AXILLARY SKIN BIOPSY AND M R SPECTROSCOPY IN LAFORA’S DISEASE - A CASE REPORT

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ABSTRACT
Lafora’s disease (lafora body disease) a rarely seen and progressive disease characterised by mental decline, myoclonus and seizures. Definitive diagnosis is made with skin biopsy showing typical spherical PAS positive inclusion bodies. We present a case who had myoclonus, generalized seizures and dementia, diagnosed lafora’s body disease, confirmed by skin biopsy. Magnetic resonance spectroscopy findings showing predominant involvement of frontal lobes are described and discussed.

Key Words: Lafora’s disease, Lafora Body, Myoclonus, Axillary Skin Biopsy, Magnetic Resonance Imaging, M R Spectroscopy

INTRODUCTION
Lafora’s disease is an autosomal recessive hereditary disease characterized by progressive dementia, myoclonus and generalize seizure. It was first described as progressive myoclonic epilepsy by Lafora and Gluech in 1911. Symptoms mainly begin in the first and second decade of life between 6 to 20 years. Initial clinic findings vary, but a generalized seizure is the first symptom in the majority of cases (Footitt et al., 1997).

The diagnosis is confirmed by the demonstration of typical PAS positive spherical inclusion bodies in the brain and spinal cord, skin, liver and skeletal muscle on biopsies. For diagnosis, axillary skin biopsy is preferred being less invasive and gives lower false negative results. We present a case of Lafora’s disease. Findings of Magnetic Resonance (MR) Spectroscopy are described and discussed.

CASES
A 19 years old, male patient was admitted to the Government Medical College M.B.S. hospital with myoclonus, generalized tonic-clonic seizure and mental decline. Two years prior to presentation he started with myoclonus involving initially both arms, subsequently both legs, followed by generalized tonic clonic seizure 6 months later. Frequency and duration of myoclonus increased up to the extent that it made patient incapable to perform his routine activity (feeding, bathing etc), normal standing and sitting.

He complained of progressive mental decline such as forgetfulness, personality deterioration, cognitive sub normality for last 2 month. He had a positive family history; his elder sister had the same symptoms onset at 17 yrs of age and presently has mental sub normality with seizure.

On physical examination; his blood pressure, heart rate and systemic examination were all within normal limits. Neurological evaluation revealed partial cooperation and orientation, with occasional absurd behavior and cognitive sub normality. His mini mental state was below 13 and D. Q. was 27(i.e. debilitated level). There was no cerebellar, pyramidal and extrapyramidal signs.

His routine Haemogram, Urine and Biochemical tests were normal. Electroencephalography (EEG) showed diffuse generalized multiple spikes and slow wave discharges. Visual evoked potential (V.E.P.) showed normal latency of P100 wave(105.3 on right side, 99.5 on left side), whereas Brain stem auditory evoked responce (BAER) showed normal inter-latency differences. Magnetic resonance (MRI) imaging showed mild cerebral atrophy. Magnetic resonance spectroscopy (Fig. 1) showed decrease in...
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choline/creatine ratio and decreased NAA specially in frontal lobe. Biopsy of axillary’s sweat gland duct cells (Fig. 2, 3) showed polyglucosan body mater which was characteristic of Lafora’s disease

Figure 1: Magnetic resonance spectroscopy showed decrease in choline/creatine ratio and decrease NAA specially in bilateral frontal lobe

Figure 2: Axillary skin biopsy showing pink inclusions in eccrine duct cell
Patient was already on Sodium Valproate 15mg/kg/day and Lamotrigine 50 mg/day. Phenobarbitone was added 60 mg/day by orally. Both myoclonus and generalized seizure frequency decreased. His cooperation and mental decline improved partially during 4 week follow up.

**DISCUSSION**

The etiology of Lafora’s disease is unknown and it affects both sexes equally. Although polyglucosan inclusions are characteristic of this disease, as of yet no enzymatic deficiency or abnormality in carbohydrate metabolism has been demonstrated. In most of the cases seizures are the first symptoms of the disease. Mental decline starts usually later in the course of the disease, but it can rarely be the initial finding. In our case also seizure was first symptoms followed by mental decline. Kaufmann et al reported that epileptic seizures can be responsible for personality deterioration and mental decline. In our case clinical course also supported this opinion that mental functions were partial improved after seizure frequency decreased during follow up. Visual ictal phenomena appear in half of the cases and are a relatively specific clinical clue to the diagnosis of disease, but this clinic feature was absent in our case.

The characteristic EEG pattern consists of slow background recurrent epileptiform discharges including spikes, polyspikes, spike-wave and polyspike-wave complexes. Additionally, it has been shown that EEG remains almost unchanged with disease progression. In the presented case, the EEG showed diffuse and non-localized polyspike and slow wave discharges.

The most remarkable MR spectroscopy finding is the predominant involvement of the frontal lobes when compared with the occipital lobes. So far, predominant frontal brain damage has not been reported in neuro-pathologic, neurophysiologic, or functional neuro-imaging studies in Lafora disease patients (Villanueva, 2006). Case reports and case series from India (Acharya et al., 1993; Malur et al., 2008) did not performed MR spectroscopy. Neurophysiologic studies have shown prolonged visual-evoked potential latencies (indicating visual pathway or occipital damage), delayed auditory brainstem responses (auditory pathway or brainstem damage), or giant somato-sensory evoked potentials (sensory pathway or parietal damage), but frontal cortex involvement has not been reported (Berkovic et al., 1991). This
Evoked potential changes occur over time (Kobayashi et al., 1990), our patient did not have any abnormality, possibly due to relatively earlier stage of disease.

The diagnosis may be confirmed by the demonstration of typical spherical PAS-positive inclusion bodies in the Brain and spinal cord, heart and liver, skeletal muscle and axillary’s sweat gland duct cells (Andrade et al., 2003). The inclusions polyglucosan bodies are not specific for Lafora’s disease. Similar changes can also be seen in normal aging, type IV glycogen storage disease, arylsulfatase A pseudodeficiency, some instances of myotrophic lateral sclerosis.

Differential diagnosis includes sub acute sclerosing panencephalitis (SSPE), progressive myoclonic ataxia (PMA), progressive encephalitis (GM2 gangliosidosis, Nieman Pick, Gaucher disease), juvenile myoclonic epilepsy, Nonketotic hyperglycemia, Inheritance pattern, absence of burst-suppression on EEG and typical biopsy findings; presence of mental decline and tonic-clonic seizure; and normal blood glucose levels help differentiate SSPE and progressive encephalitis; PMA; juvenile myoclonic epilepsy; and nonketotic hyperglycemia, respectively.

Antiepileptic drug, especially Sodium valproate is preferred for the treatment of both myoclonic and generalized seizures. We also used Sodium valproate in our case. Both myoclonic and generalized seizure frequencies diminished.

CONCLUSION
Clinical feature and diagnosis of lafora body disease in a 19 year boy is presented. The axillary’s skin biopsy is an easy to perform investigation for the confirmation. Finding of M.R. Spectoscopy showing predominant frontal lobe involvement are also described and discussed.

REFERENCES
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