Singapore Med J 1998; Vol 39(8):370-372

# Computed Tomography Findings in Maple Syrup Urine Disease

L C Ong, T B Khoo, A Zulfiqar, H Zarida, A Ruzana


## ABSTRACT

**Maple syrup urine disease (MSUD) is an inherited metabolic disorder characterised by a severe, usually lethal, neonatal course unless dietary intake of branched chain amino acids is restricted. We describe a patient with MSUD who had computed tomography (CT) changes of diffuse white matter hypodensity, particularly in the deep white cerebellar matter, brain stem, cerebral peduncles, thalamus and posterior limb of the internal capsule. With dietary treatment, there was neurological improvement with simultaneous disappearance of the oedema. These CT changes are typical of MSUD, hence are relevant findings in the neuroradiologic differential diagnosis of a possible metabolic disorder.**


**Keywords: maple syrup urine disease, computed tomography**

## INTRODUCTION

Maple syrup urine disease (MSUD) is a familial metabolic disease caused by a defect in the oxidative decarboxylation of the branched chain amino acids. As a consequence of the enzymatic defect, these amino acids and their corresponding keto acids accumulate in the urine, serum and cerebrospinal fluid (giving rise to a characteristic odour, hence its name).

Patients with the classical form appear normal at birth, but show symptoms of poor feeding, vomiting and lethargy by the end of the first week. Unless a diet low in branched chain amino acids is started, death usually ensues or those who survive suffer severe irreversible brain damage. Several variants have also been described and are classified as mild, intermittent and thiamine responsive[1]. Computed tomography (CT) studies in patients with MSUD have reported hypodensity throughout the cerebral white matter[2,3]. We report here the CT features of a patient with MSUD and the changes over time with treatment.

## CASE REPORT

A 27-day-old boy, born after an uneventful pregnancy and delivery from healthy non-consanguinous parents, weighed 3,250 grams at birth. He was well until the twelfth day when poor sucking and one episode of cyanosis was noted. He became progressively lethargic and had to be tube-fed. There were no seizures or vomiting. Two elder siblings were healthy and there were no previous neonatal deaths. CT scan showed diffuse hypodensity of the white matter (Fig 1). These were particularly hypointense over the deep white cerebellar matter, brain stem, cerebral peduncles, thalamus and posterior limb of the internal capsule. He was then referred for a possible metabolic disorder.

On arrival, he was lethargic, hypotonic with decreased deep tendon reflexes and had inspiratory stridor. He weighed only 3,200 grams. There was an unusual odour, initially attributed to the medicinal oil being rubbed on his abdomen. Blood

Department of Paediatrics
Universiti Kebangsaan Malaysia
Jalan Raja Muda Abdul Aziz
50300 Kuala Lumpur
Malaysia

L C Ong, MRCP (UK)
Associate Professor

T B Khoo, M Med (Paeds)
Registrar

Department of Radiology
Universiti Kebangsaan Malaysia

A Zulfiqar, M Med (Radiol)
Associate Professor and Head

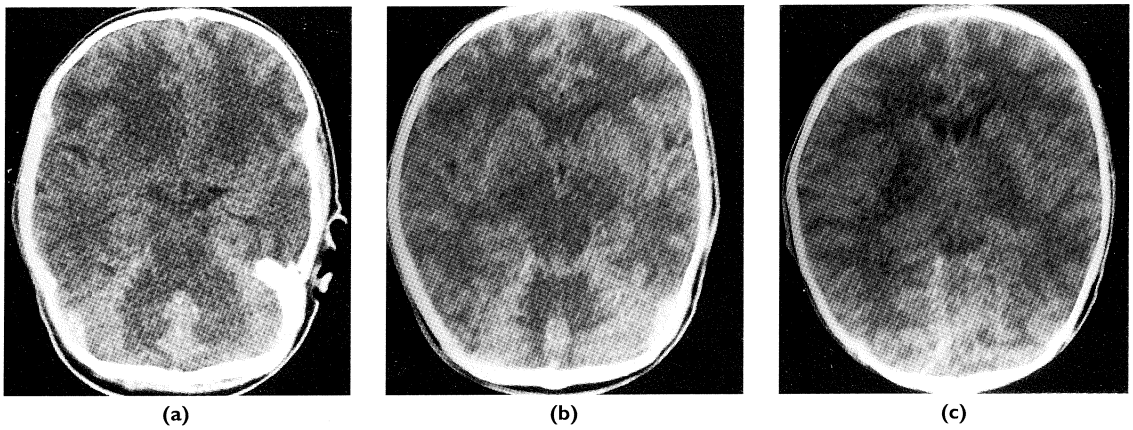
Department of Chemical Pathology
Universiti Kebangsaan Malaysia

