ORIGINAL ARTICLES

Management and outcome of brain abscess in renal transplant recipients

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Abstract

Although infection is the commonest central nervous system complication following renal transplantation, brain abscess is uncommon. Over the last 11 years, five renal transplant recipients who had brain abscesses were treated by computed tomography (CT)-guided stereotactic aspiration. Three patients had a fungal abscess, one a tuberculous abscess and the other had a methicillin-resistant *Staphylococcus aureus* abscess. One patient required a craniotomy for the excision of a fungal abscess which was persistent after two CT-guided stereotactic aspirations. The survivors in this group are the patient with a tuberculous abscess who is alive and well 5 years after diagnosis, and another with a dematiaceous fungal abscess (phaeohyphomycosis). CT-guided stereotactic surgery is minimally invasive, and can safely be performed in these patients. It often leads to an aetiological diagnosis in renal transplant recipients with brain abscesses. Specific antibiotic management directed towards the causative organism rather than empirical treatment can be instituted following the procedure. Although the ultimate prognosis in these patients is bleak even with specific antibiotic therapy, an occasional patient might have a good outcome with prompt and appropriate therapy.

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Keywords: brain abscess; computed tomography guided stereotaxy; renal transplant recipients

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The kidney is the most commonly transplanted organ of the human body and neurological events in renal transplant recipients are quite common.[1] The 1-year survival of renal transplant recipients who receive a kidney from a living related donor is greater than 95%.[2 3] It has been reported that 30% of recipients have some neurological complications.[1 4–6] Central nervous system (CNS) infection is a common complication, but brain abscess is rare.[1 6]

In general, opportunistic infections by organisms such as *Listeria monocytogenes, Aspergillus fumigatus, Cryptococcus neoformans*, and *Nocardia asteroides* lead to brain abscess formation in renal transplant recipients.[1 5 7–9] There are also reports of tuberculous abscesses in such patients.[10] Management of these patients has been based on aetiology, determined in the past by open surgery or free-hand aspiration of the abscess.[6] In this article, we discuss five patients who developed a brain abscess after renal transplantation and their diagnosis and management using computed tomography (CT)-guided stereotactic techniques.

Material and methods

CT-guided stereotaxy (stereotactic biopsy or aspiration) is a minimally invasive procedure which is performed on patients who have deep-seated brain lesions, for example, located in the sensorimotor area, basal ganglia, and brainstem. Since it can be performed under local anaesthesia, it is particularly suited for high-risk patients. A head ring is fixed to the patient's head under local anaesthesia. After fixing a localiser ring (consisting of six vertical and three diagonal carbon fibre rods) to the head ring, the patient undergoes a CT scan of the brain with intravenous contrast administration. Using the scanner computer, the X and Y coordinates of the nine rods and the target/targets are determined. The patient is transferred to the 'stereotactic suite' and the localiser ring is taken off. The arc system which is set for the target using various coordinates is then fixed on to the head ring and a 'twist drill craniostomy' is made in the skull. A biopsy forceps is inserted through this hole to the predetermined depth and the wall of the abscess is taken for histopathology. Using a syringe fitted to the cannula, the abscess is gently aspirated and sent for microbial culture studies. A post-aspiration CT scan is done to confirm the site of biopsy and to check for the presence of haemorrhage, if any.[11]

We retrospectively analysed the records of all 1200 patients who underwent CT-guided stereotactic procedures in our institute between May 1987 and May 1998. During this time, 1197 patients underwent renal transplantation at our institute. We were able to identify five renal transplant recipients with brain abscesses who had also undergone CT-guided stereotactic procedures. These were carried out under local analgesia using 2% lignocaine, and purulent material from within the abscess had been sent for microbial studies. Based on microbiological studies of the pus, appropriate antibiotic therapy was instituted. Follow-up CT scans were done as dictated by clinical outcome.

