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MR imaging of adrenoleukodystrophy

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Summary. We performed MRI in 7 cases with adrenoleukodystrophy (ALD), including 3 cases with childhood ALD, 3 cases with adrenomyeloneuropathy (AMN) and one symptomatic heterozygote. The symptomatic heterozygote was the mother of the patient with AMN. High-field-strength (2.0T) MRI was used in two cases with childhood ALD. In all 3 cases of childhood ALD, MR showed widespread lesions in both cerebral hemispheres. Areas of low intensity in the diencephalon or striatum on heavily T2-weighted images at 2.0T were seen in 2 cases with childhood ALD. Cerebral lesions confined to the internal capsule, cerebral peduncle and optic radiation in the adult onset ALD including AMN and symptomatic heterozygote, have not been reported and this confinement may indicate an early stage of the disease.

Key words: Adrenoleukodystrophy – Adrenomyeloneuropathy – Magnetic resonance imaging – Demyelination

Adrenoleukodystrophy (ALD) is a genetically determined disorder associated with the accumulation of very-long-chain fatty acids (VLFA), particularly hexacosanoic acid (C26:0), in tissue and body fluids [1, 2]. There are two ALD genotypes; X-linked and autosomal. The X-linked type may manifest in childhood or in adulthood as adrenomyeloneuropathy (AMN) [3–5]. The less common autosomal recessive type usually occurs in neonates and resembles the Zellweger cerebrohepatorenal syndrome [6]. Childhood ALD is characterized by rapidly progressive demyelination of cerebral white matter and adrenal insufficiency. Clinically, it is associated with dementia, visual loss, and quadriparesis, leading to death [3]. AMN is a variant of ALD in the older patients, and is characterized by adrenal insufficiency and slowly progressive demyelination in the spinal cord and peripheral nerves [5]. The female heterozygote may develop signs and symptoms of central nervous system or adrenal dysfunction. The underlying metabolic defects have not been fully defined. The CT features of ALD have been described [7–10].

Young et al. first mentioned MR findings in a case of ALD [11]. After that, many case reports have been presented [12–16, 24]. We tried to identify the localization of abnormalities in ALD with brain MRI.

Methods

MR imagers used were a Toshiba MRT resistive 0.15T unit, a Toshiba MRT 200S superconductive 1.5T unit and an Asahi prototype MRI superconductive 2.0T unit. In all cases, T2-weighted images were obtained using spin echo sequences with repetition times (TR) of 1600 and 2000 ms and echo times (TE) of 50 and 80 ms at 0.15T, TR of 2000 ms and TE of 40 ms at 1.5T and TR of 3000 ms and TE of 82 ms at 2.0T. In addition, T1-weighted images using inversion recovery or spin echo sequences were obtained in some cases. Slice thickness was 5 or 10 mm and matrix size was 256 by 256.

Materials

In the last 2 years, we have performed MRI on 7 cases with ALD. Included in our sample were 3 cases of childhood ALD, 3 cases of AMN, and one symptomatic heterozygote. The essential data concerning the 7 observations are presented in Table 1. In all cases, the ratios of VLFA in plasma and erythrocyte membrane were increased. The symptomatic heterozygote is the mother of case 6 with AMN.

Toshiba resistive 0.15T unit was used in all cases, Toshiba 1.5T unit in 2 cases (Case 4 and 6) and Asahi Medical 2.0T unit in 2 cases (Case 1 and 3).

Results

The average time between onset and MRI was about 5 years, with a range between 1 year (case No. 1) and 14 years (case No. 5). In 6 of the 7 cases, T2-weighted images showed abnormal high intensity areas in brain.

In all 3 cases with childhood ALD, MRI showed widespread lesions in both cerebral hemispheres (Table 2).

