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A. Muhteşem Ağıldere
Aydın Kurt
Tülin Yıldırım
Sibel Benli
Nur Altınörs

MRI of neurologic complications in end-stage renal failure patients on hemodialysis: pictorial review

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A. Muhteşem Ağıldere (✉) · A. Kurt · T. Yıldırım
Department of Radiology,
Başkent University Faculty of Medicine,
Fevzi Çakmak Cad. 10. Sok. No. 45,
06490 Bahçelievler Ankara, Turkey
e-mail: amuhtesem@ixir.com
Tel.: + 90–312–2126868 ext. 1013
Fax: + 90-312-223 7333

S. Benli
Department of Neurology,
Başkent University Faculty of Medicine,
Fevzi Çakmak Cad. 10. Sok. No. 45,
06490 Bahçelievler Ankara, Turkey

N. Altınörs
Department of Neurosurgery,
Başkent University Faculty of Medicine,
Fevzi Çakmak Cad. 10. Sok. No. 45,
06490 Bahçelievler Ankara, Turkey

Abstract End-stage renal disease patients who have been on long-term hemodialysis tend to develop central nervous system complications. The most common neurologic complications in this patient group include white matter changes, cerebral atrophy, osmotic demyelination syndrome, dialysis encephalopathy, hypertensive encephalopathy, intracranial hemorrhage, infarct, sinus thrombosis, and infection. Clinical evaluation of these patients is somehow complicated and MRI is important before establishment of the therapy. The purpose of this article is to illustrate the range of MRI findings of neurologic complications in end-stage renal failure patients on hemodialysis with etiologic factors.

Keywords MRI · End-stage renal failure · Hemodialysis · Central nervous system

Introduction

It is common to see neurologic symptoms in end-stage renal disease (ESRD) patients on hemodialysis [1, 2]. Some of these problems are related to ESRD itself, and others are secondary to hemodialysis [1, 2, 3, 4, 5, 6, 7, 8, 9]. The introduction of dialytic procedures led to a significant drop in the incidence and severity of neurologic complications caused by uremia; however, some of these disturbances are unaffected by dialysis [1]. Vascular calcification secondary to hyperparathyroidism, blood-lipid disorders, systemic hypertension, chronic uremia, immune system disorders, bleeding diathesis, and fluctuations of urea, creatinine, and body water content are factors known to contribute to neurologic complications in ESRD patients [1, 2, 3, 4, 5, 6, 7, 8, 9, 10]. Aluminum has been identified as a cause of dialysis encephalopathy and cerebral atrophy, and has been removed from dialysis solutions [3, 5, 10]. Magnetic resonance imaging is of particular value in this patient group as it often enables the examiner to pinpoint the underlying cause of neurologic complications when clinical assessment is inconclusive.

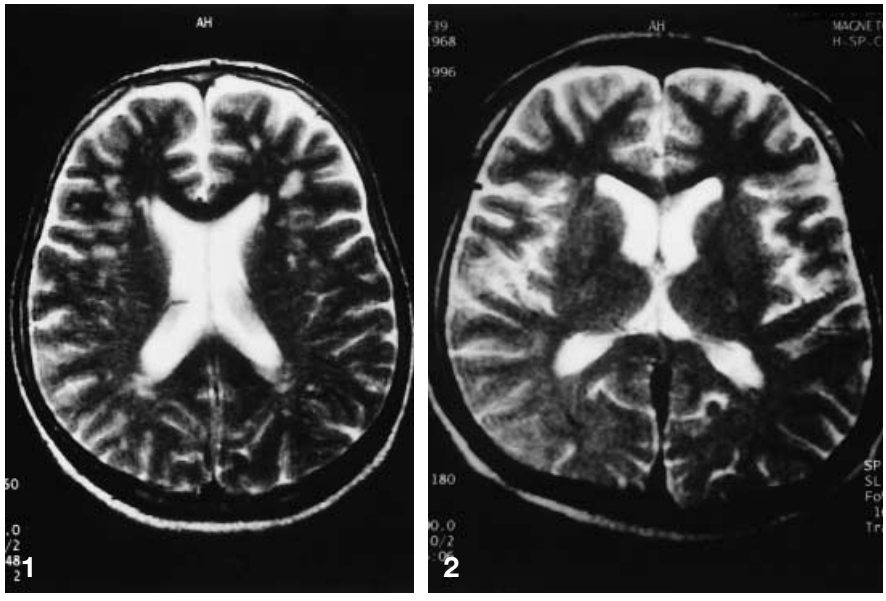


Fig. 1 Focal white matter changes in a 43-year-old man after 13 years on dialysis. Turbo spin-echo T2-weighted axial MRI reveals hyperintense areas in the periventricular and subcortical white matter