Case reports

CASE 1 (TUBERCULOUS ABSCESS)

A 39 year old man who received a renal allograft 10 years ago (native kidney disease: progressive glomerulonephritis; donor: mother) was on conventional immunosuppression. This regime (published by us previously) consisted of prednisolone 2 mg/kg/day on the day of transplantation, tapered to 20 mg/day by the fourth week, and 10 mg/day by the 24th week. Azothioprine was started at 3 mg/kg/day and titrated according to white cell count.[12] This patient presented with a history of intermittent low grade fever for 3 months, dysuria for 1 month and right focal motor seizures for 3 days. CT scan showed evidence of a left frontal well-circumscribed ring-enhancing mass lesion with hypodense centre and perifocal oedema (figure 1A). He underwent a CT-guided stereotactic aspiration of the abscess which showed numerous acid-fast bacilli. He had a full course of antituberculous therapy (ATT) with tapering doses of steroids given over 6 weeks. He is alive and well 5 years after diagnosis with no neurological deficits.

CASE 2 (ASPERGILLUS ABSCESS)

A 26 year old man who had received a renal allograft 7 months ago for end-stage renal disease (native kidney disease: crescentic glomerulonephritis; donor: mother) on triple immunosuppression consisting of prednisolone 20 mg/day on the first day of transplantation, tapered to 10 mg/day after 6 months, continued for life; azothioprine 1.5 mg/kg/day, continued for life; cyclosporin commencing at 8 mg/kg/day, and tapering to 3 mg/kg/day, continued for life. This patient presented with history of generalised seizures, altered sensorium and urinary incontinence of 3 weeks duration and rapid onset of right-sided weakness for 2 days. On examination he had a Glasgow Coma Score (GCS) of 14/15 with

