ABSTRACT
Tumefactive demyelinating lesions (TDLs) are rare and specific types of inflammatory demyelinating lesions. Its clinical manifestations are nonspecific, and the imaging findings are similar to those of other intracranial space-occupying lesions, which are usually misdiagnosed as tumors or abscesses and require a pathologic examination to confirm the diagnosis. Tumefactive demyelinating lesions after kidney transplantation are even rarer. This article reports a case of TDLs after kidney transplantation. A 60-year-old female patient underwent kidney transplantation 15 years ago and took anti-rejection drugs such as tacrolimus, tacrolimus, and corticosteroids after surgery. The patient was admitted with headache and left limb weakness, and magnetic resonance imaging of the head showed multiple space-occupying lesions with surrounding edema. The patient underwent a stereotactic biopsy of the encephalopathy lesion, and postoperative pathology confirmed TDLs. She was treated with corticosteroids and discharged after the improvement of her symptoms. Here, to our knowledge, we report the first case of TDLs after kidney transplantation. We report this case to provide clinicians with useful information on intracranial demyelinating disease after kidney transplantation.

Clinical Report
A 60-year-old female patient was admitted to our hospital on March 18, 2021 for a “headache with left limb weakness and slurred speech for 1 week.” One week ago, she developed a headache without obvious inducement, which progressively worsened, with weakness and slurred speech of the left limb, no nausea or vomiting, and no limb twitching. On March 14, a brain computed tomography (CT) scan performed in our neurosurgery clinic showed hypodense shadows in the right basal ganglia and centrum semiovale and ischemic changes in the white matter region beside the anterior horn of the bilateral lateral ventricles (Fig 1). A brain magnetic resonance image (MRI) showed multiple lesions and enhancement in the brain, considering metastases with a significantly longer time (15 years) after in situ kidney transplantation (KT). Prisoners were not used in the study, and participants were neither paid nor coerced. The data conform to the Helsinki Conference and Istanbul Declaration.
She had a history of kidney transplantation for 15 years and was regularly treated with oral prednisone, tacrolimus, and cyclosporine drugs on weekdays; she had a history of hypertension for 5 years and was regularly treated with oral nifedipine sustained-release tablets drugs on weekdays. Neurologic examination showed clear consciousness, the correct answer to questions, less clear speech, equal and round pupils, sensitivity to light, the central position of the bulbs of both eyes, shallowing of the nasolabial fold on the left side, right crooked mouth, left tongue extension, grade 3 muscle strength of the left upper limb, grade 4 muscle strength of the left lower limb, deep and superficial hypoesthesia of the left limb, grade 5 muscle strength of the right limb, normal deep and superficial sensation, normal muscle tone and tendon reflexes of the bilateral limbs, and a negative Barthel sign bilaterally.

Diagnosis on Admission
Her admission diagnosis included multiple intracranial space-occupying lesions (probable metastases), post–kidney transplantation, and hypertension. On March 17, 2021, a stereotactic biopsy of the intracerebral lesion was performed under general anesthesia, and postoperative pathology showed that it was consistent with TDLs, with stellate gliosis and brain tissue degeneration and necrosis (Fig 3). Fluid replacement for dehydration, antiepileptic therapy, and hormonal therapy were given postoperatively, and the patient was discharged in improved condition. A repeated brain MRI showed that the lesions were significantly smaller than before (Fig 4). The patient’s recent renal function test (May 7, 2023) showed the following: blood urea, 12.12 mmol/L; serum creatinine, 144.3 μmol/L; normal urine output. The patient was treated with regular oral medication of prednisone 2.5 mg once daily, tacrolimus 1.5 mg twice daily, mycophenolate sodium 180 mg twice daily, and mycophenolate mofetil 0.5 g twice daily. The patient had no neurologic symptoms or positive signs at the current examination.

DISCUSSION
Formerly known as “demyelinating pseudotumors,” TDLs are relatively special immune-mediated inflammatory demyelinating lesions of the CNS that mimic brain tumors on imaging; demyelinating changes characterize pathology. Currently, TDLs are considered a rare subtype of multiple sclerosis with imaging features of solitary lesions with the longest diameter > 2 cm associated with ring enhancement, which are easily confused with brain tumors [4]. Tumefactive demyelinating lesions mainly involve the subcortical and paraventricular white matter, and the cortex can also be affected; supratentorial demyelinating pseudotumors are more common in the frontoparietal lobe and can also appear in the brainstem, cerebellum, and spinal cord. Lesions can be single or multiple [5]. A small number of lesions may involve the spinal cord because of different sites of involvement; the clinical manifestations vary, mainly manifested as substantial mass effect and...
focal neurologic deficits; there may be a headache, nausea, vomiting, trance, language retardation, paralysis, and other symptoms and signs of parenchymal damage. The occurrence and development of demyelinating lesions after KT is a very complex process, and the exact pathogenesis is thus far unknown. Currently, liver and kidney dysfunction, micronutrient deficiencies (vitamin B1, vitamin B12), hyponatremia or its rapid correction, immunosuppressants, and infections are risk factors, with osmotic stress considered the most likely cause [6].