In case 1 with childhood ALD (Fig. 1), T2-weighted images demonstrated areas of high intensity predominantly in the white matter of the parieto-occipital lobes and the posterior parts of the temporal lobes bilaterally. Involvement of the visual pathway included the lateral geniculate bodies and the optic radiations. A T1-weighted

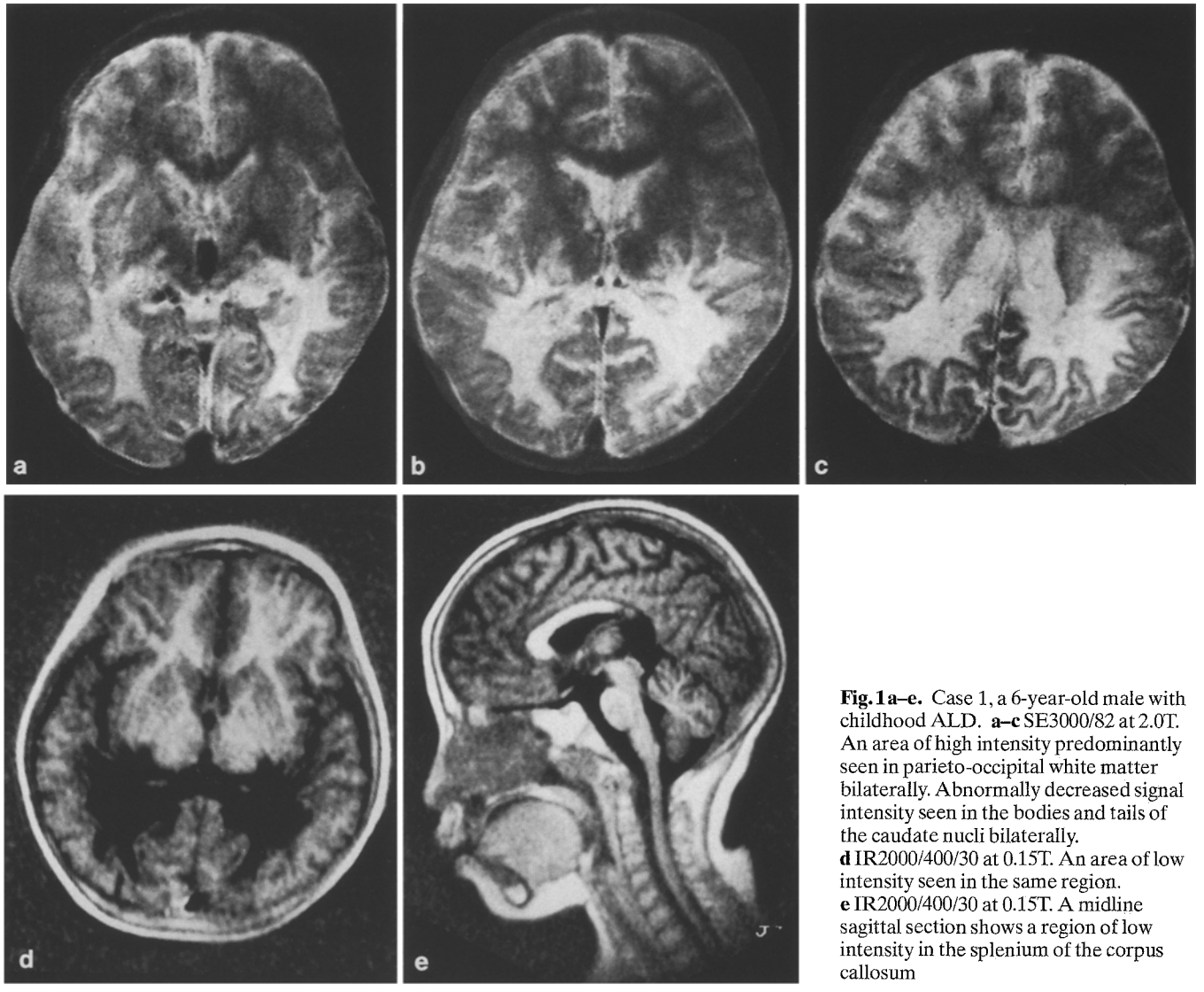


Fig. 1a–e. Case 1, a 6-year-old male with childhood ALD. **a–c** SE3000/82 at 2.0T. An area of high intensity predominantly seen in parieto-occipital white matter bilaterally. Abnormally decreased signal intensity seen in the bodies and tails of the caudate nucli bilaterally. **d** IR2000/400/30 at 0.15T. An area of low intensity seen in the same region. **e** IR2000/400/30 at 0.15T. A midline sagittal section shows a region of low intensity in the splenium of the corpus callosum

image in a midline sagittal section revealed a region of low intensity in the splenium of the corpus callosum. Heavily T2-weighted images at 2.0T showed abnormally decreased signal intensity in the bodies and tails of the caudate nucli bilaterally. CT scans showed symmetrical areas of low density in the parieto-occipital regions with peripheral contrast enhancement.

In case 2 with childhood ALD (Fig. 2), T2-weighted images displayed areas of high intensity diffusely in the white matter, predominantly in the frontal lobes. A midline sagittal section revealed marked atrophy of the genu and body of the corpus callosum.

In case 3 with childhood ALD (Fig. 3), T2-weighted images demonstrated widespread diffuse symmetrical

Table 1. Summary of 7 patients in study

Case/age/sex	Subtype	Duration(y)	Clinical signs
1/ 6/m	Childhood ALD	1	Progressive gait disturbance, dementia, pyramidal signs, hallucination, visual loss
2/11/m	Childhood ALD	2	Speech disturbance, muscle weakness, dementia, gait disturbance
3/20/m	Childhood ALD	9	Dementia, spasticity, quadriparesis
4/27/m	AMN	2	Gait disturbance, hypertonicity, deep and superficial sensory disturbance, neurogenic bladder
5/42/m	AMN	14	Gait disturbance, hypertonicity, deep and superficial sensory disturbance
6/24/m	AMN	3	Spastic paraparesis
7/54/f	Symptomatic heterozygote	?	Spastic gait. The mother of case 6