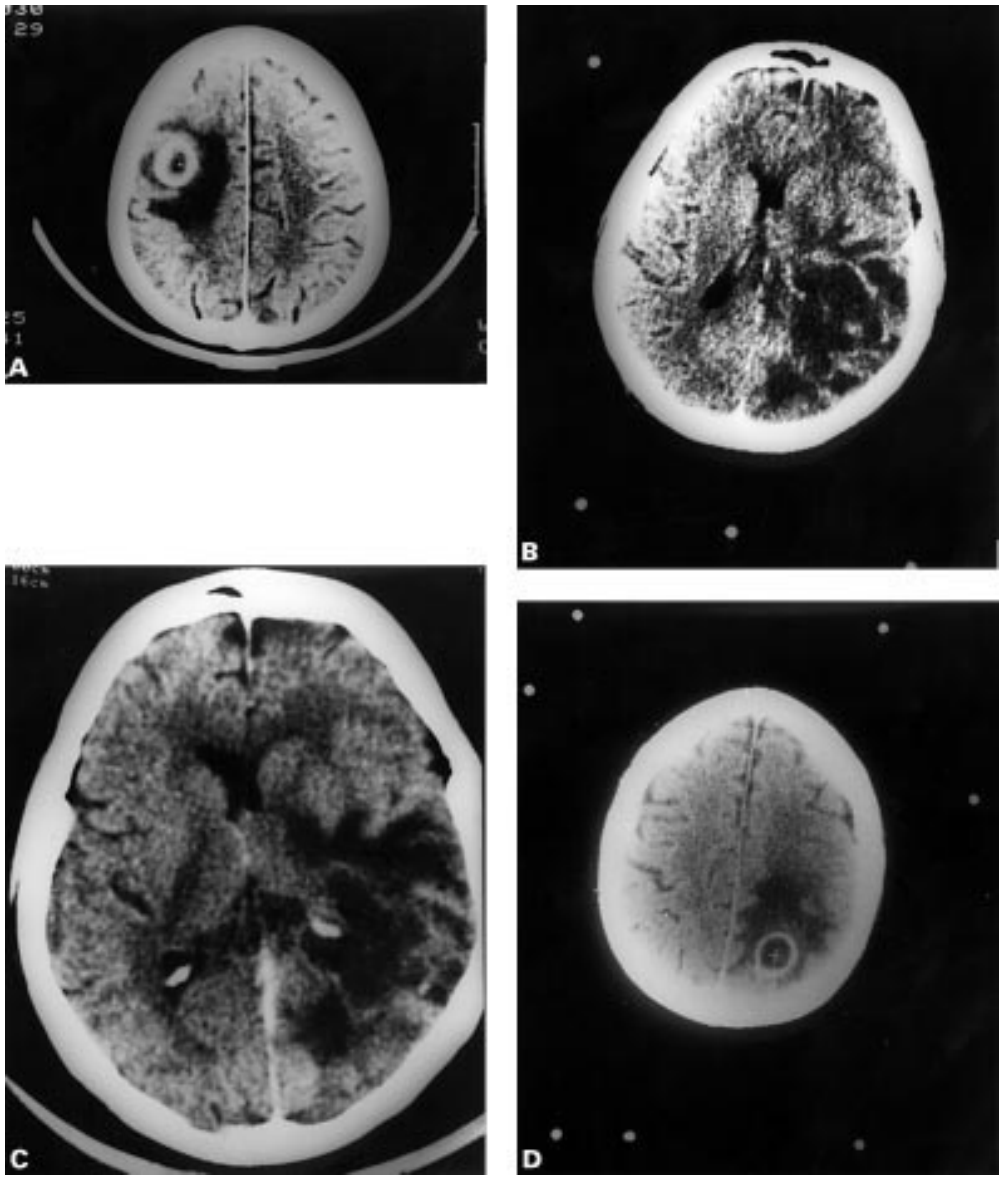

Figure 1 Contrast-enhanced CT scans of Cases 1–3 (A–C) and Case 5 (D) showing the CT morphology of brain abscesses in renal transplant recipients.

equal and reacting pupils and right hemiparesis. CT scan showed evidence of multiple enhancing lesions in the left parietal region with severe perifocal oedema and midline shift; these lesions were irregularly enhancing with hypodense centres (figure 1B). He underwent CT-guided stereotactic aspiration of one of the abscesses under local analgesia. Smears of the pus showed many septate branching fungal hyphae which were reported as *Aspergillus fumigatus*. He was started on antifungal agents (amphotericin). He also had disseminated tuberculosis with secondary infection (*Pseudomonas*) and septicaemia, which were appropriately treated (ATT, ciprofloxacin and metronidazole). Though there was a transient improvement in his motor power, he died due to disseminated infection (sepsis) 4 days after the CT-guided aspiration (8 months after transplant). It is important to note that this patient had an episode of acute rejection 2 months prior to the cerebral abscess formation, for which methyl prednisolone was given by injection at a dose of 1 g/day for 3 days.

CASE 3 (MRSA ABSCESS)

A 33 year old male had undergone renal transplantation (native kidney disease: not known; donor: unrelated) 3 months ago. He was on triple immunosuppression (as for Case 2), and presented with history of two episodes of generalised seizures. He had no neurological deficits. CT scan showed evidence of a left parietal irregularly enhancing lesion with marked perilesional oedema and midline shift (figure 1C). CT-guided stereotactic aspiration of the abscess yielded 10 ml of purulent material. Pus culture showed a heavy growth of methicillin-resistant *Staphylococcus aureus* (MRSA), sensitive only to netilmycin and vancomycin. 24 Hours following the aspiration he developed right-sided facial paresis with altered sensorium (GCS: 12/15, E4 M5 V3). Repeat CT showed no evidence of haematoma or recollection of abscess, but revealed severe cerebral oedema. He was started on anti-oedematous medications, but developed MRSA septicaemia with further worsening of his sensorium and died 3 days after the CT-guided aspiration. This patient too, had had an episode of acute rejection one month prior to the diagnosis of cerebral abscess for which methyl prednisolone was given by injection for 3 days at 1 g/day.

