Utility of Carbonic Anhydrase-IX in the Diagnosis of Metastatic Renal Cell Carcinoma by Fine-Needle Aspiration Biopsy

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ABSTRACT

Background

Expression of the commercially available antibody against Carbonic anhydrase-IX (CAIX) has been shown to be useful in the diagnosis of metastatic conventional renal cell carcinoma (cRCC) in surgical pathology specimens, but studies demonstrating its utility in cases of metastatic cRCC from cell-block sections of aspiration biopsies are limited. The objective of the current study was to compare CAIX expression with other immuno-histochemical markers routinely used in the diagnosis of metastatic cRCC (CD10, and Vimentin) in cell block material from fine-needle aspiration biopsies (FNABs), and to assess its utility in confirming the diagnosis of metastatic cRCC in cytological specimens.

Design

Thirteen metastatic cRCC specimens from 12 patients were immunostained with CAIX, CD10, and Vimentin. The immunoreactivity results were compared. Immunohistochemistry (IHC) staining was performed and immunoreactivity was graded as 0, no tumor cells immunoreactive (IR); 1+, 1% to 25% IR; 2+, 25% to 50% IR; and 3+, greater than 50% IR.

Results

Eleven of 13 (85%) cases showed 3+ strong and diffuse membranous staining with CAIX; 12 of 13 (92%) cases showed similar 3+ IR with CD10; and 9 of 12 (75%) cases showed 3+ strong and diffuse cytoplasmic IR for Vimentin. In 1 case where CAIX IR was 1+, both CD10 and Vimentin showed 3+ IR; while in the other case where CAIX IR was 1+, CD10 showed 0 IR and Vimentin showed 1+ IR. Morphologically, 12 of 13 metastatic cRCCs showed small to intermediate sized nuclei with relatively inconspicuous nucleoli, and 1 case showed larger nuclei with prominent nucleoli. In the 2 cases where CAIX showed 1+ IR, the tumor cells were intermediate in size with inconspicuous nucleoli. In the 1 case with prominent nucleoli, both CAIX and CD10 showed 3+ IR, while Vimentin showed 1+ IR.

Conclusions

The majority of cases in this study showed strong and diffuse expression of CAIX, and with the exception of 1 case the expression of CD10 and Vimentin was comparable. This study suggests that CAIX is a useful marker in addition to CD10 and Vimentin to confirm the diagnosis of metastatic cRCC in cytological cell block material from various anatomical sites.

INTRODUCTION

Renal cell carcinoma (RCC) is a type of kidney cancer that starts in the lining of small tubules in the kidney. RCC is the most common type of kidney cancer in adults, responsible for approximately 80% of cases. It is also known to be the most lethal of all the genitourinary tumors. The metastatic stage of renal cell carcinoma occurs when the disease invades and spreads to other organs. It is most likely to spread to neighboring lymph nodes, the lungs, the liver, the bones, or the brain. Metastatic renal cell carcinoma presents a special challenge to pathologists and oncologists, as about 70% of patients develop metastases during the course of their disease, and 5 year survival for patients with metastatic renal cell carcinoma is between 5 and 15%.

Carbonic anhydrase-IX (CAIX), a protein that maintains intracellular and extracellular pH, have recently been shown to be useful in the diagnosis of RCC in surgical pathology specimens. Immunohistochemical staining for CAIX have been shown to be useful in the diagnosis of metastatic conventional renal cell carcinoma (cRCC) in surgical pathology specimens, but studies demonstrating its utility in cases of metastatic cRCC from cell-block sections of aspiration biopsies are limited. We compared CAIX expression with other immunohistochemical markers routinely used in the diagnosis of metastatic cRCC (CD10, and Vimentin) in cell block material from fine-needle aspiration biopsies (FNABs), and assesed its utility in confirming the diagnosis of metastatic cRCC in cytological specimens.

