al. [19]	63	Male	Right Upper Lobe	14 × 13 × 12	Not given	14,000	cT4 N2	Lung, right adrenal, brain mets	Chemo
Oshiro et al. [20]	77	Male	Right Lower Lobe	Not Reported	Not given	Not Assayed	cT2 N0 M0	Liver metastasis	Surg
Hayashi et al. [21]	55	Male	Right Upper Lobe	5 × 4.8 × 6.5	Yes	89	pT2b N0	No progression at 32 months	Surg
Hiroshima et al. [22]	71	Male	Right Lower Lobe	10.5 × 8.5 × 7	Yes	7417	pT3 N1	Lung and brain metastases	Surg
Kishimoto et al. [23]	64	Male	Left Lower Lobe	7.5 × 7 × 4	Not given	673	cT3 N0 M0	Not reported	Surg
Haninger et al. [2]	51	Male	Right Upper Lobe	4.2 × 3.7	Yes	1.3 (post-tx)	cT2a N3 M1b	Died 14 mo after presentation	Chemo, XRT, Surg
Haninger et al. [2]	52	Male	Right Upper Lobe	2.5	Yes	Not Assayed	cT1b N0 M1b	Alive 37 mouths after presented	Surg, Chemo, XRT
Haninger et al. [2]	64	Male	Left Upper Lobe	3.2 × 2.2	Yes	1 (post-tx)	cT2a N0 M1b	Died 10 months after presentation	Surg, Chemo, XRT
Haninger et al. [2]	54	Female	Left Upper Lobe	1	Yes	Not Assayed	cT1a N0 M1b	Alive 9 years after presentation	Chemo, XRT, Surg
Haninger et al. [2]	60	Male	Right Upper Lobe	11.2 × 10.1 × 8.5	Yes	4410	cT3 N2 M1b	Alive 1 month after presentation	Chemo, XRT
Mokrim et al. [5]	52	Male	Left Upper Lobe	11.8 × 12 × 8	Yes	5000	cT3 N0 M1	Alive 6-7 months after presenting	Palliative Chemo
Lin et al. [4]	66	Male	Right Upper Lobe	7.4 × 6 × 4.8	Yes	8686	cT3 N2 MO	Alive 57 months after presenting	Surgery, adjuvant chemo
Che et al. [3]	48	Male	Left Upper Lobe	7.8 × 7.9 × 10	Yes	6283	pT4 N1 M0	Died 36 months after presentation	Chemo, XRT
Gavrancic et al. [6]	64	Male	Right Upper Lobe	3.8 × 2.9	Not given	181	cT2 N2 M1	Died 11 months after presentation	Chemo, Sorafenib, XRT
Ivan et al. [8]	54	Male	Left Upper Lobe	13 × 11	Yes	14,540	pT4 N3 M1	Not reported	Chemo, XRT
Valentino et al. [7]	71	Male	Right Lower Lobe	1.8 × 1.5 × 1.5	No	34,791	pT1 N0 M1	Died 4 months after presentation	Chemo, XRT, Surg
Current Case	54	Male	Right Upper Lobe/Paratracheal	4.1 × 5.1	Yes	2	pT4 N0 M1b	Died 4 months after presentation	XRT