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CASE REPORT

Primary Synchronous Ipsilateral Renal Fibrosarcoma and Renal Pelvic Carcinoma: A Case Report and Literature Review

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Abstract: Renal fibrosarcoma is a rare tumor, with only a few cases reported so far, and simultaneous occurrence of ipsilateral renal fibrosarcoma and renal pelvic carcinoma in a patient is extraordinarily rare. A 66-year-old man admitted to our hospital with right renal percutaneous nephrostomy and recurrent fever. And the patient underwent laparoendoscopic nephrectomy and partial ureterectomy for pyonephrotic nonfunctioning kidneys. Postoperative pathology showed fibrosarcoma of right kidney and carcinoma of the renal pelvis. This is the first case of simultaneous occurrence of ipsilateral renal fibrosarcoma and renal pelvic carcinoma in a patient. The diagnosis of fibrosarcoma is one of ultimate immunohistologic exclusion, because there are no specific immunologic markers for fibroblasts. Electron microscopy combined with light microscopy and IHC is helpful for the case of renal fibrosarcoma which is difficult to diagnose. Clinically, radical nephrectomy is the main strategy for primary localized renal fibrosarcoma. At present, it is still necessary to carry out basic biology research to better understand etiology and therapeutical strategy of renal fibrosarcoma.

Keywords: renal fibrosarcoma, renal pelvic carcinoma, multiple primary malignant neoplasms

Introduction

Primary malignant mesenchymal tumors of kidney are rare, most of them are leiomyosarcoma, fibrosarcoma is seldom seen. We will report a case of primary synchronous renal fibrosarcoma and renal pelvic carcinoma of ipsilateral renal which is extremely rare. Renal fibrosarcoma is a highly malignant tumor with poor prognosis, and the etiology of renal fibrosarcoma remains obscure. There are no standard treatment options available for patient with renal fibrosarcoma. Radical nephrectomy is historically accepted as the main treatment for primary localized renal fibrosarcoma.

Case Presentation

A 66-year-old man admitted to hospital with right renal percutaneous nephrostomy. Nine days ago, the patient underwent right renal nephrostomy because of severe hydronephrosis, the daily drainage was about 50 mL of purulent fluid per day. After the operation, the patient developed shaking chills and fever repeatedly, and the symptoms did not improve within seven days of treatment with antibiotic. The axial

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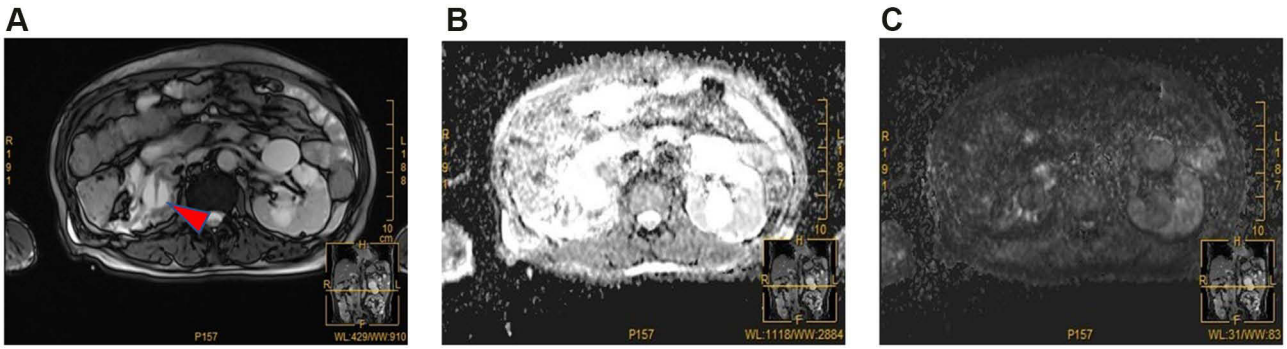

Figure 1 MRI of postoperative right renal percutaneous nephrostomy. (**A**) The axial T2-weighted MR images showing right renal atrophy, empyema in the right upper ureter with increased thickness and signal intensity in the perinephric fat and Gerota's fascia; there is a water balloon of nephrostomy tube (red head of arrow). (**B** and **C**) MRI showed no abnormal diffusion restriction in the right kidney.