TABLE 1. Clinical features and IHC expression of metastatic cRCC cases

Case number	Patient age and gender	Metastatic site	CAIX	CD10	Vimentin
1	57M	Lymph node, 12R	3+	3+	3+
2	68M	Lymph node, station 7	3+	3+	3+
3	53M	Lymph node, station 7	3+	3+	3+
4	67M	Pancreas	3+	3+	3+
5	71F	Pancreas	3+	3+	3+
6	69M	Vertebrae, T10	1+	3+	3+
7	60F	Pancreas	3+	3+	3+
8	60M	Left iliac bone	1+	0	1+
9	86F	Pancreas	3+	3+	3+
10	69M	Lymph node, R10	3+	3+	3+
11	51F	Soft tissue, right shoulder	3+	3+	3+
12	68M	Vertebrae	3+	3+	1+
13	57M	Pleural fluid	3+	3+	n/a
Total Cases: 13					

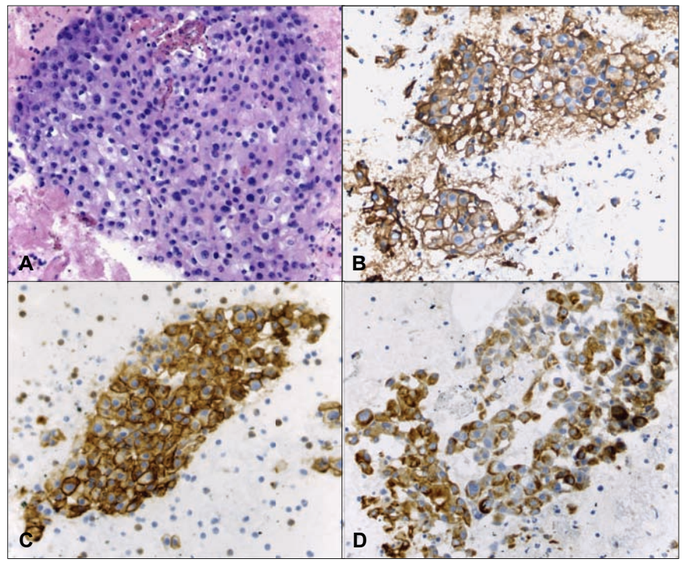

FIGURE 1. Case 1: Microscopic photographs of Hematoxylin & Eosin stain and immuno-histochemistry stains. Hematoxylin & Eosin stain [400x] (**A**) and immunohistochemistry stains for CAIX [400x] (**B**), CD10 [400x] (**C**), and Vimentin [400x] (**D**) of cRCC on cell block material of Case 1.

MATERIALS & METHODS

Search of the Yale Pathology database CoPath over 69 months (1/2005- 9/2011) yielded thirteen metastatic cRCC FNA specimens with adequate cell block material from 12 patients. The metastatic sites included pancreas (4), thoracic lymph nodes (4), bone (3), soft tissue (1), and pleural fluid (1). The patient ages ranged from 57 to 86 years old, (mean age of 67). The commercially available CAIX antibody, clone NB100-417 (Novus Biological, Littleton, CO), was used in this study. Immunohistochemistry (IHC) staining was performed and immuno-reactivity was graded as follows: 0 = no tumor cells immunoreactive (IR); 1+ = 1% to 25% IR; 2+ = 25% to 50% IR; and 3+ = greater than 50% IR.

RESULTS

The primary RCCs with histological classification of tumor type and Fuhrman grade were not available for all cases. The immunohistochemistry stains for CAIX and CD10 showed a linear membrane staining pattern. The immunohisto-chemistry stains for Vimentin were cytoplasmic (**Figure 1**).

Eleven of 13 (85%) cases showed 3+ strong and diffuse membranous staining with CAIX; 12 of 13 (92%) cases showed similar 3+ IR with CD10; and 9 of 12 (75%) cases showed 3+ strong and diffuse cytoplasmic IR for Vimentin. In 1 case where CAIX IR was 1+, both CD10 and Vimentin showed 3+ IR; while in the other case where CAIX IR was 1+, CD10 showed 0 IR and Vimentin showed 1+ IR (as summarized in **Table 1**). Morphologically, 12 of 13 metastatic cRCCs showed small to intermediate sized nuclei with relatively inconspicuous nucleoli, and 1 case showed larger nuclei with prominent nucleoli. In the 2 cases where CAIX showed 1+ IR, the tumor cells were intermediate in size with inconspicuous nucleoli. In the 1 case with prominent nucleoli, both CAIX and CD10 showed 3+ IR, while Vimentin showed 1+ IR.

CONCLUSIONS

- The majority of cases in this study showed strong and diffuse expression of CAIX, and with the exception of 1 case the expression of CD10 and Vimentin was comparable.
- This study suggests that CAIX is a useful marker in addition to CD10 and Vimentin to confirm the diagnosis of metastatic cRCC in cytologic cell block material from various anatomical sites.

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