CASE 4 (PHAEOHYPHOMYCOSIS; A DEMATIACEOUS FUNGAL ABSCESS)

This 25 year old woman had received multiple (three) renal transplants, the first 13 years ago (native kidney disease: not known; donor: father), the second 12 years ago (donor: mother), and the third 2 years ago (donor: unrelated). She was on triple immunosuppression (as in Case 2). She had developed generalised seizures 2 weeks prior to presentation. On examination, she was highly icteric with a GCS of 15/15 and equal pupils. She had right hemiparesis. CT scan showed evidence of a left parietal abscess with surrounding oedema and midline shift. CT-guided stereotactic aspiration was done under local analgesia with fresh frozen plasma infusion, as there was derangement of the coagulation profile. Thick blood-stained purulent material was aspirated. Post-operative scan showed a small haematoma at the biopsy site which was treated with anti-oedematous measures. Smear showed septate fungal hyphae identified as 'phaeohyphomycosis' (dematiaceous fungi) and the patient was treated with amphotericin. However, she had also developed fulminant hepatitis of the B and C subtypes (positive anti-Hbc, HBsAg, and HCV antibody) with liver cell failure, cytomegalovirus infection and sepsis from multiple infected sites. She died 1 month after the CT-guided aspiration (13 years after transplant).

CASE 5 (PHAEOHYPHOMYCOSIS)

A 51 year old man had received a renal allograft 10 years ago (native kidney disease: hypertension with chronic renal failure; donor: sister). He was on conventional immunosuppression (as in Case 1). He presented with one episode of generalised seizures, headache and vomiting of 10 days duration. He had no focal neurological deficits. CT scan and magnetic resonance imaging (MRI) showed evidence of a ring-enhancing lesion with perifocal oedema in the left parietal region (figure 1D and figure 2). CT-guided stereotactic aspiration yielded 2 ml of purulent material (fig 3). Smear showed many septate branching hyphae identified as *Cladosporium* sp (phaeohyphomycosis) in culture. He was started on liposomal amphotericin and his clinical condition improved. A repeat CT scan 3 weeks later showed evidence of a persisting abscess which was again aspirated. Pus showed the same septate branching hyphae. Therefore a left parietal craniotomy and excision of the abscess was done. Following surgery, he had no new neurological deficits; he was discharged after having received 3 g of amphotericin.

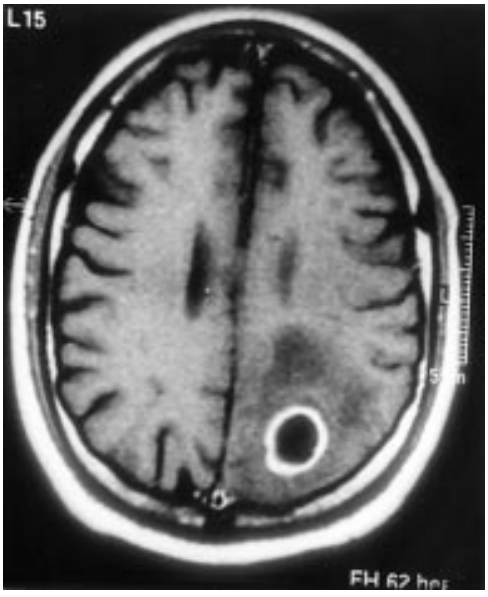

Figure 2 Axial section of the MRI (with Gado) showing a ring enhancing mass in the left parietal region with perifocal oedema (case 5).