T2-weighted MR images showed empyema in the right upper ureter with increased thickness and signal intensity in the perinephric fat and Gerota's fascia (Figure 1). Then, the patient underwent laparoendoscopic nephrectomy and partial ureterectomy for pyonephrotic nonfunctioning kidneys. Grossly, the tumor appeared as exophytic, cauliflower-shaped like mass in the right renal pelvis (3.5×2.5×2.0 cm^3) (red arrow); and there was another tumor with invasive growth at the ureteropelvic junction (black arrow) (Figure 2). Postoperative pathology showed high-grade urothelial carcinoma of the upper ureter with immunohistochemistry (IHC): CK-HMW (+), CK5/6 (+++), Vimentin (focal +), CK8/18 (+++), CK7 (++), Ki-67 (60%+) (Figure 3); the immunohistochemistry results of pelvic neoplasms: CK5/6 (focal +), CK-HMW (focal +), CK8/18 (focal +), CK7 (focal +), Vimentin (+++), Ki-67 (85%+), SMA (-), CD10 (-) (Figure 4). The patient refused further treatment and was discharged after 7 days.

Discussion

This is a rare case report of multiple primary malignant neoplasms (MPMNs). MPMNs were defined as two or more primary malignant neoplasms in one individual. Two kinds of primary tumors in one organ are extremely rare. The prevalence of MPMTs has been reported to vary from 0.734% to 16% in various research and different countries.[6] The molecular mechanism of MPMN, however, remains unclear, but may be associated with multiple factors, such as, genetic susceptibility, environmental factors, immune status, radiation therapy and drug therapy. In addition, continuous smoking and alcohol consumption could increase the risk of MPMNs.[7]

Fibrosarcoma is a malignant mesenchymal tumor composed of cells and fibers and characterized by immature proliferating fibroblasts or undifferentiated anaplastic spindle cells. According to clinical manifestations, fibrosarcoma can be divided into two categories: infantile or congenital fibrosarcoma (a low malignant/rarely metastasizing tumor) and adult-type fibrosarcoma (a rare and highly aggressive subtype of sarcomas). It has been reported that the most common types of soft tissue sarcoma are adult fibrosarcoma. In recent decades, however, due to extensive use of immunohistochemistry and

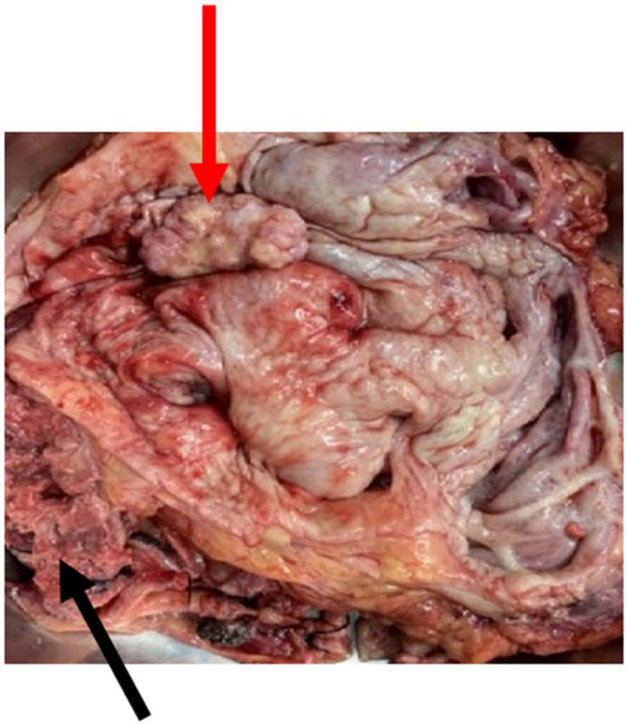

Figure 2 Grossly, the tumor appeared as exophytic, cauliflower-shaped like mass in the right renal pelvis (3.5×2.5×2.0 cm^3) (red arrow); at the ureteropelvic junction, there was another tumor with invasive growth that caused an obstruction of ureter (black arrow).