?: uncertain onset

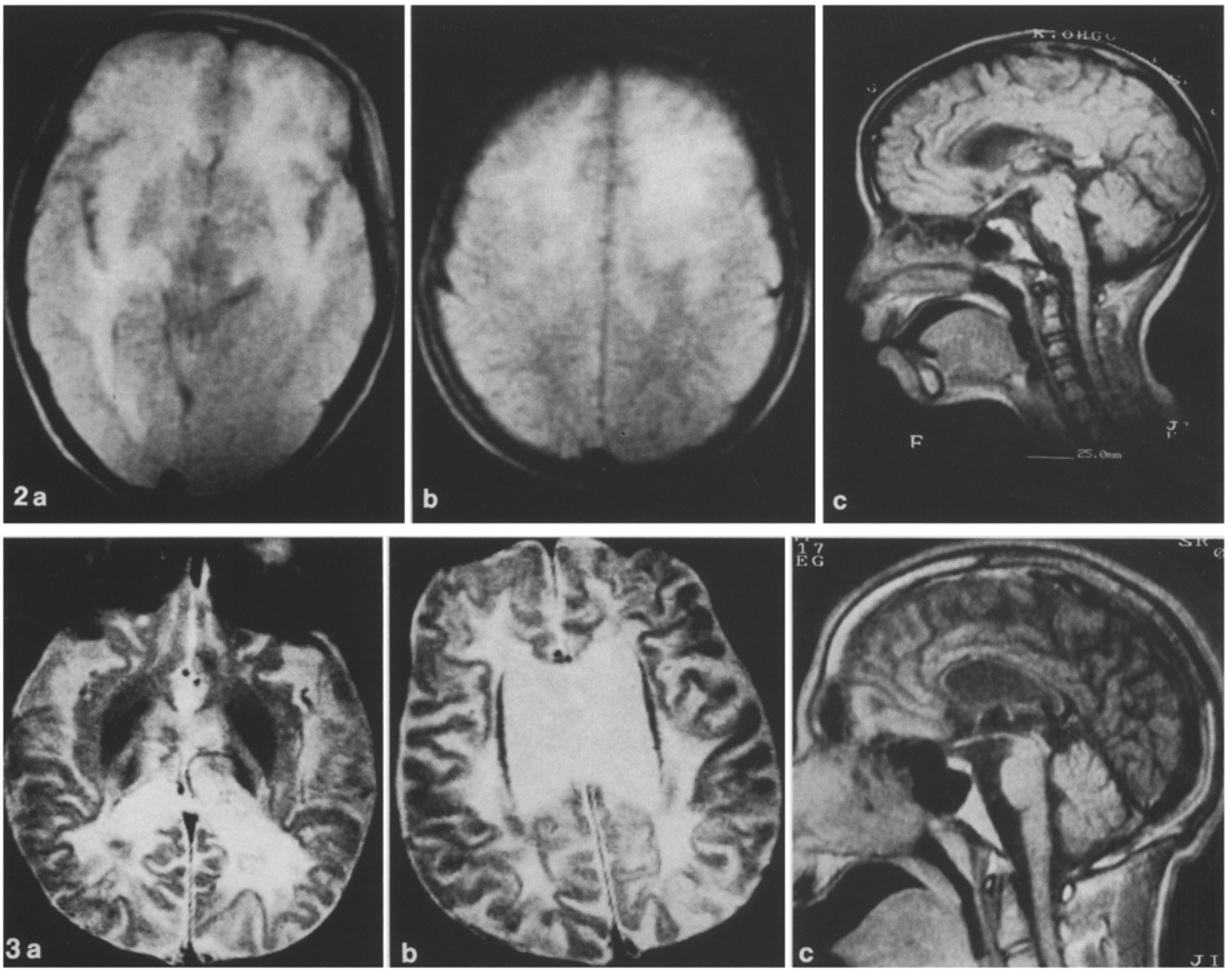


Fig. 2 a–c. Case 2, an 11-year-old male with childhood ALD. **a, b** SE2000/50 at 0.15T. Areas of high intensity diffusely seen in white matter, predominantly in both frontal lobes. **c** SR500/30 at 0.15T. A midline sagittal section shows marked atrophy of the genu and body of the corpus callosum

Fig. 3 a–c. Case 3, a 20-year-old male with childhood ALD. **a, b** SE3000/82 at 2.0T. Widespread diffuse symmetrical areas of high intensity seen in the white matter and abnormally decreased signal intensity in the thalamus, putamen and caudate nucleus bilaterally. **c** SR500/30 at 0.15T. A midline sagittal section shows diffuse atrophy of the corpus callosum

areas of high intensity in the white matter and marked atrophy of the corpus callosum. Heavily T2-weighted images at 2.0T revealed abnormally decreased signal intensity in the thalamus, putamen, and caudate nucleus.

Areas of low intensity in the diencephalon and striatum on heavily T2-weighted images at 2.0T were seen in 2 cases of childhood ALD.

In 3 of the 4 cases with adult onset ALD that is AMN and symptomatic heterozygote, we have noted focal abnormality in brain on MRI (Table 3). In all 4 cases, CT scans revealed no evidence of abnormality.

In case 4 with AMN (Fig. 4), T2-weighted images demonstrated a spotty area of high intensity in the right optic radiation. Positron emission tomographic image (PET) of the same patient showed decreased cerebral blood flow in the right temporo-occipital region including the optic radiation. Loss of eyesight was not noted.

In case 5 with AMN, MRI was normal.

In case 6 with AMN (Fig. 5), T2-weighted images revealed spotty areas in the both internal capsules and in the left cerebral peduncle.

In case 7, the symptomatic heterozygote who was the mother of case 6 (Fig. 6), T2-weighted images showed spotty areas of high intensity in the genu of the internal capsules bilaterally.

