Case Report

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# Papillary Renal Cell Carcinoma in Transplanted Kidney and Xp11.2 Translocation/ Transcription Factor E3-Rearranged Renal Cell Carcinoma in the Native Kidney: A Case Report

## 이식신장에 생긴 유두모양 신세포암종과 고유신장에 생긴 Xp11.2전위/전사인자E3-재배열 신세포암종: 증례 보고

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Concomitant renal cell carcinomas (RCC) of both native and allograft kidneys are extremely rare, and only a few cases have been reported in the available English literature. A particularly rare variant within the adult population is the Xp11.2 translocation/transcription factor E3 (TFE3)-rearranged RCC. Although few case reports of TFE3-rearranged RCC have been reported in children who underwent kidney transplantation (KT), no case of adults with TFE3-rearranged RCC following KT has been reported. Herein, we presented the radiological and pathological findings of a rare metachronous papillary RCC in the allograft kidney and TFE3-rearranged RCC in the native kidney. The TFE3-rearranged RCC in the native kidney exhibited slow expansion in size over five years. Radiologically, it appeared as a slightly enhanced, lobulated mass on contrast-enhanced CT. MRI revealed high signal intensity on T1-weighted images and low signal intensity on T2-weighted images.

**Index terms** Neoplasm; Kidney; Transplant; Computed Tomography; Magnetic Resonance Imaging

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## INTRODUCTION

Patients undergoing kidney transplant (KT) have a significantly higher risk of renal cell carcinoma (RCC), with incidences ranging from 5 to 10 times more than that of the general population (1). Most cases involve the patient's native kidneys, with an incidence of 0.7%, whereas transplanted kidneys are rarely affected, with an incidence of 0.2% (2). Clear cell and papillary RCC account for the majority of RCCs in native kidneys of KT recipients, with incidences of 50% and 44%, respectively (3). In allograft kidneys, clear cell RCC accounts for 45.7%, and papillary RCC makes up 42.1% (4). To our knowledge, no incidence of concomitant RCCs has been reported in native or allograft kidneys. Only a few cases of RCCs have been reported in native and allograft kidneys (5, 6).

A novel category of RCC, Xp11.2 translocation/transcription factor E3 (TFE3)-rearranged RCC, has been included in the World Health Organization (WHO) classification in 2022. It is rare in adults, accounting for 1%–4% of all types of RCC (7). Few cases of TFE3-rearranged RCC have been identified in the native kidneys of pediatric patients who received KT, but instances of its occurrence have not been reported in adult patients (8).

Herein, we presented a rare case featuring imaging and pathological findings of a 48-year-old male patient who developed papillary RCC in a transplanted kidney, followed by the emergence of TFE3-rearranged RCC in a native kidney.

## CASE REPORT

A 34-year-old male with a history of chronic kidney disease necessitating dialysis underwent a renal transplant from a deceased donor. He underwent immunosuppression therapy with sirolimus (Rapamune; Pfizer, Manhattan, New York, USA) and tacrolimus (Advagraf; Astellas, Tokyo, Japan, Tacrobell; Chong Kun Dang, Seoul, Republic of Korea), with no documented graft rejection episodes. At 43, a routine CT screening identified a mass in the allograft kidney. The mass measured 1.1 cm and exhibited hypodensity with distinctly demarcated margins (Fig. 1A). Subsequent MRI revealed isointensity on both the T2-weighted image (T2WI) and pre-contrast enhanced T1-weighted image (T1WI) (Fig. 1A, B). The mass showed poor enhancement across the arterial, venous, and delayed phases on dynamic contrast-enhanced T1WI (Fig. 1B). Additionally, a high signal intensity on diffusion-weighted imaging (DWI) and low value on apparent diffusion coefficient (ADC) map were observed (Fig. 1B). The mass was preoperatively diagnosed as hypovascular RCC. Both the CT and MRI scans showed no evidence of lymphadenopathy or metastasis. Accordingly, a partial nephrectomy without chemotherapy was performed. Papillary RCC was confirmed through pathological examination (Fig. 1C).