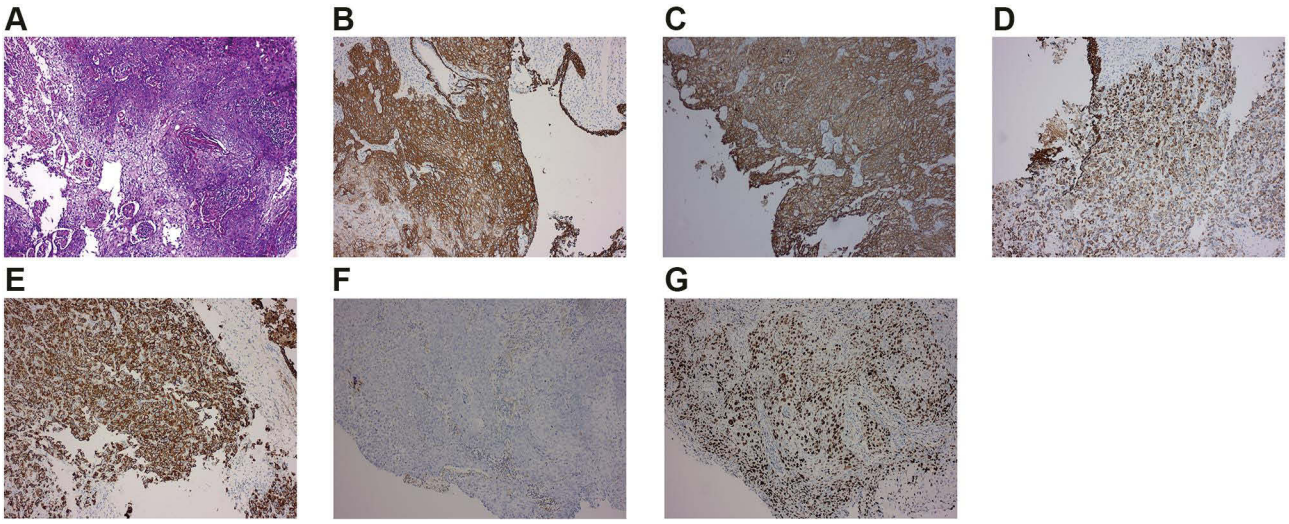

Figure 3 Pathological features of the carcinoma of upper ureter: (**A**) H&E showing urothelial squamous metaplasia; (**B**) positive immunostaining in tumor cells with CK5/6; (**C**) intense positive immunostaining for CK-HMW (+) in tumor cells; (**D**) positive immunostaining in tumor cells with CK8/18 (+++); (**E**) positive immunostaining in tumor cells with CK7 (+); (**F**) positive immunostaining in tumor cells with Vim (focal +); (**G**) tumor cell proliferation rate as determined by Ki-67 immunostaining showed 60% of positive cells.