Fig. 2 Cerebral atrophy in a 28-year-old man after 3 years on dialysis. Turbo spin-echo T2-weighted axial MRI reveals cortical and subcortical atrophy

White matter changes

Focal white matter lesions are more common in hemodialysis patients (56%) than in the normal population (27%) [10]. These changes manifest as bright areas throughout the cerebral white matter on proton-density, T2-weighted, and fluid attenuated inversion recovery (FLAIR) images. They appear in various locations, particularly in the periventricular and subcortical white matter near the lateral ventricles, or in the centrum semiovale and retrotrigonal area (Fig. 1). Although no correlation has been established between these findings and the metabolic disturbances that are seen, many investigators suspect that these lesions represent a subclinical form of leukoencephalopathy [3, 4, 5]. Geissler et al. [10] found that the extent of focal white matter lesions and changes in brain metabolites reflected by MR spectroscopy do not correlate with the abnormal blood pressures observed in ESRD patients. There is a significantly lower N-acetylaspartate (NAA):creatine ratio in the gray and white matter of long-term hemodialysis patients. This drop in NAA may represent impairment of neuronal cells and neuronal damage due to dialysis, with resultant gliosis [10]. It is known that uremic intoxication causes damage to nerve tissue. Also, the accelerated atherosclerosis often observed in ESRD patients can lead to damage of cerebral vasculature and cause focal white matter changes [3]; however, it can be difficult to distinguish between toxic leukoencephalopathy and white matter changes solely on the basis of MRI findings.

Cerebral atrophy

Cerebral and cerebellar atrophy are known neurologic complications of uremia that may appear as cortical or subcortical atrophy, or as a combination of both (Fig. 2). The higher incidence of atrophy in dialysis patients has been attributed to exogenous Al $(OH)_3$ intoxication; however, even though $AI(OH)_3$ has been removed from dialysate solutions, cerebral atrophy continues to occur in this patient group [3, 5]. Hypertension has been identified as an early cause of cerebral parenchymal damage in patients on regular hemodialysis. The degree and duration of hypertension are known to be important factors in cerebral atrophy [3, 4]. Uremic intoxication, anemia, and malnutrition are also considered to contribute through failure of tissue oxygenation. Dialysis may also cause atrophy by altering tissue hydration [3]. Papageorgiou et al. showed that subcortical atrophy occurred in 80% of chronic hemodialysis patients vs 28% of ESRD patients [5].

Osmotic demyelination syndrome

Osmotic demyelination syndrome (ODS) is a known complication in chronic renal failure patients [1,8]. Endo et al. reported five ESRD patients with ODS and concluded that there was no any clinical explanation for the pathogenesis of myelinolysis in the uremic state. There were no imaging studies done on any of these patients [8]. Magnetic resonance imaging findings of an ODS patient with disequilibrium syndrome, which is a reversible early manifestation of hemodialysis, has been described [6]. Disequilibrium syndrome is usually seen

