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Case Report

SMARCA4-deficient tumors in the adrenal gland and small intestines: A rare case report ☆

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ABSTRACT

Thoracic SMARCA4-deficient undifferentiated tumors (SMARCA4-UTs) are rare undifferentiated thoracic malignancies with poor prognosis. They predominantly affect young men who are heavy smokers. Recently, the category of SMARCA4-deficiency–related malignancy has been expanded to include extra-thoracic sites, such as the paranasal sinuses, gastrointestinal tract, ovary, and uterus. We report a rare case of SMARCA4-deficient tumors in the adrenal gland and small intestines. SMARCA4-deficient tumors should be included in the differential diagnosis when multiple large masses with heterogeneous contrast effect and strong accumulation are seen in cancers of unknown primary on 18F-fluorodeoxyglucose (FDG) positron emission tomography with computed tomography (PET/CT).

Introduction

Thoracic SMARCA4-deficient undifferentiated tumors (SMARCA4-UTs) are rare undifferentiated thoracic malignancies that were first reported in 2015 [1]. They are characterized by the loss of the *SMARCA4* gene, which is located on chromosome 19p and encodes the Brahma-related gene 1 (Brg1) protein. The tumors have an undifferentiated epithelioid or rhabdoid morphology with no expression of markers of thymic, lung, or mesothelial origin and complete loss of Brg1 protein. However, the histomorphological differential diagnosis of SMARCA4-UT includes a wide variety of neoplasms. Diagnosis based on morphology alone is difficult [2]. They most commonly consist of a large heterogeneous infiltrative mass involving the mediastinum, lung, or pleura. The prognosis is poor, with a median survival of 6-7 months. Most patients are young men (median age, 39-58 years; range, 27-90 years) with a history of heavy smoking [1].

SMARCA4-UT is considered a distinct entity from other lung tumors because of significant immunohistochemical, clinical, and prognostic differences. Recently, the category of SMARCA4–deficiency–related malignancy has been expanded to include extra-thoracic sites such as the paranasal sinuses,

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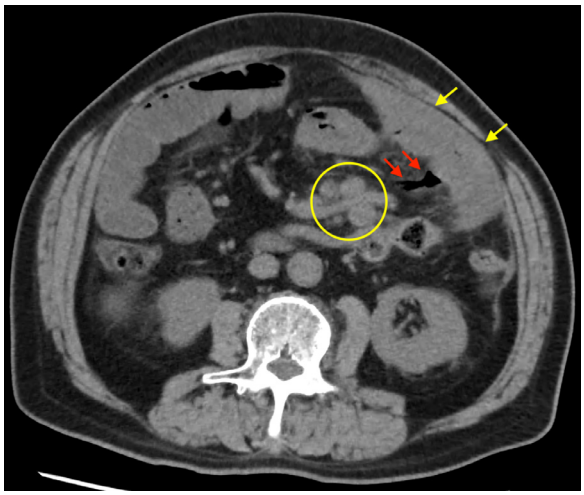

Fig. 1 – Computed tomography image shows intra-abdominal free air (red arrows) with thickening of the jejunal wall (yellow arrows) and enlarged para-aortic lymph nodes (circle).

gastrointestinal tract, ovary, and uterus [3]. Here, we report a rare case of SMARCA4-deficient tumors in the adrenal gland and small intestines on the basis of imaging findings.

Case report

A 76-year-old male with a smoking history of 56 pack-years presented with severe abdominal pain. Bowel perforation due to an intestinal tumor was observed (Fig. 1). Following emergency bowel preparation, tumor resection surgery was performed. Pathologically, hematoxylin–eosin staining of the small intestines showed adenocarcinoma. However, immunohistology was positive for CK7 and negative for CK20, which is not typical for tumors originating from the small intestines. Cancer of unknown primary was suspected.

The patient was referred to our hospital for further examination and treatment. Contrast-enhanced computed tomography (CT) showed a mass with a diameter of 4.5 cm and a heterogeneous internal contrast effect in the left adrenal gland and multiple masses up to 3.0 cm in diameter with similar characteristics in the small intestines (Fig. 2). 18F-fluorodeoxyglucose (FDG) positron emission tomography with CT (PET/CT) revealed markedly high maximal standardized uptake values, 8.6 in the adrenal tumor and 6.2-11.5 in multiple residual tumors of the small intestines (Fig. 3). There were no abnormal uptakes in the neck, lungs, mediastinum, bone, or soft tissue.