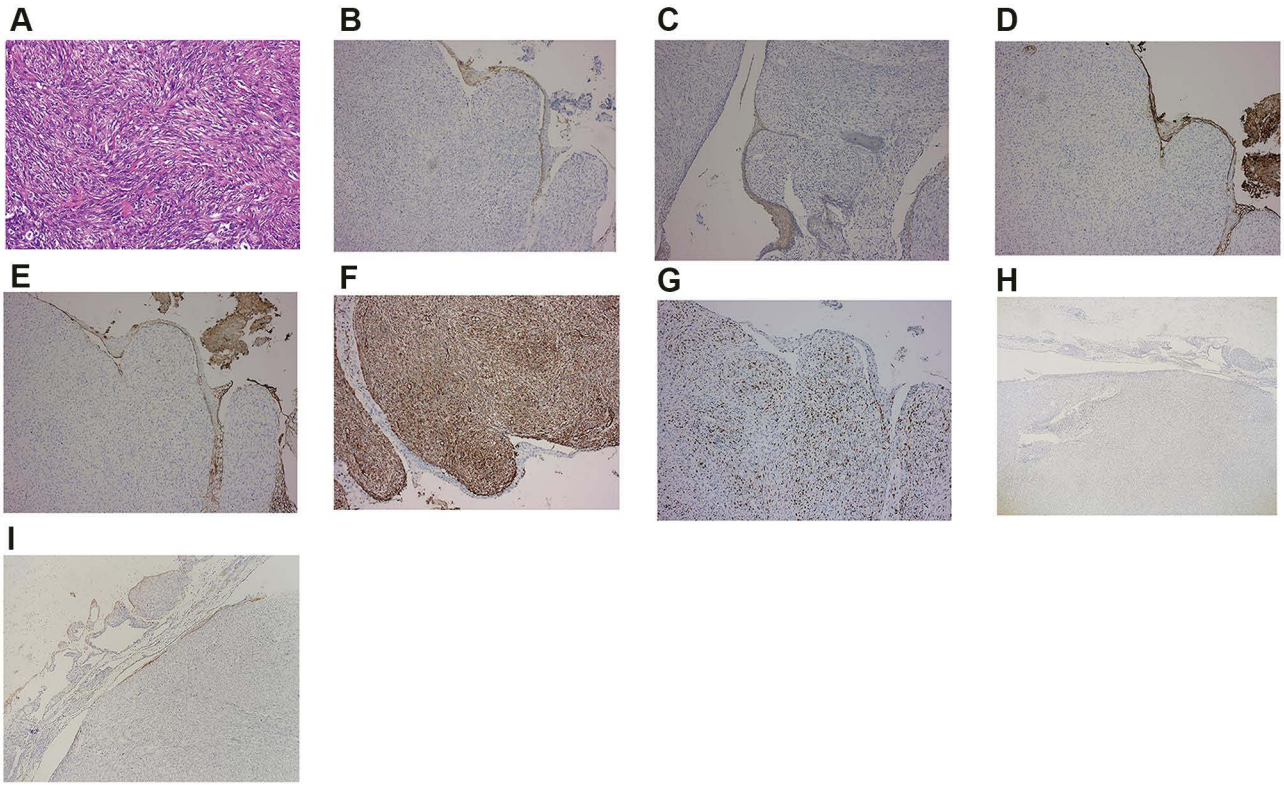

Figure 4 Pathological features of the carcinoma of pelvic neoplasms: (**A**) H&E showing abundant fibroblastic epithelioid cells densely arranged in cords, nests, or sheets within a collagenous extracellular matrix; (**B**) positive immunostaining in tumor cells with CK5/6 (focal +); (**C**) positive immunostaining for CK-HMW (focal +) in tumor cells; (**D**) positive immunostaining for CK7 (focal +) in tumor cells; (**E**) positive immunostaining in tumor cells with CK8/18 (focal +); (**F**) intense positive immunostaining in tumor cells with Vim (+++); (**G**) tumor cell proliferation rate as determined by Ki-67 immunostaining showed 85% of positive cells; (**H**) negative immunostaining in tumor cells with CD 10; (**I**) negative immunostaining for SMA in tumor cells.

electron microscopy, the proportion of fibrosarcoma has been greatly reduced, accounting for less than 1% of adult soft tissue sarcomas.[8] Primary renal fibrosarcoma is extremely rare. We searched the case of renal fibrosarcoma with the search phrase "fibrosarcoma [title] and kidney [title]" and "fibrosarcoma [title] and renal [title]" using the PubMed since 1980. A total of 5 cases of renal carcinoid were retrieved from PubMed (Table 1). Primary synchronous renal fibrosarcoma and renal pelvic carcinoma of ipsilateral renal have not been reported. The results showed that renal fibrosarcoma was more common in middle aged and elderly people, and there is no significant difference between male and female, and it occurs seemingly more often in right kidney than left. The volume of the tumor is generally large when patient visits the doctor. Of course, those conclusions are only based on currently available case report. In this case, the diagnosis of renal fibrosarcoma was an incidental finding on postoperative pathological examination. The carcinoma of upper ureter caused severe hydronephrosis, and complicated with pyometra in the right kidney.