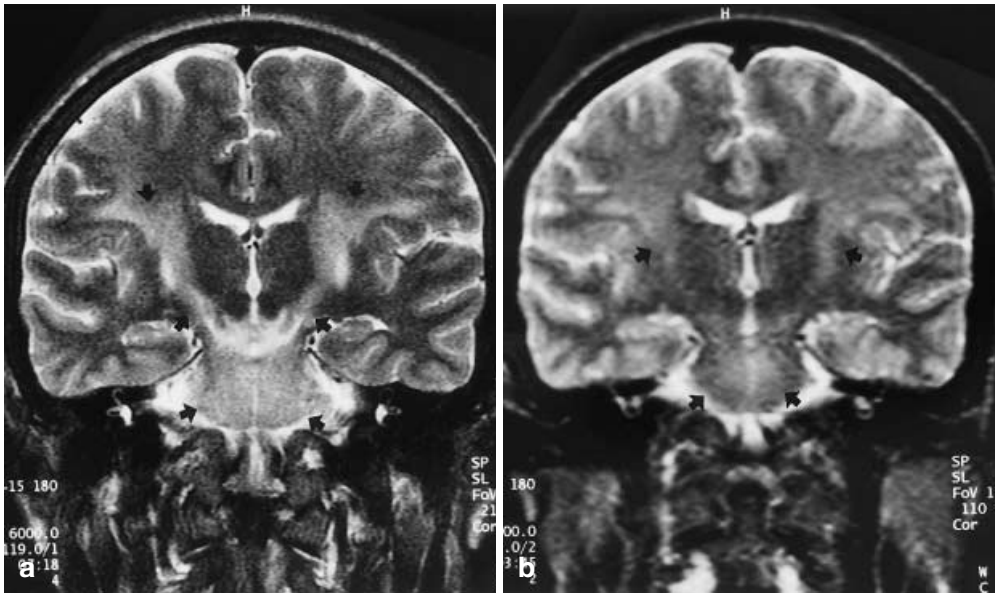


Fig. 3a, b Osmotic demyelination syndrome in a 43-year-old man on dialysis therapy who developed mental disturbance after dialysis. His symptoms decreased following conventional therapy: In **a** TSE T2-weighted coronal MRI reveals symmetric bilateral hyperintense areas which affect the pons, basal ganglia, capsula interna, and subcortical white matter *(arrows)*. In **b** TSE T2-weighted coronal MRI of the same patient 2 months later show obvious improvement *(arrows)*

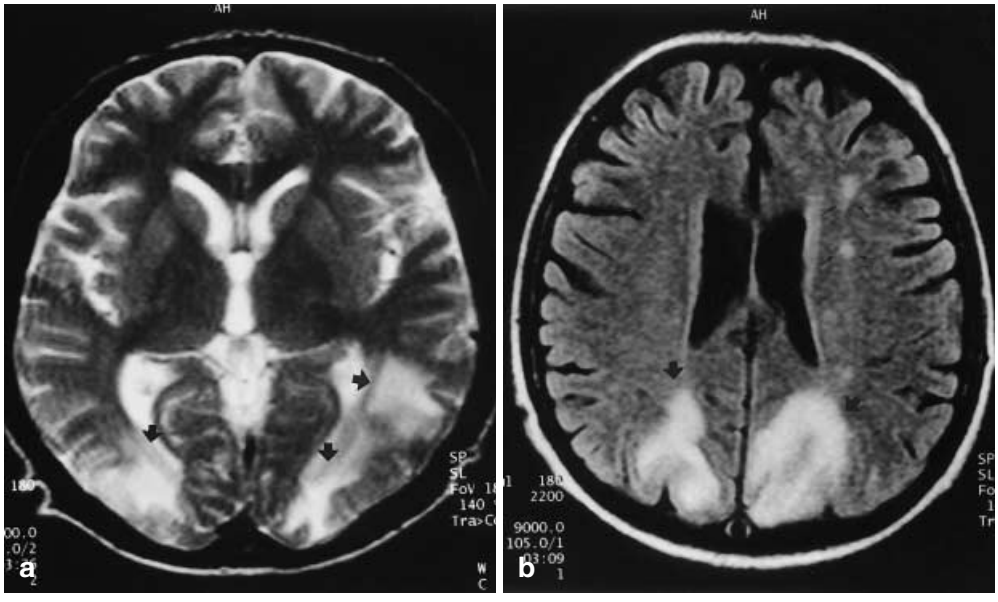
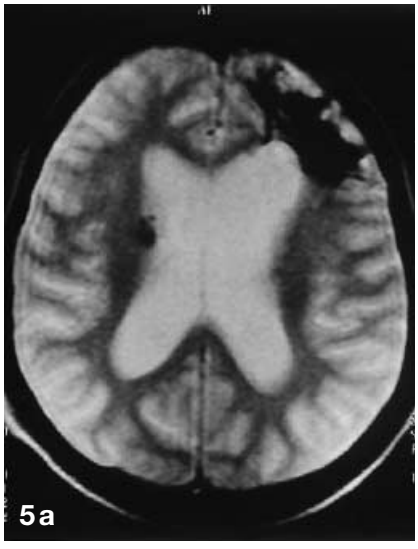


Fig. 4a, b Hypertensive encephalopathy in a 29-year-old man on dialysis therapy who developed headache as well as visual and mental disturbances during dialysis. **a** Turbo spin-echo T2-weighted axial MRI reveals bilateral occipital and posterior parietal subcortical white matter edema *(arrows)*. **b** fluid attenuated inversion recovery (FLAIR) image of another hypertensive end-stage renal disease (ESRD) patient shows edema *(arrows)* and periventricular white matter changes *(small arrows)*

during the latter portion of dialysis or in the immediate postdialysis setting, and clinical findings are similar to those found in cases of subdural hematoma, intracerebral hemorrhage, infarct, uremia, anoxia, and primary seizure [1]. In this group, cross-sectional imaging is important for ruling out intracerebral hemorrhage and infarct. In hemodialysis patients, direct osmotic effects and accumulation of metabolites may cause edema and demyelination, thus leading to ODS [1, 6, 8]. The imaging findings are similar to those seen as the other causes of ODS: symmetrical, bilateral pontine and extrapontine lesions that are hypointense on T1-weighted and hyperintense on T2-weighted images, representing edema and myelinolysis (Fig. 3) [6].