CT-guided biopsy of the adrenal tumor was performed. Hematoxylin–eosin staining showed atypical cells with nuclear enlargement and increased chromatin proliferation involving pre-existing adrenal tissue, which were morphologically suggestive of poorly differentiated adenocarcinoma (Fig. 4). Immunostaining was negative for Brg1 (Fig. 5). SMARCA4-deficient tumor was included in the differential

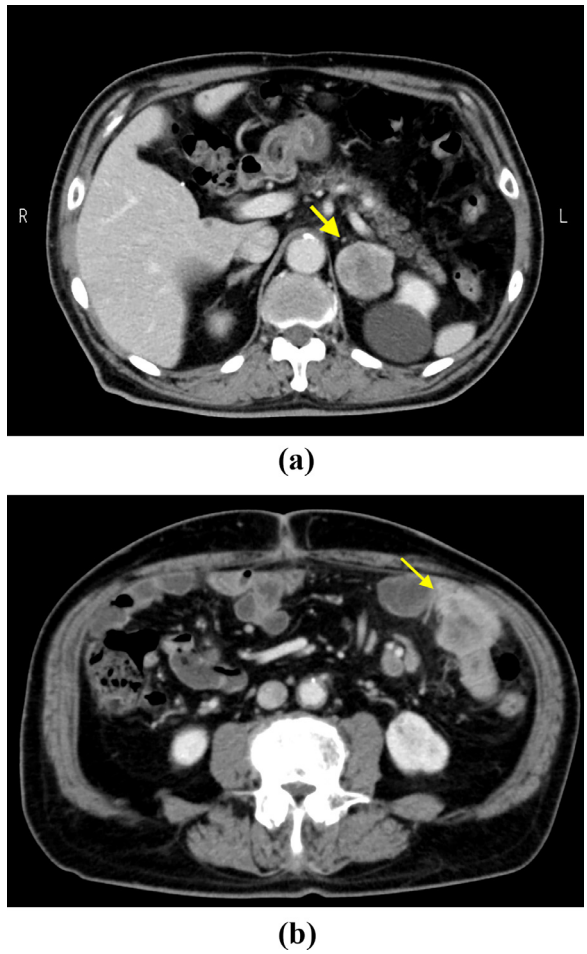

Fig. 2 – Computed tomography images (A) A 4.5 cm diameter mass with a heterogeneous internal contrast effect in the left adrenal gland (arrow) and (B) Multiple masses up to 3.0 cm in diameter with a heterogeneous internal contrast effect in the small intestines (arrow).

diagnosis. Genetic testing confirmed a *SMARCA4* deficiency. Finally, the patient was diagnosed with SMARCA4-deficient tumor.

Discussion

We report a rare case of SMARCA4-deficient tumors in the adrenal gland and small intestines. Recently, the category of SMARCA4-deficiency-related malignancy has been expanded to include extra-thoracic sites, including the paranasal sinuses, gastrointestinal tract, ovary, and uterus [3]. Tumors in this category have been reported to share some common clinicopathological features, such as (1) undifferentiated round cell or rhabdoid morphology and (2) highly aggressive malignant behavior with a relatively poor clinical course [3]. Perret et al. [4] found that metastases were prevalent. They occurred in the affected sites in the following order: lymph nodes,