Adult fibrosarcoma occurs most often in the trunk and lower extremities, and only 15% of the cases occur in the head and neck. It is most common in people between the ages of 20 and 60, and male are more frequently affected than female.[9,10] The etiology of renal fibrosarcoma remains obscure. During the past decade, gene fusions have been widely researched in mesenchymal malignancies. Sclerosing epithelioid fibrosarcoma (SEF) is an extremely rare variant of fibrosarcoma. The study showed that SEF tumors harbor EWSR1 rearrangements, with EWSR1-CREB3L1 and more rarely EWSR1-CREB3L2 gene fusions, conversely, FUS gene rearrangement was not found.[11,12] The ETV6-NTRK3 gene fusion was first identified as a result of the t (12; 15) (p13; q25) chromosomal translocation in congenital fibrosarcoma.[13,14] Low-grade fibromyxoid sarcoma (LGFMS) is a rare low-grade malignant fibroblastic tumor, it was discovered to carry the recurrent chromosomal translocation t (7; 16) (q33; p11) encoding a characteristic FUS-CREB3L2 or FUS-CREB3L1 gene fusion.[15,16] It is suggested that there is a relationship between LGFMS and SEF on a genetic level. However, these gene fusions were not found in the limited number of adult fibrosarcomas.[14] In this case, there was no definite diagnosis before operation, and the patient refused genetic testing for economic reasons postoperation, so the etiology is still unknown, this may be the most important limitation of this study. The causes of cancer of renal pelvis are also unclear, pelvic cancer is a common tumor, related to tobacco smoking, environmental arsenic exposure, and chemical carcinogens (phenacetin, benzidine), pyelolithiasis, chronic inflammation and other factors.

Currently, there is no evidence-based pathophysiological explanation for the simultaneous occurrence of renal fibrosarcoma and renal pelvic carcinoma in one kidney. We believe that this case has its own characteristics. It is now clear that inflammatory tumor microenvironment (TME) has a major influence on the development of cancer and promotes all stages of tumorigenesis.[17] Within the TME, cells are highly plastic, and their phenotypic and functional characteristics are continuously changing to adapt to new condition.[18] Studies have shown that QR-32 tumor cells, a clone derived from a murine fibrosarcoma, presented highly malignant in inflamed site, further study found that inflammation, especially when neutrophils infiltrate into inflamed site, is primarily important for cells to acquire metastatic phenotype.[19] In addition, inflammation-induced oxygen species produced by the inflammatory environment participated in the progression of QR-32 cells.[20] We speculate that the TME may play an important role in the development of renal fibrosarcoma in this patient. From the degree of hydronephrosis and the depth of tumor invasion, we hypothesize that the renal pelvic carcinoma precedes the development of fibrosarcoma, the renal fibrosarcoma is the second primary cancer. Chronic hydronephrosis with infection may be an important factor in the development of renal fibrosarcoma in this case. Further experiments will be carried out to verify this conjecture.

The diagnosis of renal fibrosarcoma is relatively difficult because there are no specific immunologic markers. Renal fibrosarcoma is a diagnosis of exclusion on Immunohistochemical (IHC). IHC staining and transmission electron microscopy are helpful for the diagnosis of fibrosarcoma, it is consistently positive for Vim, and negative for HMB-45 (melanocyte marker), CD31 (vascular origin), CK (cytokeratin; epithelial origin sarcoma), Bcl-2 (lymphoma lineage) and SMA (smooth muscle actin; smooth muscle origin). In addition, it is important to exclude the possibility of the same tumor implantation and invasion in right kidney, light microscopy and immunohistochemistry showed that they had different pathological features.

There are several types of diseases that need to be identified. Immunohistochemistry and light microscopy can

Table 1 Reported Cases of Renal Fibrosarcoma in the English Literature

Reference	Age	Gender	Size (cm)	Symptoms	Treatment	Pathologic Diagnosis	Side	Metastatic	Follow Up (Months)
Gupta et al[1]	75	F	15×10	Vague abdominal discomfort	RN	Vim (+), Ki-67 (+), CK (-), Desmin (-), HMB-45 (-), SMA (-)	R	–	NS
Agarwal et al[2]	54	M	17.5×12.5×9	Intermittent hematuria and pain in the lumbar region	RN	Vim (+), CK (-), Desmin (-), EMA (-), SMA (-), PAN (-), S100 (-)	R	–	6
Ares Valdés et al[3]	53	F	10	Left flank pain, fever and palpable mass	RN	NS	L	Brain	After 24 months, death
Kaneoya et al[4]	64	F	NS	Hematuria	Nephrectomy	NS	L	–	After 4 months, death
Chaudhari et al[5]	70	M	17×10×6	Abdominal swelling and pain	RN	Vim (+), CK (-), Desmin (-),	R	–	NS
Our case	72	M	3.5x2.5x2cm	Severe hydronephrosis	Nephroureterectomy	CK5/6 (+), CK (+), CK8/18 (+), CK7 (+), Vimentin (+++), Ki-67 (85%+), Desmin (+), HMB-45 (-)	R	–	3