Dialysis encephalopathy

Dialysis encephalopathy (dialysis dementia) is a progressive and frequently fatal encephalopathy seen almost exclusively in patients who have been repeatedly dialyzed [1]. Aluminum is considered the causal agent in this condition, and some reports claim that removal of this compound from dialysate solutions has reduced the



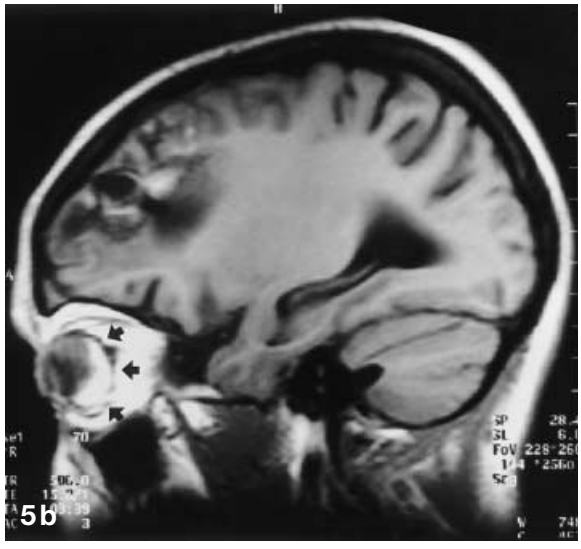
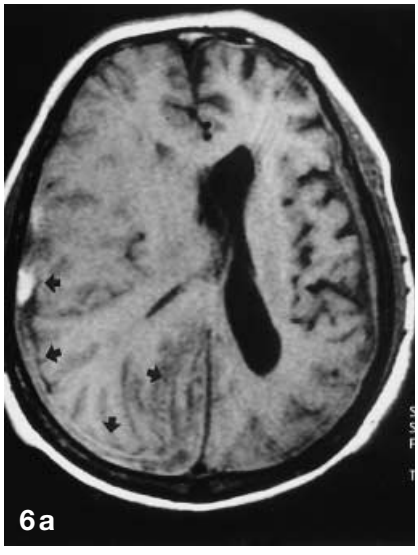


Fig. 5a, b Intraparenchymal and intravitreal hemorrhage in a 38-year-old woman who had been on dialysis therapy for 6 months and had experienced visual disturbance for 1 month. **a** Gradient-echo axial image shows hypointense areas of hemorrhage in left frontal region and in the cella media of the right ventricle. **b** A sagittal T1-weighted SE image demonstrates retinal detachment *(arrows)*, and left frontal chronic hemorrhage with hypo–hyperintense areas



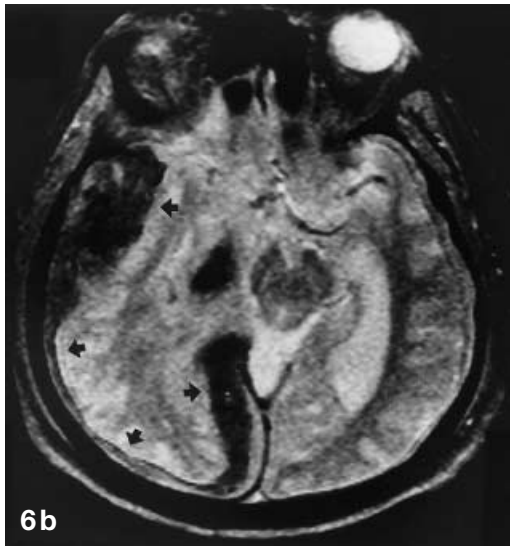
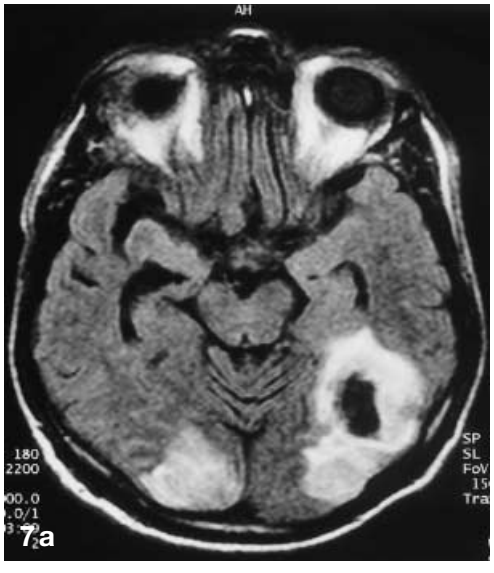