The diagnosis of TDLs relies on imaging, clinical parameters, and biology. Histopathologic findings on stereotactic biopsy of multiple lesion areas are the gold standard to confirm demyelinating lesions. Because biopsy is not always performed in the setting of demyelinating lesions, it is essential to understand the clinicopathologic features of TDLs and malignancies. On MRI, most cases showed homogeneous low T1WI and high T2WI signals, heterogeneous low T1WI and high T2WI signals in cystic areas in the lesions, edema signals around the lesions, a certain mass effect, and mass volume not proportional to the mass effect; that is, the mass could be large, whereas the edema and mass effect were relatively mild, and the lesion was clearer on Flair sequences. On contrast-enhanced scans, the non-necrotic areas inside the lesions showed scattered nodular enhancement, ring enhancement, or no closed-rim enhancement, that is, open ring enhancement. Open loop, mass effect, and contrast enhancement are known as 3 signs on an MRI describing TDLs. Maseu et al. reported an incomplete or open-mouth sign in 70% of cases [7]. In contrast, only 1 of 32 tumors showed an open-loop pattern, and none of the 32 infectious diseases showed an open-loop pattern. Tumefactive demyelinating lesions should be differentiated from the following diseases [8].

**Brain Abscess**

The patient had a previous history of bacterial infection. Cranial CT scans showed hypodense cystic lesions with slightly higher cyst wall density than the central area. The annular cyst wall of the lesion was enhanced after enhancement, whereas the ring toward the cortex was thickened.

**Lymphoma**

The lesions are often distributed in the brain parenchyma and perivascular areas, single or multiple, arranged in sleeves around the blood vessels. Brain CT scans show focal or diffuse isodense to hyperdense masses, surrounded by mild edema, often located around the ventricles, showing significant diffuse enhancement. Magnetic resonance imaging scans showed slightly hypointense to isointense signal intensity on T1WI, iso-intense to slightly hyperintense signal intensity on T2WI, and significant diffuse enhancement on enhancement.

**Tuberculoma**

Patients usually have a history of tuberculosis exposure or have had tuberculosis, and miliary tuberculosis shows multiple spotty hyperdense lesions on CT scans with ring enhancement. Magnetic resonance imaging showed high signal intensity around T1WI but isointensity in the center, low signal intensity in the edema area outside the ring, and homogeneous or heterogeneous low signal intensity on T2WI in the granuloma area.

**Astrocytoma**

The CT scan findings of low-grade astrocytoma showed ill-defined, more homogeneous hypodense masses with mild edema bands in peripheral tissues. In contrast, pilocytic astrocytoma had well-defined borders and homogeneous enhancement on enhancement. High-grade astrocytomas with necrosis or hemorrhage show heterogeneous density with extensive edema. Magnetic resonance imaging scans showed differential signal intensity from the gray matter at T1WI lesions, enhancement of high-grade gliomas, vascular shadows supplying blood vessels, and solid parts of T2WI tumors could be hyperintense.

**Metastases**

Metastases may be located at the gray and white matter junction, often distributed in the middle cerebral artery area, and may be single or multiple lesions. The CT showed round, round low-density or slightly high-density lesions, enhanced MRI significantly enhanced, and significant edema.

Histopathology of TDLs showed perivascular lymphoid “sleeve” formation, varying degrees of myelin loss, secondary macrophage phagocytosis of myelin debris, and reactive astrogliosis. In contrast, axons were relatively preserved, and many monocytes and foamy macrophages were observed in the lesions, accompanied by obese astrogliosis. The most characteristic features are the presence of diffuse macrophage infiltration and perivascular chronic inflammatory cell infiltration. Other histologic features include Creutzfeldt astrocytes and granular mitoses and the absence of necrosis and florid microvascular proliferation, which can be used to distinguish them from other diseases [9].

The occurrence of TDLs after organ transplantation is rare. To our knowledge, there are no reports of TDLs after kidney transplantation. Wan et al. reported a case of TDLs after liver transplantation in a 45-year-old middle-aged man who underwent liver transplantation for liver failure [10]. Five years after surgery, he developed right limb weakness, and cranial MRI revealed multiple patchy lesions in the bilateral basal ganglia, cerebral peduncle, and left frontal lobe, which improved after glucocorticoid treatment and was diagnosed as TDLs. Ten years after surgery, the patient developed dizziness and diploria again, and a cranial MRI revealed a new cerebellar lesion, which resolved after retreatment with glucocorticoids. This case suggests that TDLs may be associated with autoimmune status after organ transplantation, and transplant recipients with neurologic symptoms should routinely undergo multimodal cranial MRI to improve the accuracy and timeliness of diagnosis and treatment of neurologic complications.

In our report, head MRI showed multiple lesions with mass effect, lumbar puncture excluded infectious lesions, and...
magnetic resonance spectroscopy (MRS) findings suggested demyelination (elevated Cho peak, hypoxic Lac peak) that contributed to our diagnosis. Therefore, we propose a triple test with MRI, MRS, and lumbar puncture when encountering patients with a first diagnosis of post-KT TDLs. According to our experience, once the diagnosis is confirmed, corticosteroid therapy is the main treatment, and immunoglobulin and neurotrophic drugs can be given for symptomatic treatment. Recovery, neurotrophic medicine, and functional training are important. Our patient recovered uneventfully after receiving corticosteroid therapy and other symptomatic treatments.

**CONCLUSIONS**

Clinicians should be aware of the presence of TDLs after kidney transplantation, which may be completely relieved after hormonal therapy. They should pay attention to differentiating them from CNS tumors and abscesses. Physicians should also consider the possibility of demyelinating pseudotumors in cases of acute or subacute onset, imaging findings of mass effect, and multiple forms, especially patchy, ring, or open ring enhancement, and careful history. Magnetic resonance imaging, MRS, and cerebrospinal fluid examination help confirm the diagnosis, and hormone experimental therapy or tissue biopsy are required when necessary, thereby reducing unnecessary surgical treatment and radiation therapy damage. Histopathologic findings of stereotactic biopsy specimens from multiple lesion areas are the gold standard for confirming demyelinating lesions and excluding tumors.

**DECLARATION OF COMPETING INTEREST**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

**REFERENCES**