H Zarida, DCP (Lond), PhD
Associate Professor

Unit of Dietetics
Faculty of Medicine
Universiti Kebangsaan Malaysia

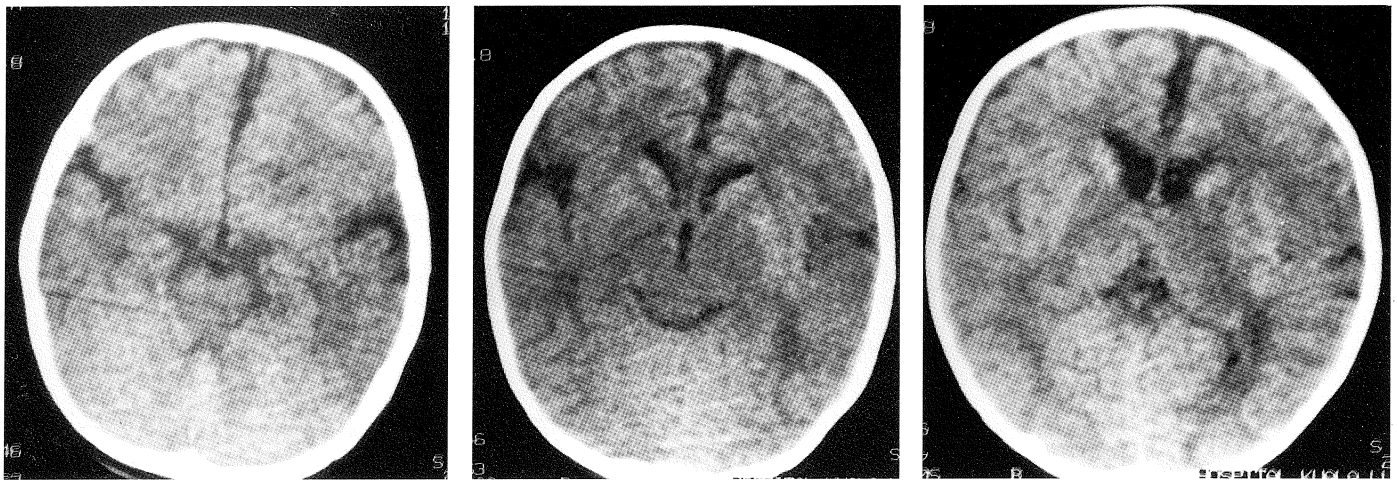
A Ruzana, BSc, Dip Dietetics (Lond)
Dietician

Correspondence to:
A/Prof L C Ong



(a) (b) (c)

**Fig 1** – The computed tomography of the brain at the onset of illness showed diffuse oedema, with marked hypodensity in the (a) deep cerebellar white matter and brain stem; (b) cerebral peduncles and (c) thalami and posterior limbs of the internal capsule. The frontal horns of the lateral ventricles and Sylvian fissues are effaced (b).