Fig. 6a, b Interhemispheric subdural hematoma in a 69-year-old hemodialysis patient. **a** Axial T1-weighted SE image demonstrates obvious midline shift to left with right iso-hyperintense interhemispheric subdural hematoma *(arrows)*. **b** Gradient-echo image reveals hypointense appearance of the right interhemispheric subdural hematoma *(arrows)*



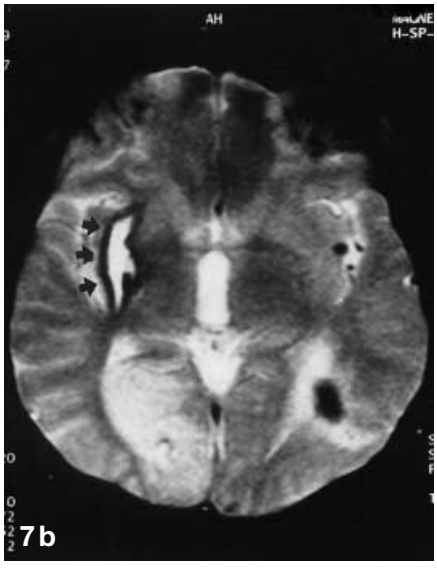


Fig. 7a, b Infarct and hemorrhage in a 48-year-old ESRD patient who developed sudden visual loss after 1 year of dialysis therapy. **a** A FLAIR image shows acute infarct in the left posterior parietal region. **b** Gradient-echo axial image demonstrates right occipital–posterior parietal and left posterior parietal acute infarcts with hemorrhage in the left, and chronic hematoma in the right external capsule and putamen with hypointense rim *(arrows)*

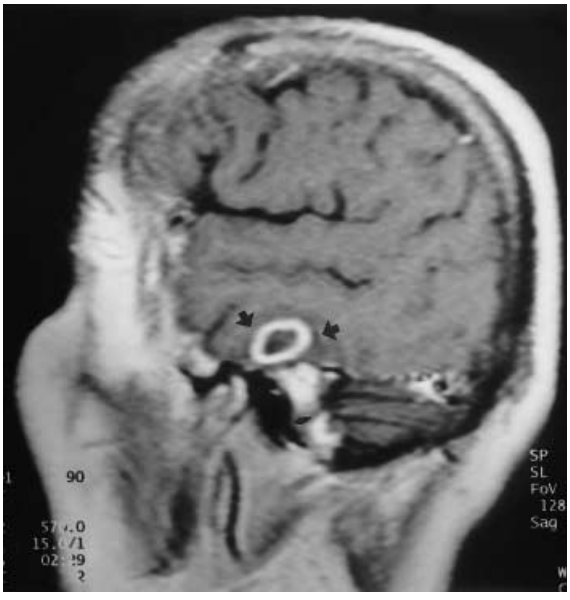


Fig. 8 Staphylococcal abscess in a 44-year-old man, who was on hemodialysis for 3 years, and who was admitted with headache and fever. Sagittal postcontrast T1-weighted SE image shows edema in the right temporal lobe with ring enhancement *(arrows)* and mastoid cells opacification due to mastoiditis

incidence of this form of dementia [2, 10]. A study done in the Nashville, Tennessee (USA), area is, to our knowledge, the only investigation of the incidence of dialysis dementia that has looked at a large group of sporadic cases. The reported incidence was 5 %, and this figure remained unchanged after aluminum was eliminated from the dialysate solutions [11]. As well, dialysis centers that use aluminum-free dialysis material have reported that they still encounter dialysis encephalopathy [1, 10]. Dialysis dementia is thought to be caused by alterations of metabolic state associated with ionic changes and impaired synaptic function [2]. Conventional imaging techniques yield no imaging findings specific to patients with this condition. An MR spectroscopy investigation of patterns of cerebral metabolites in dialysis patients found elevations of choline, a major osmotic regulator, only in the gray matter. This is in line with the fact that most histopathologic changes in dialysis-induced encephalopathy are detected in cortical and subcortical gray matter in the brain [10]. Diffusion-weighted MRI techniques are being researched as a means of assessing dialysis encephalopathy.

