CT AND MR FINDINGS IN CENTRAL PONTINE AND EXTRAPONTINE MYELINOLYSIS - A STUDY OF TWO PATIENTS

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ABSTRACT

Central pontine and extrapontine myelinolysis is a distinctive clinical syndrome and has characteristic CT and MR features. We describe two patients who presented with nasopharyngeal carcinoma, severe hyponatremia, and had quick correction of hyponatremia. Low T1 and high T2 signal alterations were seen in the basal ganglia and caudate nuclei in both patients whilst one of them had concommitant ventrolateral thalami and central pontine region involvement. Neurologic recovery was good in one case, and initially seen in the other patient before death resulted from septicaemia. Peripheral enhancement of the basal ganglia and caudate nuclei was seen in one patient, which we believe is a new feature.

Keywords: brain stem, magnetic resonance; degenerative brain disease; demyelinating disease; hyponatremia; extrapyramidal disease

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INTRODUCTION

Central pontine myelinolysis (CPM) was first described by Adams et al in 1959[1]. It is most often found in patients with a history of alcoholism and malnourishment[1-3], and also in patients with electrolyte abnormalities, especially rapidly corrected hyponatremia[2-11]. Typical clinical features include spastic quadriparesis and pseudobulbar palsy. It is a condition characterised by symmetrical loss of myelin in the central pons, spreading centrifugally. In severe cases, necrosis and cavitation may be seen, and extension to tegmentum and midbrain can occur. When it occurs sometimes in extrapontine regions, it is termed extrapontine myelinolysis (EPM), notably in the basal ganglia, thalami, cerebral and cerebellar gray-white matter junctions. CPM and EPM may occur alone or in conjunction[12].

CASE REPORTS

Case 1

A 49-year-old man, with recent history of extensive nasopharyngeal carcinoma, base of skull and intracranial invasion, was given radiotherapy for five days in the preceding week before admission. He presented with vomiting and abdominal distension for a day, obtundation for 3 days, and was admitted to hospital in late February 1995.

On examination, the patient was obtunded and had low grade fever. Vital signs were normal. Abdomen was soft but distended. No focal neurological signs were present.

Laboratory findings revealed normal haemoglobin level, raised white blood count (17.4 x 10^9/L); normal serum glucose; severe hyponatremia (serum sodium 95 mmol/L), normal serum potassium; mildly raised serum urea (7.4 mmol/L) and creatinine (165 umol/L) levels; low serum and urine osmolality (209 mmol/kg [range 275-305], 274 mmol/kg [range 500-1200], respectively), very low urine sodium content (5 mmol/L), consistent with syndrome of inadequate antidiuretic hormone secretion and mild dehydration; hypopituitarism (undetectable serum LH, ACTH and TSH levels, FSH1.1 IU/L [range 1.2-8.1], testosterone 1.8 nmol/L [range 10.4-34.7], PRL 20.2 ug/L [range 5-27.7], total T4 144.1 nmol/dL [range 59.3-154.8], free T4 18.0 pmol/L [range 10.3-31]). He was started on steroids immediately. Abdominal radiograph showed paralytic ileus, secondary to electrolyte imbalance. Chest radiograph showed basal pneumonia. Urine culture grew enterococcus, which responded to intravenous antibiotics within 2 weeks.

Vigorous sodium replacement with hypertonic and normal saline, together with fluid restriction converted the serum sodium to 131 mmol/L within 2 days, a rise of 18 mmol/L per day. Initial serum urea and creatinine rises were corrected shortly. Continued drowsiness prompted early CT brain scanning which was normal. The patient recovered consciousness on day 7 for a day but was not oriented or responsive. Thereafter, drowsiness set in again.

Clinical signs of extrapyramidal and brain stem dysfunction were exhibited 13 days after admission, with neck stiffness, decerebrate posture, quadriparesis, limb hypertonicity, lower limb hyporeflexia, mastication movements and negative Doll's eye reflex.