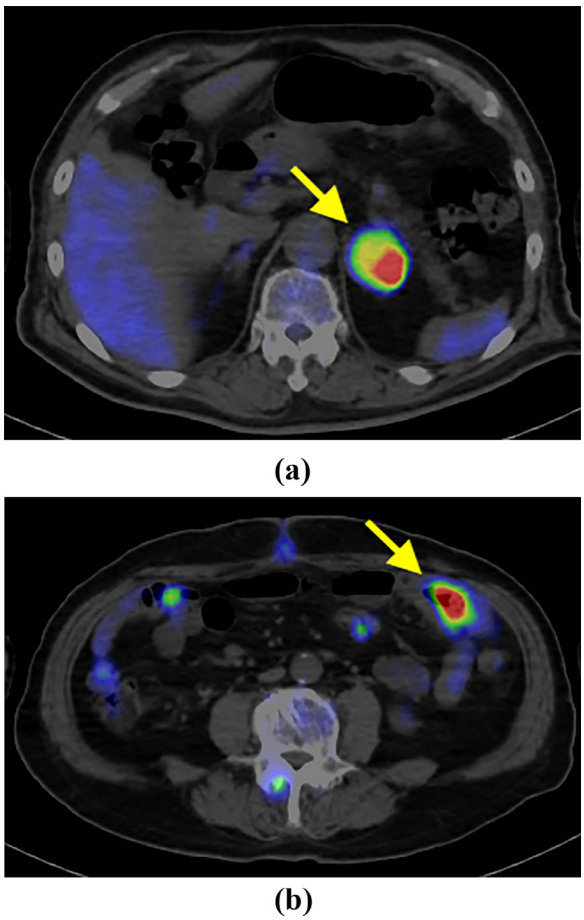

Fig. 3 – Fused axial 18F-fluorodeoxyglucose positron emission tomography with computed tomography images (A) Marked uptake is seen in the left adrenal gland (arrow) and (B) Marked uptake is seen in the small intestines (arrow).

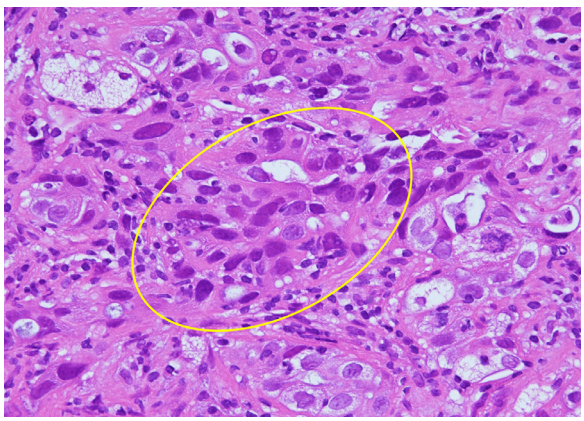

Fig. 4 – Hematoxylin–eosin stain of the adrenal biopsy specimen shows atypical cells with nuclear enlargement and increased chromatin proliferation involving preexisting adrenal tissue (oval).

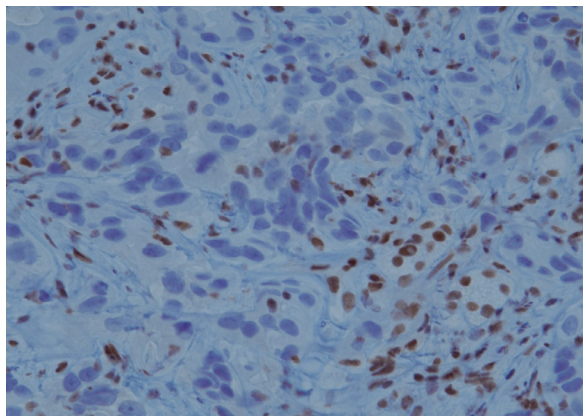

Fig. 5 – Tumor cells were negative for Brahma-related gene 1.

bones, adrenal glands, liver, gastrointestinal tract, central nervous system, and kidney [4]. Decroix et al. [5] report that even though the tumors were resectable without metastasis, they recurred within 1 month .

The imaging characteristics of SMARCA4-deficient tumors have not been well described. The primary tumor tends to have a large heterogeneous contrast effect on CT [6] and strong uptake on PET/CT. Many patients have metastases at the time of diagnosis [7]. In the present case, the patient was diagnosed with cancer of unknown primary (CUP) because the primary site could not be determined from the initial small bowel surgical specimens. However, Brg1 immunostaining was not performed. This resulted in a 3-month delay before definitive diagnosis. Imaging revealed large tumors in the adrenal gland and small intestines with heterogeneous contrast enhancement on CT and high uptake on PET/CT. Although these findings are relatively nonspecific, SMARCA4-deficient tumors are part of the differential diagnosis for CUP. Recently, immunotherapy consisting of pembrolizumab, ipilimumab, and nivolumab and targeted therapy consisting of enhancer of zeste homolog 2 inhibitors have shown promising results. A phase I clinical trial of zeste homolog 2 inhibitors has shown encouraging results, with some patients achieving complete or partial remission and some patients having stable disease for more than 2 years [8]. The possibility of a SMARCA4-deficient tumor can be identified by the radiologist, which might lead to an earlier diagnosis and thus better prognosis.

Conclusion

We report a rare case of extra-thoracic SMARCA4-deficient tumors in the adrenal gland and small intestines. SMARCA4-deficient tumors should be part of the differential diagnosis when multiple large masses with heterogeneous contrast effect and strong accumulation on PET/CT are seen in CUPs.

Patient consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

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