Following a partial nephrectomy of the allograft kidney, the patient underwent follow-up imaging at 8, 29, 41, and 60 months post-surgery. Due to concerns regarding renal toxicity related to contrast material, an MRI without contrast enhancement was used for screening. Serial imaging revealed a gradually enlarging lesion at the upper pole of the right native kidney.

Initially, the lesion was well-circumscribed and round, exhibiting a high signal intensity on T1WIs and a low signal intensity on T2WIs. Therefore, we considered it to be a hemorrhagic cyst rather than a solid tumor. During his first visit, eight months after the partial nephrecto-

Fig. 1. A 48-year-old male with papillary RCC in the transplanted kidney and TFE3-rearranged RCC in the native kidney.
A. Axial contrast-enhanced CT image reveals a 1.1 cm-sized, well-defined hypodense mass (arrow) in the transplanted kidney at the right iliac fossa (left). On axial T2-weighted magnetic resonance imaging, the mass (arrow) showed isointensity (right).
B. The mass in the allograft kidney (arrows) exhibits iso-signal intensity on a pre-contrast enhanced T1 weighted image. Dynamic contrast-enhanced MRI reveals poor enhancement during the arterial, venous, and delayed phases. The mass displays a high signal intensity on the DWI and a low value on the ADC map.
A = arterial phase, ADC = apparent diffusion coefficient, D = delayed phase, DWI = diffusion-weighted imaging, PRE = pre-contrast enhanced image, RCC = renal cell carcinoma, TFE3 = Xp11.2 translocation/transcription factor E3, V = venous phase