Brain MRI on day 15 showed symmetrical changes of swollen caudate and lenticular nuclei, with low T1 and T2 signals. Similar signal change was noted in lateral aspect of the thalami (Figs 1a and b) and also in the centre of the pons (Figs 2a and b). Faint enhancement was seen at the periphery of the abnormal signal regions (Figs 1c and 2c). The nasopharyngeal carcinoma had invaded the base of the skull and superior clivus, with encasement of the right intrapetrous carotid artery. Sellar involvement accounted for panhypopituitarism.

Neurological improvement occurred, starting at the 8th week of admission. The patient became conscious, was able to obey simple commands and move his limbs. However, the patient developed bilateral deep vein thrombosis, and perished at the 17th week after admission, from methicillin resistant *Staphylococcus aureus* septicaemia.

Case 2

A 48-year-old man, with past history of nasopharyngeal carcinoma diagnosed in 1985, 11 years ago, had previous radiotherapy. Neck recurrence the following year was treated with neck dissection. He was well till February 1995, when liver metastasis was detected on follow-up CT scan of the abdomen.

He was admitted to hospital in late March 1995, for change

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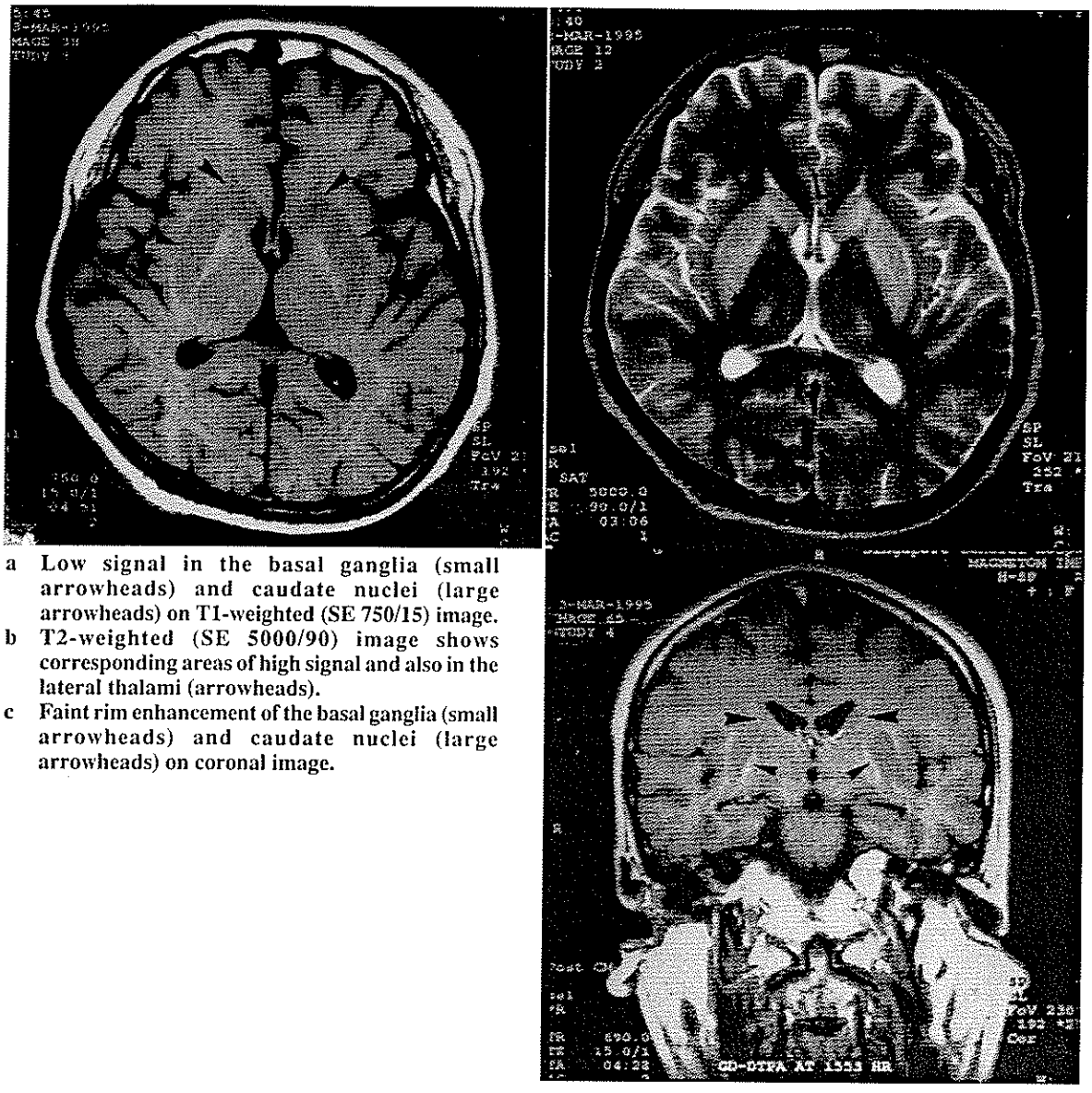
Fig 1 – Case 1: Cranial MRI examination performed 15 days after admission.