Hypertensive encephalopathy

Hypertensive encephalopathy is an acute neurologic disorder characterized by a sudden rise in blood pressure, and is a frequent finding in ESRD patients. The syndrome is usually reversible if the hypertension is treated early. Malignant hypertension can lead to renal failure, and secondary hypertension can also develop in patients who have underlying renal disease [1, 3, 4]. Occipital lobe edema is the most significant radiologic finding (Fig. 4). Additionally, diffuse swelling and abnormal intensity in the basal ganglia, brainstem, and cerebellum may be seen. Many of these abnormalities resolve with control of blood pressure [12]. With appropriate treatment of hypertensive encephalopathy, most ESRD patients do not develop intracranial hemorrhage or infarction.

Intracranial hemorrhage

Hemodialysis patients are at greater risk of bleeding due to the uremic bleeding tendency and to the systemic anticoagulant therapy they receive (Figs. 5, 6, 7) [1, 9, 13]. The pathophysiology of the bleeding diathesis of uremia is complex, and is only partially understood [9]. Anemia is an important factor, and defective platelet adhesion has also been associated with uremia. Inadequate control of hypertension and disseminated intravascular coagulation are additional risk factors [9, 13]. Hemorrhage may be intraparenchymal or subdural, with known intensity properties. Gradient-echo sequences allow the examiner to delineate small hemorrhagic foci which are often not visible on CT [14]. Before hemorrhage can be attributed to uremia, other causes of intracranial hemorrhage seen in patients without kidney disease must be considered, particularly including hemorrhagic infarction, hypertensive hemorrhage, and hemorrhage due to vasculitis. Conventional angiography can be used in some cases with known restrictions of contrast agents in this particular patient group with kidney problems. Magnetic resonance angiography allows the examiner to rule out vascular malformations in these patients.

Cerebral ischemia and infarction

Cerebral infarction and ischemia are other neurologic complications in ESRD patients [1]. In uremia, high serum lipid levels, vascular calcification, hyperparathyroidism, and arterial hypertension contribute to arterial damage [3]. Generalized atherosclerosis manifested in carotid and coronary arteries [15] leads to altered cerebral blood flow [1, 3] and is a potential source for cerebral emboli (Fig. 7).