In the adult onset ALD patients, abnormalities were limited to the internal capsule, cerebral peduncle and optic radiation.

Discussion

The specific enzyme defects in ALD have not been defined. Currently available evidence indicates an impairment in oxidation of VLFA. The diagnosis of ALD has

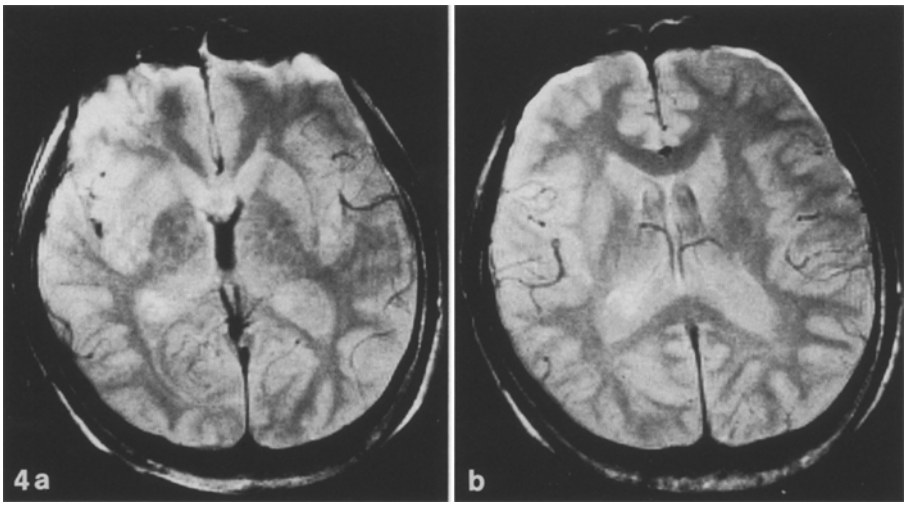
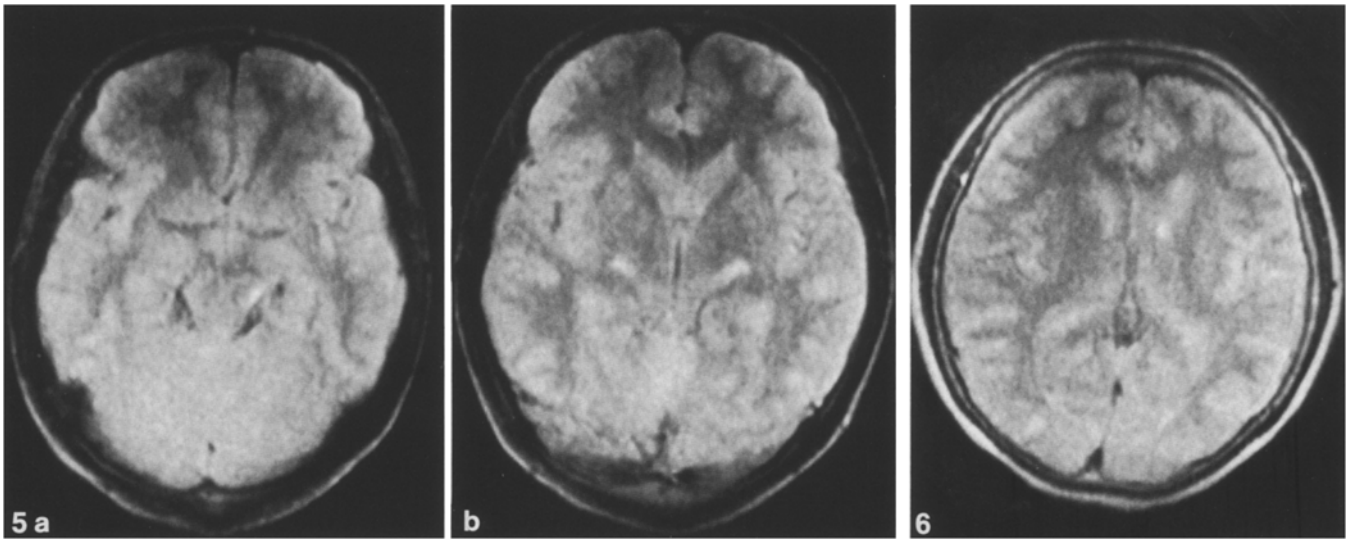