a Low signal in the basal ganglia (small arrowheads) and caudate nuclei (large arrowheads) on T1-weighted (SE 750/15) image.
b T2-weighted (SE 5000/90) image shows corresponding areas of high signal and also in the lateral thalami (arrowheads).
c Faint rim enhancement of the basal ganglia (small arrowheads) and caudate nuclei (large arrowheads) on coronal image.

in mentation and vomiting, where he was found to be severely hyponatremic (serum sodium 102 mmol/L), low serum potassium (3.2 mmol/L), with low serum and urine osmolality (250 mmol/kg [range 275-305], and 415 mmol/kg [range 500-1200], respectively), consistent with syndrome of inappropriate antidiuretic hormone syndrome. Mentation improved for a day, after a two-day intravenous hypertonic and normal saline replacement of serum sodium to 126 mmol/L (increase of 12 mmol/L per day), shortly followed by reversal back to a semiconscious state. There was limb hypertonicity and hyporeflexia. Lumbar puncture was normal. Blood culture was negative.

Immediate CT brain scan did not show any low attenuation areas. CT scan of the post nasal space was normal. MRI brain revealed T1 hypointensity and T2 hyperintensity in the basal ganglia and caudate nuclei (Fig 3b). The pons, thalami, cerebral and cerebellar cortex were not involved. No contrast medium was given. Subsequent CT showed symmetrical hypodense basal ganglia and caudate nuclei (Fig 3a).

Only in the fourth week of hospital stay, did the mental state improve with ability to obey simple commands, and spontaneous vocalisation. Resting tremor in the hands improved with methyldopa. He was able to walk subsequently, and transferred to a rehabilitation hospital after 7 weeks.