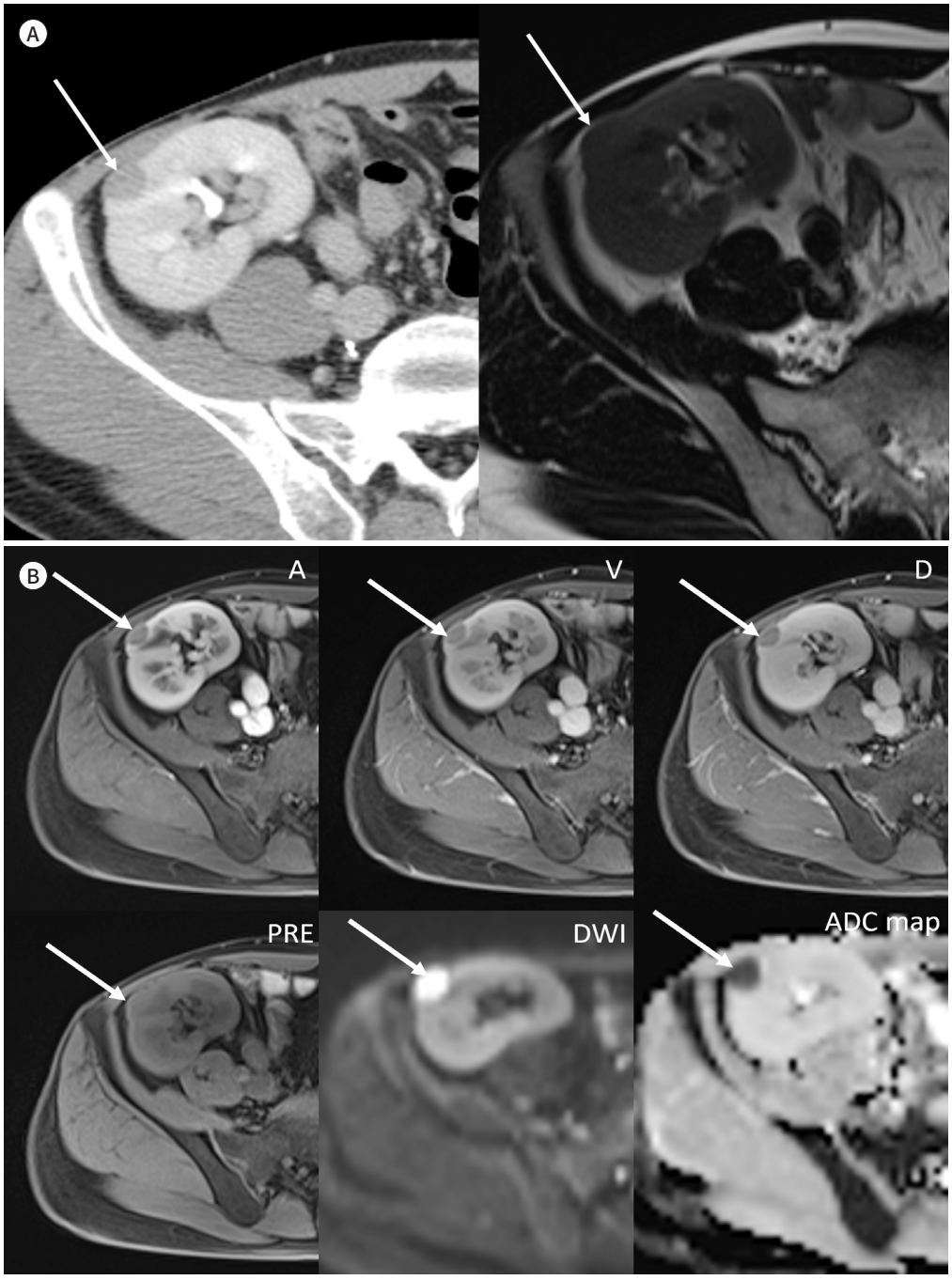

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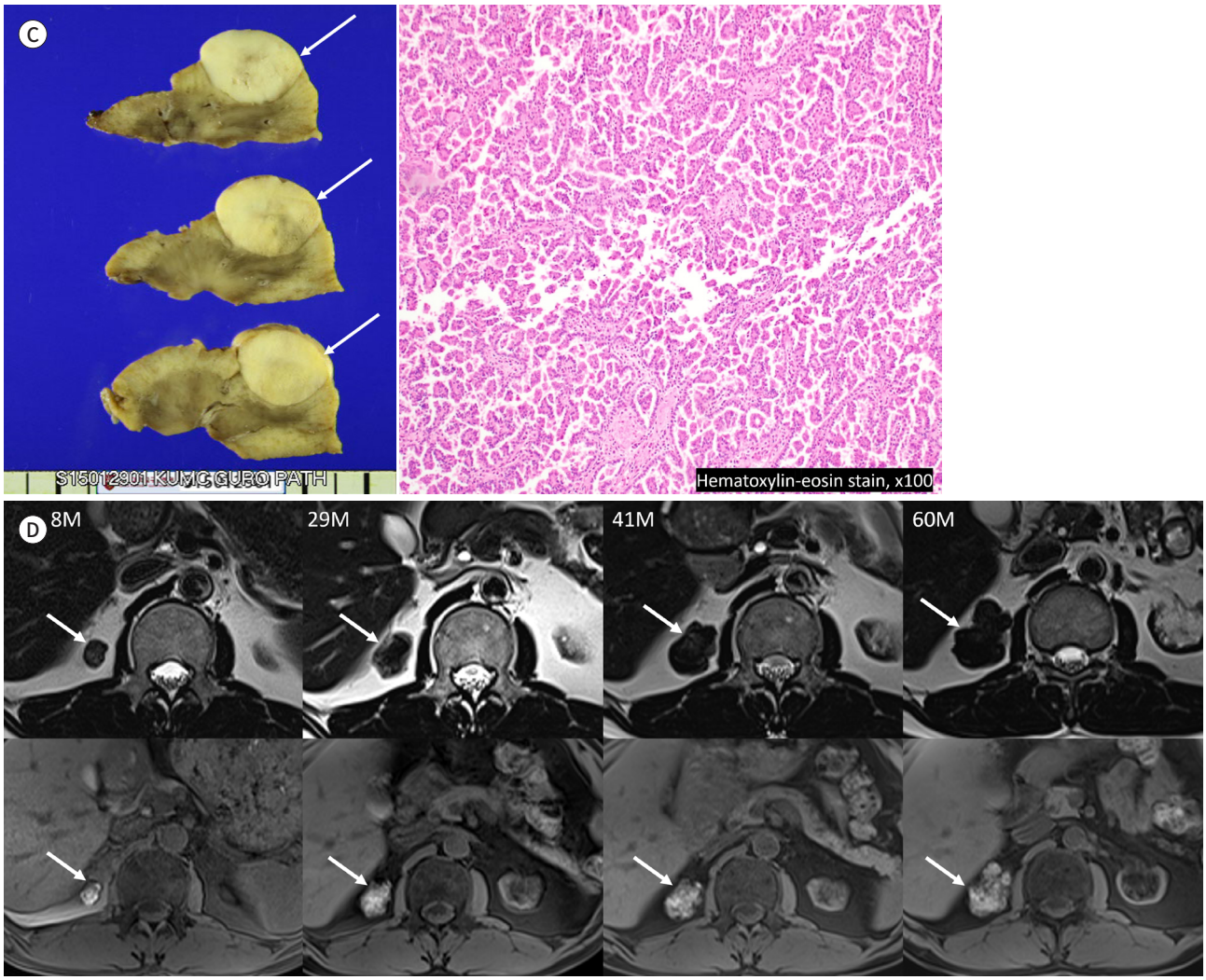
Fig. 1. A 48-year-old male with papillary RCC in the transplanted kidney and TFE3-rearranged RCC in the native kidney.
C. Gross specimen of the allograft kidney (left) exhibits a well-demarcated, whitish, bulging mass (arrows). Microscopic image with hematoxylin-eosin staining (right, × 100) of the mass reveals eosinophilic cytoplasm and sparse capillaries.
D. The mass in the right native kidney (arrows) exhibits a low signal intensity on the T2 weighted image (upper row) and a high signal intensity on the T1 weighted image with fat suppression (lower row). Serial images of 8, 29, 41, and 60 months post-surgery (from left to right, sequentially) display gradually enlarging mass from 1.5 cm → 2.7 cm → 3.3 cm → 4.3 cm. At the initial stage, the lesion is round and well-circumscribed, exhibiting a multilobulated contour in the final stage.
M = months, RCC = renal cell carcinoma, TFE3 = Xp11.2 translocation/transcription factor E3