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differentiate fibrosarcoma from other meningeal tumors with similar intracranial location and morphology–especially malignant fibrous histiocytoma (MFH), leiomyosarcoma and malignant schwannoma. Malignant fibrous histiocytoma, the most frequent soft tissue sarcoma of adulthood, is a high-grade sarcoma, but seldom arises in the urinary system. The tumor cells are arranged radially in whorls around an imaginary stem.[21] Leiomyosarcoma usually occurs in the retroperitoneum and abdomen, histologic evaluation of leiomyosarcomas were well-circumscribed and encapsulated and composed of well-differentiated smooth muscle cells, which are arranged in interesting fascicles. The tumor cells mainly showed positivity for smooth muscle actin and vimentin.[22] At last, malignant schwannoma sometimes needs to be differentiated from fibrosarcoma, the cancer cells are usually pleomorphic, with parallel or disordered arrangement, but without collagen fibers.[23]

MRI may be helpful for diagnosis of renal fibrosarcoma. The lesions showed hyperintensity to isointensity on T1WI and heterogeneous signal on T2WI. In addition, the tumor always showed hypointensity of the septa with lesions. However, this patient had no characteristic MRI changes, there may be associated with right renal empyema, which interfered with MR signals and made the occurrence of missed diagnosis of ureter cancer, and the collapse of renal cortex after renal fistula may also lead to misdiagnosis of imaging. Electron microscopy was usually useful in establishing the final diagnosis in specific instances that are difficult to diagnose or differentiate with other lesions. Electron microscopically, the tumor cells were rich in rough endoplasmic reticulum, and were surrounded by large amounts of collagen fibrils and Golgi apparatus.[24]

The gold standard for localized renal pelvis cancer is nephroureterectomy with removal of the bladder cuff. Radical nephrectomy is the main strategy for the primary renal fibrosarcoma. Renal fibrosarcoma, even when confined to the kidney, have a poor prognosis with an overall 5-year survival less than 10%. Radiotherapy and chemotherapy have no significant effect on primary renal fibrosarcoma. Recent study manifested that the soluble pattern recognition receptor long-pentraxin 3 (PTX3) may act as an oncosuppressor, functioning as an antagonist of the fibroblast growth factor/fibroblast growth factor receptor (FGF/FGFR) system to inhibit FGF-dependent tumor growth.[25] Jain et al[26] found that miR-197-3p can significantly inhibit the viability, colony formation, migration as well as triggers G2/M phase cell cycle arrest of fibrosarcoma cells. For the recurrent fibrosarcoma with high expression of vascular endothelial growth factor (VEGF), apatinib could effectively reduce the risk of disease progression in patient with recurrent fibrosarcoma, which highly expressed vascular endothelial growth factor (VEGF).[27] These findings provide new insight into treatment of fibrosarcoma.

Conclusion

In summary, simultaneous occurrence of ipsilateral renal fibrosarcoma and renal pelvic carcinoma in a patient is extremely rare. The diagnosis of fibrosarcoma is one of ultimate immunohistologic exclusion, because there are no specific immunologic markers for fibroblasts. With combined use of light microscopy and IHC, electron microscopy is helpful for the case of renal fibrosarcoma which is difficult to diagnose. Although low incidence rates of this disease, renal fibrosarcoma is a highly malignant tumor with poor prognosis, further gene detection and animal experiments should be carried out to explore its pathogenesis and therapeutical strategy. Clinically, radical nephrectomy is the main strategy for primary localized renal fibrosarcoma.

Abbreviations

M, male; F, female; L, left; R, right; RN, radical nephrectomy; NS, not stated; Vim, vimentin; CK, cytokeratin; SMA, smooth muscle actin; HMB-45 (Human Melanoma Black 45); EMA, epithelial membrane antigen; PAN, Pancytokeratin; CD34, cluster of differentiation 34; CD68, cluster of differentiation 68; MtoD1, myogenic differentiation 1; CK-HMW, high molecular weight cytokeratin.

Consent for Publication

Written informed consent was obtained from the patient for publication.

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Disclosure

The authors declare that they have no competing interests.

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