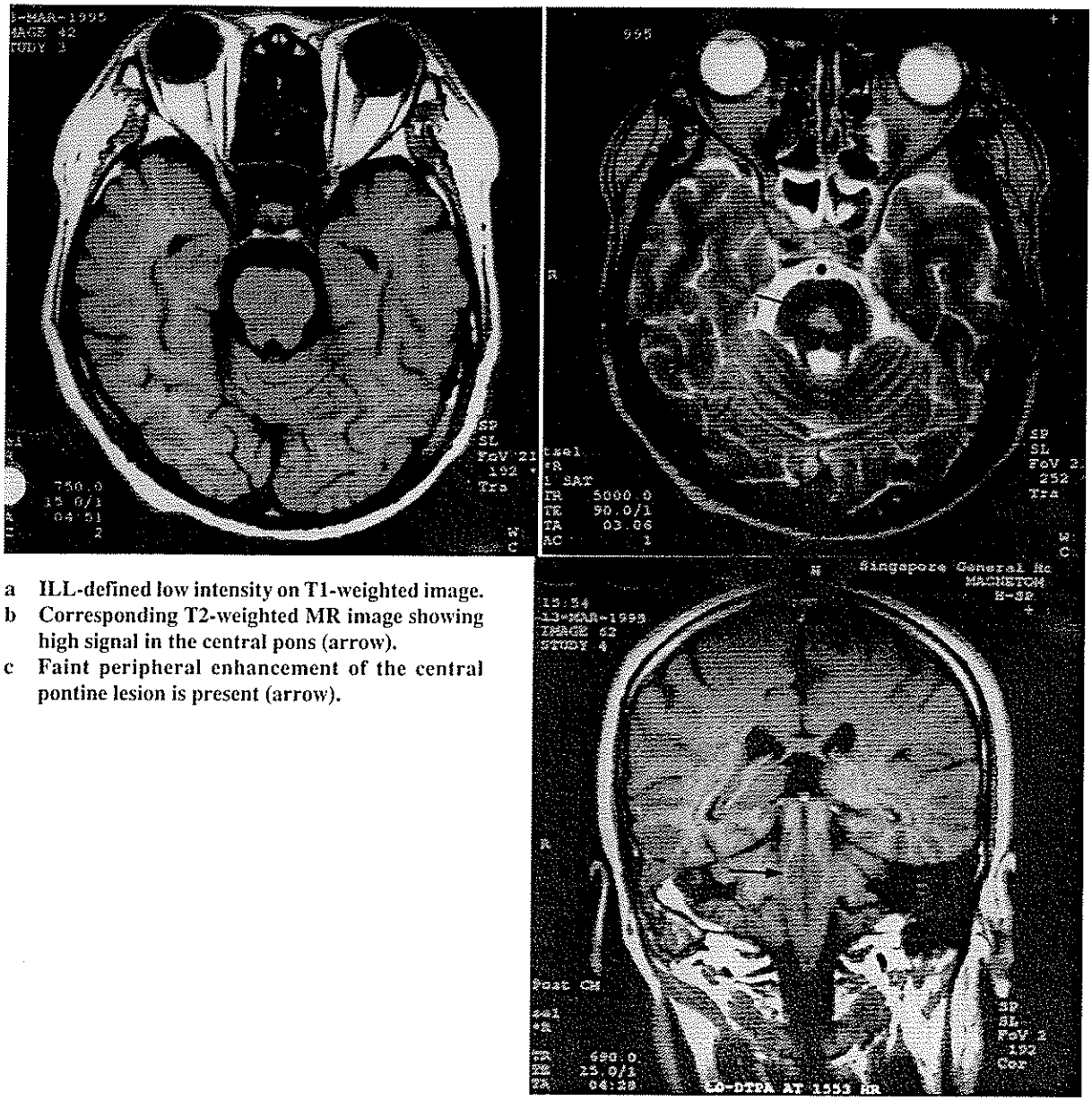
DISCUSSION

Central pontine and extrapontine myelinolysis is also known as osmotic myelinolysis. It is a demyelinating disease classically occurring in alcoholics, malnourished and debilitated adults[1]. A variety of other conditions in which CPM and EPM have been reported in association with, include chronic renal failure, hepatocellular dysfunction, dehydration, diabetes mellitus, syndrome of inappropriate antidiuretic hormone secretion, and electrolyte imbalances especially hyponatremia with rapid correction of hyponatremia[2-11].

CPM is more common than combined CPM and EPM, or isolated EPM. In a study by Gocht and Colmant[12] on 58 cases, 27 had CPM alone, 18 had combined CPM and EPM, whilst 13 presented with EPM.

The postulated mode of osmotic injury to the endothelium from rapid rise of serum sodium is the release of myelinotoxic factors and/or production of vasogenic oedema, causing osmotic

Fig 2 - Case 1: Characteristic central pontine signal alterations, with sparing of the longitudinal fibres of the descending corticospinal tracts and peripheral pons.



a ILL-defined low intensity on T1-weighted image.
b Corresponding T2-weighted MR image showing high signal in the central pons (arrow).
c Faint peripheral enhancement of the central pontine lesion is present (arrow).