Table 1 Presenting symptoms, duration of illness, aetiology, and outcome of brain abcess in renal transplant recipients

No	Age/sex	Symptoms	Duration (days)	Aetiology	Outcome
1	39/M	Fever	90	Tuberculous	Alive (5 yrs)
		Focal seizure	3		
2	26/M	Generalised seizures	21	*Aspergillus*	Died
		Incontinence	14		
		Hemiparesis	2		
3	33/M	Generalised seizures	1	MRSA	Died
4	25/F	Generalised seizures	14	Phaeohyphomycosis	Died
5	51/M	Generalised seizures	14	Phaeohyphomycosis	Alive (5 months)

MRSA, Methicillin-Resistant Staphylococcus Aureus

Table 2 CT morphology of abscesses in renal transplant recipients

No	Location	Single/ multiple	Character	Post-scan
1	L frontal	Single	Ring enhancing	Normal
2	L parietal	Multiple	Irreg enhancing	Normal
3	L parietal	Single	Irreg enhancing	Normal
4	L parietal	Single	Irreg enhancing	Blood clot
5	L parietal	Single	Ring enhancing	Normal

Results

The mean age of the patients in this series was 34.8 years (range 25–51 years), four men and one woman. All five patients had 'seizures' as the presenting complaint, with or without focal deficits (one had a hemiparesis). The mean duration of illness was 27 days (1–90 days). The causative organism for abscess in renal transplant recipients were tuberculous in one, fungal in three and pyogenic in one (table 1).

All five patients had a left-sided lesion (four of them had a left parietal location), indicating that, as the left carotid artery originates directly from the aortic arch, the chances of an infective emboli lodging in the carotid system is high. Three patients had an irregularly enhancing mass on post-contrast CT scan, and the other two had a ring-enhancing lesion. At follow-up, only two patients were alive (one with a tuberculous lesion, and the other a fungal lesion), and the rest had succumbed to the infection (table 2).

Three of the patients had triple immunosuppression and two conventional immunosuppression. Both patients on conventional immunosuppression are alive at the time of this report without any episode of rejection, and they did not require methylprednisolone or antithymocytic globulin. Two of the three patients who were on triple immunosuppression had one episode each of acute rejection and had been treated with parenteral methyl prednisolone (1 g/day for 3 days) prior to the development of the cerebral abscess (table 3).

Monoclonal cyclosporin assays were done in all patients on triple immunosuppression, the normal therapeutic range (our hospital values) being 150–350 μg/ml. Cyclosporin was started at 8 mg/kg/day tapering to 3 mg/kg/day and continued lifelong (table 4).

Table 3 Immunosuppressive regimes and outcome in renal transplant recipients

No	Immunosuppressive regime	Rejection	Outcome
1	Conventional regime	No	Alive
2	Triple immunosuppression	+	Died
3	Triple immunosuppression	+	Died
4	Triple immunosuppression	No	Died
5	Conventional regime	No	Alive

Table 4 Monoclonal cyclosporin assay in patients with triple immunosuppression. The normal therapeutic range in our hospital is 150–350 units. The dosage was 8 mg/kg/day tapered to 3 mg/kg/day continued lifelong

No	Cyclosporin level (μg/ml)
2	389*
3	180
4	200

*The dose of cyclosporine was reduced from 3 mg/kg/day to 2 mg/kg/day, after which the drug level fell within the normal therapeutic range.

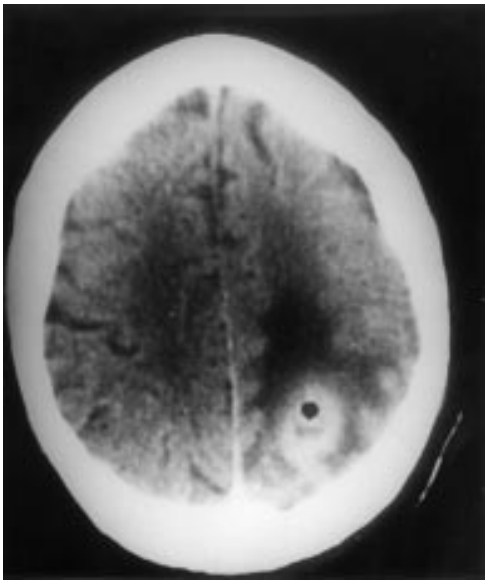

Figure 3 Post-aspiration CT scan in case 5 showing a dot of air at the biopsy site.