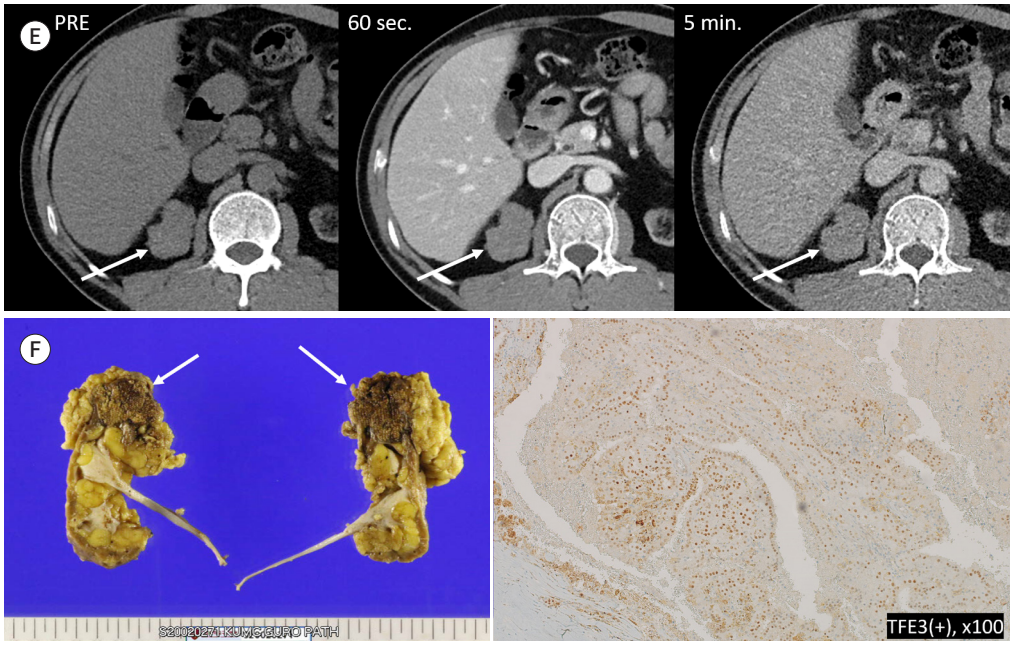



my, the lesion measured 1.5 cm; however, the last follow-up at 60 months revealed a lobulated contour and an enlargement up to 4.3 cm (Fig. 1D). Consequently, we re-diagnosed it as a hemorrhagic solid tumor, indicative of RCC.

Preoperative contrast-enhanced CT revealed a lobulated mass with mild enhancement at 60 seconds and 5 minutes following intravenous contrast injection. The Hounsfield units of the pre-enhanced, 60 seconds enhanced, and 5 minutes enhanced images were approximately 54, 67, and 70, respectively (Fig. 1E).

The patient underwent a radical nephrectomy of the right kidney. The gross specimen revealed a lobulated, yellowish mass with internal hemorrhage. Upon microscopic analysis,

Fig. 1. A 48-year-old male with papillary RCC in the transplanted kidney and TFE3-rearranged RCC in the native kidney.
E. Dynamic contrast-enhanced CT of the mass in the right native kidney (arrows) exhibits mild contrast enhancement at 60 seconds and 5 minutes following intravenous contrast injection.
F. Gross specimen of the right native kidney (left) reveals a yellowish, lobulated mass with internal hemorrhage (arrows). TFE3 immunohistochemistry of the tumor cells (right, × 100) exhibits strong and diffuse nuclear labeling.
PRE = pre-contrast enhanced image, RCC = renal cell carcinoma, TFE3 = Xp11.2 translocation/transcription factor E3, 5 min = 5 minutes following contrast injection, 60 sec = 60 seconds following contrast injection




immunohistochemical staining for TFE3 displayed positive reactivity within the tumor cells (Fig. 1F). Therefore, the final histological diagnosis was confirmed as TFE3-rearranged RCC. Due to the absence of lymphadenopathy and metastasis, the patient has been undergoing annual imaging follow-up without additional treatments. There is no evidence of recurrence or metastasis until now, three years after the surgery.

This study was approved by the Institutional Review Board of our institution, which waived the requirement for informed consent (IRB No. 2023-1941-001).

## DISCUSSION

Patients who undergo kidney transplantation have a 5- to 10-fold higher incidence of RCC than the general population. RCC predominantly involves native kidneys and rarely allograft kidneys (1). A recent study reported an overall incidence of 0.7% for RCC following KT. RCC can develop either in the native kidneys, with an incidence of 0.7%, or in the transplanted kidneys, with a lower incidence of 0.2% (2). Although its exact etiology remains unclear, immunosuppression has been implicated as one of the contributing factors (1, 2).

In the general population, clear cell RCC is the most common subtype (75%–85%), followed by papillary RCC (10%–15%) (1). Papillary RCC exhibits a higher prevalence at 44%, whereas

clear cell RCC exhibits a lower prevalence at 50% in native kidneys of KT recipients than in the general population (3). In allograft kidneys, papillary RCC accounts for 42.1%, whereas clear cell RCC constitutes 45.7%, similar to the pattern observed in native kidneys (4).

To our knowledge, only two cases of RCCs in native and allograft kidneys have been reported. One patient had metachronous RCCs in bilateral native and allograft kidneys, whereas the other had synchronous RCCs in the right native and allograft kidneys. All five previously reported RCCs were of the clear cell subtype (5, 6).

Our patient exhibited de novo papillary RCC in the allograft kidney nine years after KT. Subsequent serial follow-ups revealed the growth of another RCC in the right native kidney, confirmed as TFE3-arranged RCC, occurring five years following partial nephrectomy of the transplanted kidney.