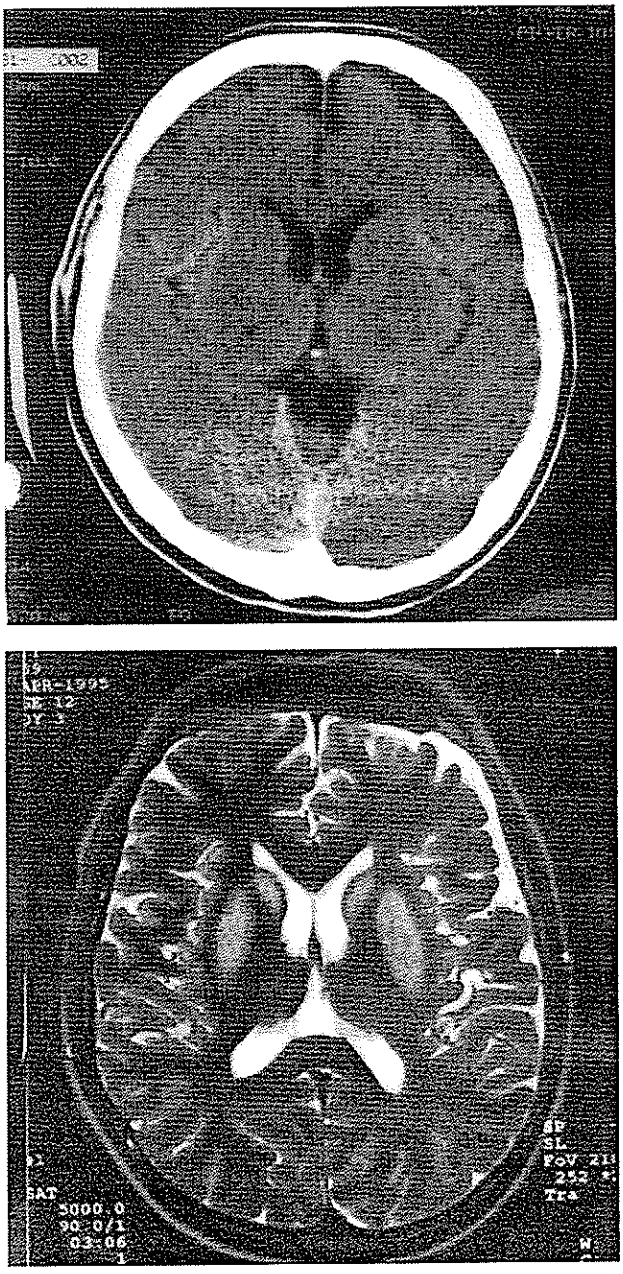
stress, against which a debilitated patient may be unable to generate protective cerebral mechanisms[3].

The treatment of hyponatremia is controversial: some authorities warn that severe hyponatremia has a high mortality rate unless it is corrected rapidly, and others have cautioned that rapid correction causes central pontine myelinolysis. Central pontine myelinolysis has developed after patients presented with severe hyponatremia (less than 106 mmol/L)[4] and had rapid correction of hyponatremia (greater than 18 mmol of sodium per 24 hours, sometimes as slow as 10 mmol per 24 hours or 21 mmol per 48 hours)[7]. When correction proceeded more slowly, patients had uneventful recovery. Another study revealed that water restriction and diuretic cessation produced no cases of CPM or EPM, whilst correction with either slow or fast normal saline or hypertonic saline infusion in 3 cases of hyponatremia resulted in fatalities[6]. Therefore overcorrection of hyponatremia is to be avoided.

