Oncology

Malignant fibrous histiocytoma arising from the renal capsule and gene mutation screening: A case report

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A R T I C L E   I N F O

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A B S T R A C T

Malignant fibrous histiocytoma (MFH) is an aggressive soft tissue sarcoma. Renal MFH is rare and information about its molecular characterization is limited. We present here the case of a 77-year-old man who was incidentally found to have a huge right renal mass on computed tomography. Radical nephrectomy was performed. Pathological diagnosis was MFH arising from the renal capsule. We used Ion AmpliSeq Cancer Hotspot Panel version 2 primers to perform gene mutation screening. We detected 13 mutations in 11 hotspot oncogenes (CSF1R, FGFR3, KDR, APC, PDGFRα, TP53, FLT3, ERBB4, KIT, STK11, RET), but these were not matched to driver mutations.

Introduction

Malignant fibrous histiocytoma (MFH) was first described by O’Brien and Stout in 1964 as a soft tissue sarcoma arising from fibroblasts and histiocytes. MFH is an aggressive tumor with a high recurrence rate. Primary sarcoma of the kidney is rare, and MFH arising from the renal parenchyma or renal capsule represents less than 6% of renal sarcomas. To date, there are only about 60 reported cases of MFH arising from the kidney, and studies on gene mutation screening in MFH are rarely conducted.

We report here a rare case of MFH arising from the renal capsule. We used next-generation sequencing (NGS) to identify specific mutations that drive oncogenesis and report the results of gene mutation screening in renal MFH.

Case presentation

A 77-year old man was incidentally found to have a huge right renal mass on computed tomography (CT). The patient had undergone abdominal CT 2 years earlier and bilateral renal cysts had been identified (Fig. 1a). Contrast-enhanced CT revealed a slightly enhanced mass (10.6 × 9.7 × 9.6 cm) on the upper pole of the right kidney (Fig. 1b). No metastasis was seen. Physical examination, laboratory investigations, and urinalysis were unremarkable. Magnetic resonance imaging (MRI) revealed the mass to be hypointense on T1-weighted images and iso- or hyperintense on T2-weighted images. Malignant renal tumor was strongly suspected. The patient underwent laparoscopic right radical nephrectomy. At surgery, severe adhesions were seen between the renal mass and the liver. Partial resection of the hepatic capsule was performed to remove the mass completely. Macroscopically, a cut section of the specimen showed a multinodular architecture with a grayish-white surface (Fig. 2a). The mass had neither invaded into the renal parenchyma nor extended through Gerota’s fascia. Microscopic findings were spindle-shaped fibroblastic cells arranged in a storiform pattern with fibrous stroma and clusters of rounded histiocyte-like cells and pleomorphic giant cells with bizarre nuclei (Fig. 2b). On immunohistochemistry, the histiocytic cells were positive for CD68. The tumor cells were negative for AE1/AE3, desmin, α-SMA, S100 m, and α-sarcomeric actin. Ki-67 labeling index was about 60%. The pathological diagnosis was MFH arising from the renal capsule. No adjuvant chemotherapy was administered.

Formalin-fixed, paraffin-embedded blocks were used for DNA extraction and genomic tumor DNA was extracted using NucleoSpin® DNA FFPE XS (Macherey-Nagel, Duren, Germany). Molecular
characterization was investigated using NGS Ion AmpliSeq Cancer Hotspot Panel version 2 primers on the Ion PGM™ System (Takara Bio Inc., Shiga, Japan). A total of 13 mutations in 11 hotspot oncogenes were identified (Table 1). We investigated the impact of these 13 mutations using COSMIC (the catalogue of somatic mutations in cancer) database, but none of the 13 mutations were matched to driver mutations.

After a 23-month follow-up period, liver metastasis was identified on abdominal CT.

Discussion

The most frequent site of MFH is the extremities and the second most prevalent site is the retroperitoneum. Primary renal MFH is rare. It occurs most commonly in the 5th-7th decades of life with equal sex distribution, often presenting with nonspecific symptoms like flank pain, fever, weight loss, and a palpable mass. Diagnostic imaging includes CT and MRI, but it cannot be differentiated radiologically from other common renal tumors. Definitive diagnosis is difficult and is usually by histopathology, which involves immunohistochemical examination.