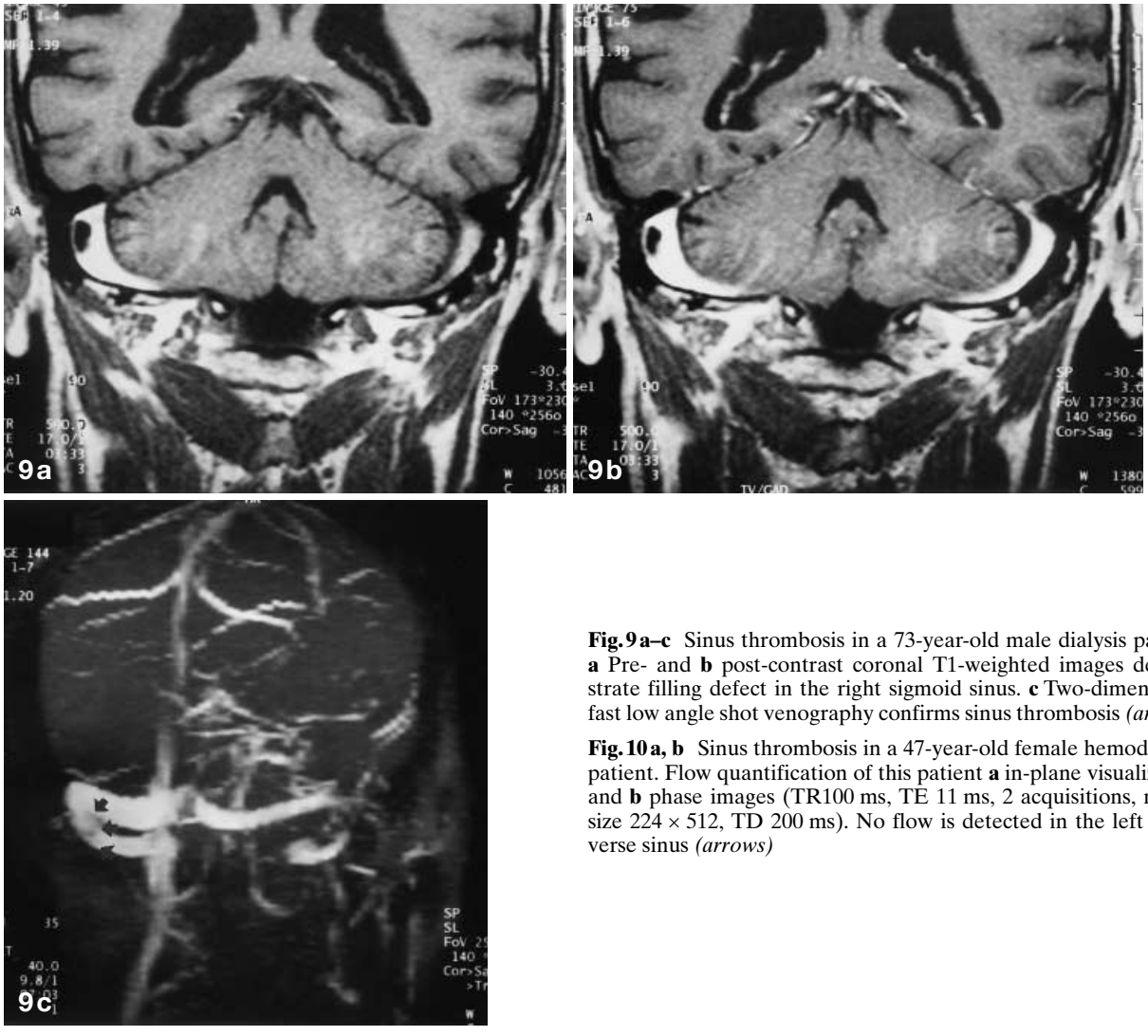
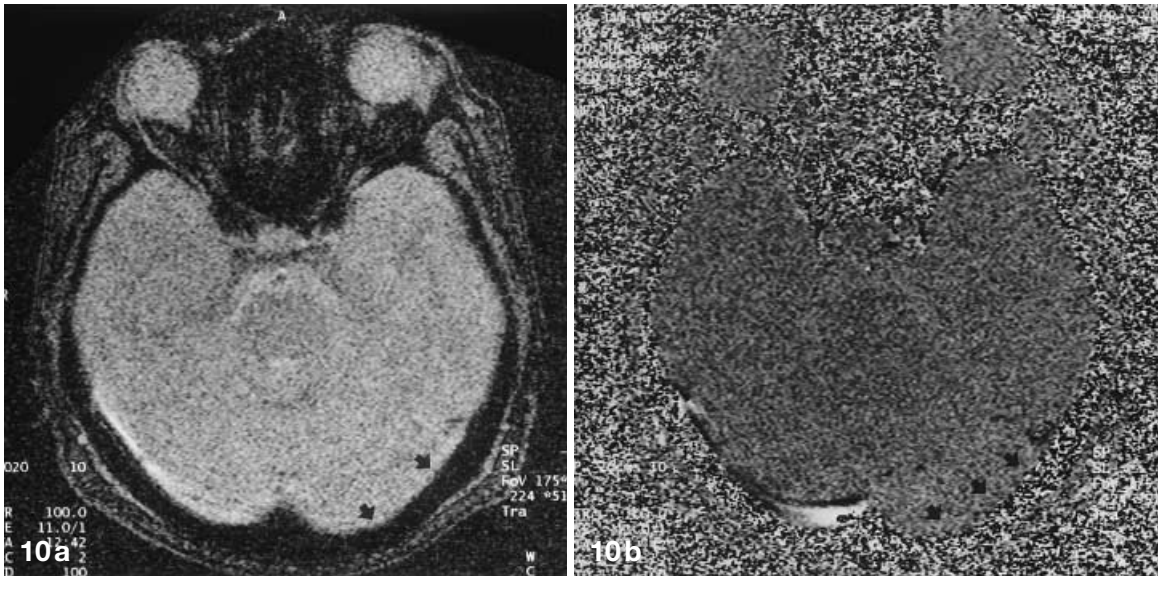


Fig. 9 a–c Sinus thrombosis in a 73-year-old male dialysis patient. **a** Pre- and **b** post-contrast coronal T1-weighted images demonstrate filling defect in the right sigmoid sinus. **c** Two-dimensional fast low angle shot venography confirms sinus thrombosis *(arrows)*

Fig. 10 a, b Sinus thrombosis in a 47-year-old female hemodialysis patient. Flow quantification of this patient **a** in-plane visualization and **b** phase images (TR100 ms, TE 11 ms, 2 acquisitions, matrix size 224 × 512, TD 200 ms). No flow is detected in the left transverse sinus *(arrows)*



Infection

Infectious complications are common and can be lethal in uremic patients on hemodialysis. In these individuals polymorphonuclear leukocytes are known to function poorly (Fig. 8). Iron overload, elevated levels of intracellular calcium, and hemodialysis treatment are known to contribute to infection. Uremic toxins that accumulate in the serum of uremic patients also inhibit the nonspecific immune system. In addition, uremic patients have deficient specific immunity, with T-lymphocyte deficiency response and a depressed specific antibody response [7].