In osmotic myelinolysis, an early improvement in hyponatremic encephalopathy occurs, followed by an acute brainstem dysfunction with typical neurological features - severe spastic tetraplegia, cranial nerve palsies, pseudobulbar palsy, occurring 3 to 10 days after correction of hyponatremia. Progressive neurologic deficits result in an impaired level of consciousness. Seizures, "locked-in" syndrome and coma may ensue. The condition is usually fatal within 2 to 3 months. Mild or longer survival cases of CPM have been reported[1-11]. Clinical improvement begins 2 weeks after correction and can continue for up to a year[7]. Both our cases presented with nasopharyngeal carcinoma, inappropriate antidiuretic secretion, severe hyponatremia, and quick hyponatremia correction within 2 days. Both had signs of pseudobulbar palsy and change of mentation. Brainstem dysfunction was also seen in Case 1, who initially survived from CPM and EPM, later succumbing to septicaemia. Patient 2 had EPM, and recovered with little neurological deficit.

Routine spinal fluid analysis in myelinolysis is normal, except for increased myelin basic protein concentration. EEG commonly shows nonfocal slowing. Brainstem auditory evoked potential latencies are prolonged in some cases. MR brain

Fig 3 - Case 2: a) Symmetric poorly defined low attenuation in the caudate nuclei and basal ganglia on CT consistent with EPM changes. b) Corresponding areas show high signal on T2-weighted MR image (5000/900).



imaging is normal in the initial week, later showing CPM and EPM changes[7].

CPM has characteristic imaging features: symmetric hypodense CT, low signal T1-weighted regions involving the basilar pons with sparing of the descending corticospinal tracts as well as the peripheral pontine tissues. T2-weighted images show corresponding areas of raised signals[8-10]. EPM changes are typically symmetrical, in the basal ganglia and lateral thalami[9,12-15]. Case 1 showed such central pontine and extrapontine signal changes, whilst Case 2 showed typical EPM changes in the basal ganglia and caudate nuclei.

Enhancement has been reported to be faintly homogeneous[15] and peripheral[16] in pontine lesions. The enhancing area may correspond to the interface between normal brain and the focus of acute demyelination or reflect blood brain barrier disruption. Case 1 had both central pontine and extrapontine myelinolysis, and enhancement with Gd-DTPA was faint and peripheral, around the basal ganglia, caudate nuclei and central pons. Enhancement in the basal ganglia and caudate nuclei has not been reported before.

Improvement on MR images lags behind clinical improvement and is incomplete. Pontine abnormality usually persists on MR imaging[8,10,11]. The initial high T2 signal alteration has been attributed to oedema and/or demyelination, whilst a smaller area of persistent high T2 signal after clinical improvement is probably from gliosis. Extrapontine myelinolysis, however, has been reported to resolve following clinical improvement or recovery[13]. No follow-up MR study was done in either of our cases.

Differential diagnoses of clinical and MRI picture of CPM and EPM include hypoxic encephalopathy and thrombosis of the basilar artery. Hypoxic areas occur in the basal ganglia, cerebellum, brainstem and always in the cerebral cortex. Brainstem involvement include the inferior colliculi, mammillary bodies, periaqueductal grey matter, substantia nigra and floor of the IVth ventricle[17], which are different compared to central pontine involvement in Case 1. In addition, both cases did not have any prior episode of hypotension or cardiorespiratory failure. Basilar artery thrombosis can be excluded because of sparing of the most ventral portion of the pons. In addition, it results in bilateral medial thalamic infarction[14,15], instead of lateral thalamic involvement seen in Case 1. Leigh disease and Wilson disease are differential considerations for pontine and basal ganglia involvement, which can be differentiated on clinical grounds[9].

CONCLUSION

Central pontine and extrapontine myelinolysis represent distinctive clinical syndromes with characteristic clinical presentations, typical CT and MR features. These conditions are not universally fatal and long-term survival can be seen. The combination of central pontine, basal ganglia and lateral thalami involvement should suggest the diagnosis of myelinolysis in the correct clinical setting of predisposing conditions, especially debilitation, chronic alcoholism and overcorrection of hyponatremia. MRI is superior to CT in depicting pontine and extrapontine involvement. One of our patients had peripheral rim enhancement of the basal ganglia and caudate nuclei, which is a new finding.

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