Fig. 4a, b. Case 4, a 27-year-old male with AMN. SE2000/40 at 1.5T. An area of high intensity seen in the right optic radiation

Fig. 5a, b. Case 6, a 24-year-old male with AMN. SE1600/80 at 0.15T. Spotty areas of high intensity seen in the left cerebral peduncle (**a**) and the internal capsule bilaterally (**b**)

Fig. 6. Case 7, a 54-year-old female symptomatic heterozygote, the mother of case 6. SE1600/80 at 0.15T. Spotty areas of high intensity seen in the genu of the internal capsule bilaterally



been based on the increase of VLFA in erythrocyte membrane sphingomyelin [17] and phospholipid [18], and in total lipid from cultured skin fibroblasts [19] and plasma [3]. In all our cases, VLFA in erythrocyte membrane and plasma was increased, confirming the diagnosis of ALD.

Classically, the area of involvement in ALD was predominantly the parieto-occipital white matter, according to Shaumburg [3]. However, predominant involvement of frontal lobes, temporal lobes, one cerebral hemisphere, or white matter tracts such as the internal capsule, corpus callosum, corona radiata, forceps major and the auditory pathway including the lateral lemnisci, brachium of the inferior colliculus, acoustic radiations and transverse temporal gyrus of Heschl, and the visual pathway including the lateral geniculate bodies and the optic radiations have been described [9, 10, 12, 13, 20–24]. In only one of the 3 cases with childhood ALD, white matter abnormalities were seen predominantly in the parieto-occipital lobes (case 1). In case 2, abnormalities were predominantly in the frontal lobes. In case 3, there were diffuse white matter abnormalities.

Areas of low intensity were seen in the body and tail of the caudate nucleus bilaterally on heavily T2-weighted at 2.0T in case 1. Areas of low intensity were seen in the tha-

Table 2. MRI findings of childhood ALD

Case	White matter abnormalities					Low intensity with 2.0T unit
	Frontal	Parietal	Occipital	Temporal	Corpus callosum	
1	−	+ + +	+ + +	+	Splenium	+ (Caudate nucleus, body~tail)
2	+ + +	+	+	+	Genu~Body	
3	+ + +	+ + +	+ + +	+ + +	Diffuse	+ (Thalamus, Putamen, Caudate nucleus)

+ + + large, + + middle, + small, − normal

Table 3. MRI findings of adult onset ALD

Case	Subtype	Focal abnormalities
4	AMN	Optic radiation, right
5	AMN	–
6	AMN	Internal capsule, bilateral Cerebral peduncle, left
7	Symptomatic heterozygote	Genu of internal capsule, bilateral

lamus, putamen and caudate nucleus bilaterally in case 3. Heavily T2-weighted high-field images provide a unique opportunity for evaluation of the extrapyramidal motor system. Drayer et al. showed low intensity areas in the thalamus and putamen on T2-weighted images at 1.5T in multiple sclerosis (MS) [25]. They thought that it was consistent with an abnormally increased accumulation of a transition element, most likely iron, in the thalamus and striatum associated with MS. Our MR findings in childhood ALD at 2.0T might be also related to the abnormal iron metabolism in the brain.

Cerebral lesions confined to the internal capsule, cerebral peduncle and optic radiation in adult onset ALD including AMN and symptomatic heterozygote, have not been previously reported and may indicate an early stage of the disease [14, 26–28].

We conclude that MRI, especially operating at high-tesla, was useful in clarifying the localization of the brain lesion in the ALD.

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