Sinus thrombosis

Conditions such as infection, which predispose patients to sinus thrombosis, are common in ESRD patients and can lead to occlusion of central nervous system venous drainage [1]. This occlusion easily leads to cerebral ischemia and infarction. Magnetic resonance venography and flow quantification techniques are useful in the diagnosis and follow-up of this patient group. (Figs. 9, 10) [16, 17].

Conclusion

Neurologic evaluation of ESRD patients on hemodialysis is difficult because of the broad spectrum and complexity of neurologic complications in this group. Prompt diagnosis is essential, and the use of MRI in combination with new and conventional imaging methods is very helpful. In addition to spin-echo and FLAIR, gradient-echo techniques can be added to rule out hemorrhage in these patients. Magnetic resonance venography and flow-phase images can be useful for assessing sinus patency. Diffusion MRI shows infarcts earlier than other sequences. This method needs to be studied in more detail to determine its diagnostic value, particularly in dialysis encephalopathy. Proton MR spectroscopy may be useful for monitoring metabolic alterations in the brain due to chronic dialysis.

References

1. Raskin NH (1995) Neurological complications of renal failure. In: Amino MJ (ed) Neurology and general medicine, 2nd edn. Churchill Livingstone, New York, pp 311–313
2. Burn DJ, Bates D (1998) Neurology and kidney. J Neural Neurosurg Psychiatry 65: 810–821
3. Savazzi GM (1988) Pathogenesis of cerebral atrophy in uraemia. Nephron 49: 94–103
4. Savazzi GM, Cusmano F, Bergamaschi E, Vinci S, Allegri L, Garini G (1999) Hypertension as an etiopathological factor in the development of cerebral atrophy in hemodialyzed patients. Nephron 81: 17–24
5. Papageorgiou C, Ziroyannis P, Vathylakis J, Grigerladis A, Hatzikonstantinou V, Capsakalis Z (1982) A comparative study of brain atrophy by computerized tomography in chronic renal failure and chronic hemodialysis. Acta Neurol Scand 66: 378–385
6. Ağıldere M, Benli S, Erten Y, Coşkun M, Boyvat F, Özdemir N (1998) Osmotic demyelination syndrome with a disequilibrium syndrome: reversible MRI findings. Neuroradiology 40: 228–232
7. Cohen G, Haag-Weber M, Horl WH (1997) Immune dysfunction in uremia. Kidney Int Suppl 62: 79–82
8. Endo Y, Oda M, Hara M (1981) Central pontine myelinolysis. Acta Neuropathol 53: 145–153
9. Weigert AL, Schafer AI (1998) Uremic bleeding: pathogenesis and therapy. Am J Med Sci 316: 94–104
10. Geissler A, Frund R, Kohler S, Eichhorn HM, Kramer KB, Feuerbach S (1995) Cerebral metabolite patterns in dialysis patients: evaluation with H-1 MR spectroscopy. Radiology 194: 693–697
11. Fraser CL (1992) Neurologic manifestations of the uremic state. In: Arieff AI, Griggs CR (ed) Metabolic brain dysfunction in systemic disorders, 1st edn. Little, Brown, New York, pp 139–166
12. Schwartz RB, Jones MK, Kalina P et al. (1992) Hypertensive encephalopathy: findings on CT, MR imaging, and SPECT imaging in 14 cases. AJR 159: 379–383
13. Castillo R, Lozano T, Escolar G, Revert L, Lopez J, Ordinas A (1986) Defective platelet adhesion on vessel subendothelium in uremic patients. Blood 68: 337–342
14. Kuhn S, Reith W, Ertl-Wagner B, Elste V, Sartor K (1999) Comparison of computer tomography and magnetic resonance imaging in the diagnosis of acute intracerebral hemorrhage. Radiologe 39: 855–859
15. Toshiyuki Uehara, Masayasu Tabuchi, Etsuro Mori (1999) Risk factors for silent cerebral infarcts in subcortical white matter and basal ganglia. Stroke 30: 378–382
16. Vogl TJ, Bergman C, Villringer A, Einhaupl K, Lissner J, Felix R (1994) Dural sinus thrombosis: value of venous MR angiography for diagnosis and follow-up. AJR 162: 1191–1198
17. Tsuruda JS, Shimakawa A, Pelc NJ, Saloner D (1991) Dural sinus occlusion: evaluation with phase sensitive gradient-echo MR imaging. AJNR 12: 481–488