(a) (b) (c)

**Fig 2** – The computed tomography of the brain 6 months later showed that the oedema had resolved (a), (b) and (c). Widening of the cerebrospinal fluid spaces in (b) indicates loss of brain substance.

urea and glucose, serum electrolytes, transaminases and lactate were normal. Serum ammonia was mildly elevated. Serial arterial blood gases did not reveal any metabolic acidosis. The metabolic urine screening was strongly positive for ferric chloride and DNP-hydrazine. Serum and urine amino acid chromatography showed dense bands corresponding to leucine, isoleucine and valine. This was confirmed on HPLC analysis whereby the leucine level was 142.2 mmol/L, isoleucine 3.41 mmol/L and valine 21.9 mmol/L (age-matched controls' levels of leucine and valine were 2.18 – 2.34 mmol/L and 1.81 – 195 mmol/L respectively). The patient was then put on MSUD diet powder. Within a week, the leucine, isoleucine and valine levels had dropped to 46.9 mmol/L, 0.62 mmol/L and 2.2 mmol/L respectively. He became more active, gained weight and was able to bottle feed. The urine odour disappeared. Normal milk feeds were then added, the ratios of the two formulas were adjusted according to weekly serum levels of leucine. By the eleventh day of admission, his serum levels had come down to normal (leucine 2.32 mmol/L, isoleucine 0.71 mmol/L and valine 1.98 mmol/L). He was subsequently discharged with monthly reviews clinically and biochemically.

Six months later, he continued to gain weight and could be introduced to semi-solids. His tone was normal but he remained developmentally delayed. A repeat CT (Fig 2) showed the oedema had resolved, with some loss of brain matter.

## DISCUSSION

MSUD is the commonest inborn error of metabolism reported in Western neonatal screening programmes[4]. It has also been reported among Malaysian children[5]. The unusual urine odour in our patient has been aptly described as that of boiled Chinese herbs by the Thais[6], which is probably more meaningful in our local context than maple syrup.

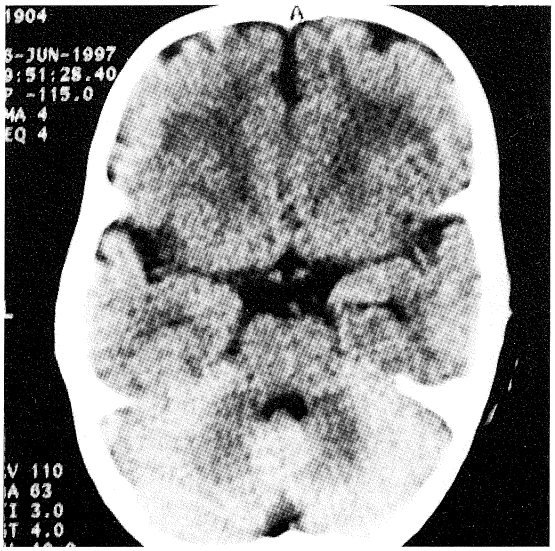



**Fig 3** – Computed tomography of the brain of a normal newborn showing complete myelination of the cerebellar pons and midbrain.

The CT changes in MSUD have been described in both the classical and variant forms[2,3]. During the first few days of life, myelination of the cerebellum and pons as evidenced on CT is almost complete (Fig 3). A marked diffuse oedema then develops simultaneously as the clinical condition deteriorates, and this oedema remains for as long as 6 or 7 weeks in untreated patients. In addition, a characteristic, more intense local hypodensity involving the deep white cerebellar matter, dorsal part of the brainstem, cerebral peduncles, posterior limb of the internal capsule and also gray matter (globus pallidus and most of the thalamus) is seen. This becomes fully developed during the third week of life and subsides gradually, often with some loss of brain substance. Dietary treatment appears to accelerate this process. MRI has been used to confirm the abnormalities seen on CT – areas with low density on CT had long T2 suggestive of increased water content, which is consistent with the dysmyelination and status spongiosus mentioned in pathological reports[7].

In other diseases that have to be considered in the clinical differential diagnosis, the CT features are different. Usually only low density areas in the basal ganglia are found in Leigh's disease[8] and methylmalonic aciduria, whereas the CT in phenylketonuria[9] does not show hypodensity. Hence the CT features described during the early stage are typical enough to suggest MSUD, and are relevant findings in the neuroradiologic differential diagnosis of a metabolic disorder.


## ACKNOWLEDGMENTS

We thank Dr Zawawi Salleh for referring the patient to us.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