Surgery is the most common treatment for MFH. Radical nephrectomy was performed in almost all reported cases. Chemotherapy has been attempted in a few patients but has shown only slight apparent survival benefit. Ifosfamide, cisplatin, vinca alkaloids, mitomycin C, Adriamycin, cyclophosphamide, and dacarbazine have all been used in various combinations. Adjuvant radiotherapy has not been found to be of obvious benefit. Sugihara et al. reported on a patient with renal MFH and pulmonary metastasis who was treated with surgical resection and MAID chemotherapy (mesna, doxorubicin, ifosfamide, and dacarbazine) and had achieved complete response for 3 years. Mauri et al. reported another patient with locally recurrent MFH plus lung and bone metastases, who was treated with sunitinib and had been doing well with no tumor progression for 13 months.

There are limited data available on the molecular characterization of MFH. Lewin et al. investigated actionable mutations using NGS in patients (n = 88) with a historical diagnosis of MFH (primary site, extremity). Following pathology re-review, histological subtypes were reclassified to include myxofibrosarcoma (n = 43), MFH (n = 18), and others (n = 27). TP53 mutation was identified in 4 out of 18 patients with MFH. Some recent unvalidated data suggested that TP53 mutation status may predict response to VEGFR inhibition. Koehler et al. retrospectively reviewed 19 cases of soft tissue sarcoma treated with pazopanib (with only 1 case of MFH) and found that patients with TP53 mutations had significantly better progression-free survival than those with TP53 wild-type (208 vs 136 days, p = 0.036). In our case, 13 mutations in 11 hotspot oncogenes (CSF1R, FGFR3, KDR, APC, PDGFRα, TP53, FLT3, ERBB4, KIT, STK11, RET) were detected, but none of these mutations were matched to driver mutations. Liver metastasis that appeared after a 23-month postoperative period is scheduled for surgical resection.

Conclusion

We encountered a rare case of MFH arising from the renal capsule. Gene mutation screening revealed 13 mutations in 11 hotspot oncogenes; however, none of these mutations were matched to driver mutations.

Consent

Informed consent was obtained from the patient.

Declarations of interest

None.

Disclosure

There is no financial or personal relationships to disclose.

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Fig. 2. (A) Macroscopic tumor appearance shows multilobular architecture with a gray-white surface. (B) Microscopy demonstrates proliferation of fibrohistiocyte cells with storiform pattern.
Table 1
Gene mutation screening reveals 13 mutations in 11 hotspot oncogenes.

| Gene | Chromosome | Position  | Reference  | Variant | Allele pattern | Allele frequency | Type  |
|------|------------|-----------|------------|---------|----------------|------------------|-------|
| CSF1R| chr5       | 149433596 | TG         | GA      | Homozygous     | 100              | MNP   |
| FGFR3| chr4       | 1807894   | G          | A       | Homozygous     | 100              | SNP   |
| KDR  | chr4       | 55972974  | T          | A       | Homozygous     | 100              | SNP   |
| APC  | chr5       | 112175770 | G          | A       | Homozygous     | 100              | SNP   |
| PDGFRA| chr4      | 55141055  | A          | G       | Homozygous     | 100              | SNP   |
| KDR  | chr4       | 55962546  | –          | G       | Homozygous     | 100              | SNP   |
| TP53 | chr17      | 7579472   | G          | C       | Homozygous     | 100              | SNP   |
| FLT3 | chr13      | 28610183  | A          | G       | Heterozygous   | 54               | SNP   |
| ERBB4| chr2       | 212812097 | T          | C       | Heterozygous   | 53.6             | SNP   |
| KIT  | chr4       | 55592239  | T          | G       | Heterozygous   | 49.9             | SNP   |
| STK11| chr19      | 1220521   | T          | C       | Heterozygous   | 48.2             | SNP   |
| RET  | chr10      | 43613843  | G          | T       | Heterozygous   | 47.2             | SNP   |
| KDR  | chr4       | 55980239  | C          | T       | Heterozygous   | 46.4             | SNP   |

MNP, multi nucleotide polymorphism. SNP, single nucleotide polymorphism. INS, insertion.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eucr.2019.101004.

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