TFE3-rearranged RCC was previously considered a member of the microphthalmia transcription factor family of translocation RCC and TFE3-altered RCC. In the 2022 WHO classification, TFE3-rearranged RCC was classified as an independent subtype and included in the "molecularly defined renal carcinomas." It is more common in children, accounting for 20%–75% of all RCC cases, whereas it is rare in adults, representing only 1%–4% of cases (7). Few cases of TFE3-rearranged RCC have been reported in the native kidneys of two children following KT (8). To our knowledge, this is the first case report of an adult with TFE3-rearranged RCC following KT.

Risk factors for TFE3-rearranged RCC include exposure to chemotherapeutic agents, such as DNA-damaging agents, alkylating agents, and topoisomerase II inhibitors. One case report suggested that immunosuppressive treatment may play a role in the carcinogenesis of TFE3-rearranged RCC (8). In our case, the patient had no history of chemotherapy and received immunosuppression with sirolimus (Rapamune) and tacrolimus (Advagraf, Tacrobell). Because only a limited number of cases of TFE3-rearranged RCC post-immunosuppression have been reported, the contribution of immunosuppressive therapy remains unclear.

The papillary RCC in the allograft kidney of our patient exhibited typical findings of papillary RCC (9). Contrast-enhanced CT revealed a well-demarcated, hypodense, nodular lesion. MRI scan revealed poor enhancement during the arterial, venous, and delayed phases, indicating hypovascularity of the tumor. The lesion exhibited hyperintensity on DWI and displayed a low value on the ADC map, indicating diffusion restriction.

In our case, the TFE3-rearranged RCC manifested as a slowly growing mass with a multilobulated contour. MRI revealed a high signal intensity on T1WI and a low signal intensity on T2WI scans, suggesting internal hemorrhage. Contrast-enhanced CT revealed mild enhancement during both the venous and delayed phases. These findings are similar to those of a previous report on TFE3-rearranged RCC in an adult patient (10).

In conclusion, we reported a rare case of sequential occurrence of papillary RCC in the allograft kidney, followed by metachronous TFE3-rearranged RCC in the right native kidney in a male patient. The TFE3-rearranged RCC revealed a multilobulated mass with internal hemorrhage on MRI. It exhibited a mild enhancement pattern during both the venous and delayed phases of CT. Notably, this represents the first case report describing de novo TFE3-rearranged RCC following KT in an adult patient.

## Author Contributions

Conceptualization, K.M.H., K.K.A.; data curation, K.M.H., K.K.A.; investigation, K.M.H., K.K.A.; writing—original draft, K.M.H., K.K.A.; and writing—review & editing, K.K.A., K.J.W., L.S.Y., C.J.W.

## Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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# 이식신장에 생긴 유두모양 신세포암종과 고유신장에 생긴 Xp11.2전위/전사인자E3-재배열 신세포암종: 증례 보고

김민혜 · 김경아* · 김정우 · 이석영 · 최재웅

고유신장과 이식신장 모두에 신세포암종이 발생하는 경우는 매우 드물며, 소수의 증례만이 영문 문헌에서 보고되었다. Xp11.2전위/전사인자E3 (이하 TFE3)-재배열 신세포암종은 성인 인구에서 드문 아형이다. 신장이식을 받은 어린이에서 TFE3-재배열 신세포암종이 소수의 증례로 보고되었으나, 어른에서 신장이식 후 TFE3-재배열 신세포암종이 보고된 증례는 없다. 저자들은 이식신장에 유두모양 신세포암종이, 고유신장에 TFE3-재배열 신세포암종이 있던 드문 증례를 영상 소견과 함께 보고하고자 한다. 고유신장에 생긴 TFE3-재배열 신세포암종은 5년에 걸쳐 천천히 자랐다. CT에서 약한 조영증강을 보이는 소엽 모양 종괴였으며, MRI에서는 T1 강조영상에서 높은 신호 강도를, T2 강조영상에서 낮은 신호 강도를 보였다.

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