Discussion

CNS diseases are an important cause of morbidity and mortality in renal transplant recipients. Among the CNS complications, infection seems to be the most common,[5 10] although cerebrovascular accidents contribute substantially to morbidity and mortality.[1 4] Infections were a major cause of death (84%) of the 38 autopsied renal allograft recipients reported in 1982 from our institution.[7]

Although immunosuppression is an essential therapeutic modality for prevention of graft rejection, it introduces a great risk factor for neurologic complications, such as opportunistic infection, *de novo* malignancy, and adverse effects of immunosuppressive agents.[1] The incidence of infection in renal transplant recipients is directly related to net immunosuppressive effect achieved and the duration of time over which treatment is administered.[2]

Listeria, Cryptococcus and *Aspergillus* account for 90% of the non-viral CNS infections in renal transplant recipients. Brain abscess is most commonly caused by *Aspergillus*. *Toxoplasma, Cryptococcus* and *Nocardia* can also produce brain abscesses.[1 13] Fever, headache and convulsions are the prominent presenting symptoms. *Aspergillus* forms abscesses and granulomas by penetrating through walls of blood vessels, predisposing transplant recipients to arterial and venous thrombosis and also intracranial haemorrhage; therefore some of these patients have a 'stroke-like' presentation.[1]

Aspergillus, *Nocardia* and *Toxoplasma* usually cause CNS infection between the first and fifth month following transplant, whereas infection with *Cryptococcus* occurs at least 4 months after transplantation.[1 2] Ram Prasad *et al*,[10] from our institution, reported cerebral abscess in four out of 38 renal transplant recipients with CNS complications over a 15-year period. Fungal abscesses (cryptococcal and aspergillosis) were found in two, staphylococcal cerebral abscess in one and the other had multiple cerebral abscess of unknown aetiology.[10] However, in our case series we had a different spectra, *viz*, *Aspergillus*, tuberculosis, MRSA and two cases with 'phaeohyphomycosis', a brain abscesses caused by a rare dematiaceous fungi with melanin-like pigment on the wall of the hyphae and/or spores. The cerebral cortex is the most common site of infection, although it can involve cerebellum, brainstem or the spinal cord. Diffuse or focal areas of basilar meningitis were seen in half the autopsied cases. The abscess usually has a necrotic centre containing the fungi, and is most commonly found in frontal or parietal regions, in association with severe brain swelling.[14]

In renal transplant recipients with brain abscess diagnosed radiologically (by CT or MRI), the aetiology should be investigated in order to institute specific antibiotic management. As evident from our series of five patients, the causative organisms can be quite varied, although the CT morphology and the clinical features may be similar. Most renal transplant recipients with CNS complications are poor candidates for general anaesthesia due to multisystem involvement. Therefore, a minimally invasive procedure under local analgesia is ideal. Coagulation disorders like disseminated intravascular coagulation are more likely in renal transplant recipients with severe sepsis. Stereotactic probes, which are blunt tipped and very narrow (1.2 mm outer diameter), are not likely to cause much disruption of brain parenchyma or vessels. The rigid fixation also avoids the 'leukotome' effect of a free-hand aspiration. Therefore, the incidence of haemorrhage in the probe track is very much reduced with stereotactic techniques.

Stereotactic surgery has a very low mortality and morbidity and therefore plays an important role in the management of many intracranial lesions. It can be used for biopsy and aspiration of deep-seated lesions in eloquent locations.[15] The mortality rate for CT-guided stereotactic biopsies has been reported to be 0.6–2.6% and the morbidity 1–5.9%.[15 16] Most of the stereotactic biopsy series report a positive yield of 90–96% which helps in avoiding empiric therapy.[15–17]

Learning points

- In renal transplant recipients who develop a brain abscess, CT-guided stereotactic aspiration is an ideal minimally invasive procedure to arrive at the aetiology.
- Although the overall prognosis is grim, some patients may have a good outcome if treated promptly with appropriate and vigorous antibiotic management.

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