

Lafora's disease

Introduction

Lafora disease is an inherited, late onset, progressive myoclonic epilepsy. Myoclonus (jerking) is a feature of the disease and characteristically this can be induced by flashing lights, sudden sounds and movement (especially that close to the dog's head). Generalised or complex partial seizures may be seen in some dogs. The disease progresses slowly over many years and gradually other neurological deficits such as ataxia, blindness and dementia occur.



Lafora disease can occur spontaneously in any breed however the miniature wire-haired dachshund, Bassett hound and beagle are predisposed. Typically the first signs occur in animals over 5 years (usually over 7 years) age and both sexes can be affected. The beagle has a more severe version of the disease and the associated epilepsy can be drug resistant.

Signs

A characteristic of this disease is myoclonus (clinical sign of a sudden contraction of a group of muscle), typified by rapid shuddering/jerking the head backwards. The myoclonus occurs spontaneously and in response to noise, flickering light (including television), and sudden movement in the visual field. Hypnic (sleep related) myoclonus may also occur. Some dogs also develop epilepsy (generalised tonic clonic seizures and complex partial seizures). The complex seizures are often characterised by high pitched vocalisations and behaviour as if the dog is panicking.

The main differential diagnoses of this disease are other causes of epileptic seizures and idiopathic epilepsy. Haematological and biochemical screens should be performed to rule out reactive causes of epileptic seizures, but will be normal in Lafora disease. Magnetic resonance imaging is useful to identify structural brain disease which may cause acquired epilepsy. Idiopathic epilepsy typically occurs in younger dogs (6 months to 6 years) and in most breeds myoclonus is not a feature.

The genetic mutation in the Dachshund and Bassett Hound was identified at The Hospital for Sick Children, Toronto. [Click here to read about the discovery of the gene](#). The Hospital offers a test for affected dogs in return for a \$200 (Canadian dollars) donation to the hospital (credit cards are accepted).

10mls of EDTA blood should be submitted to:

Dr. Berge Minassian
Room 6536B
The Hospital for Sick Children
555 University Ave.
Toronto, ON
M5G 1X8
Canada
Tel: 416-813-7721 berge.minassian@sickkids.ca

The disease may also be confirmed by identification of the Lafora bodies in a liver, muscle or nerve biopsy).

Causes and risk factors of Lafora disease

Lafora's disease is caused by a mutation in the EPM2B (NHLRC1) a gene that encodes malin E3 ubiquitin ligase, a protein involved with carbohydrate metabolism. Early data suggests that these proteins safeguard neurons against accumulating too many carbohydrates. A characteristic feature of the disease is accumulation of toxic starch-like material (polyglucosan) within cells, particularly nervous, hepatic and muscle tissue. Lafora disease has an autosomal recessive inheritance i.e. both the sire and the dam will either carry (i.e. have no signs of the disease and have one copy of the abnormal gene) or have the disease.

Treatment

Anecdotally miniature wire-haired dachshunds with early Lafora's disease respond to a proprietary antioxidant rich diet (Hills b/d™). Hills b/d™ protects nerve cells against oxidative damage however this may not be the mechanism by which it is effective for Lafora disease as the same beneficial effect is not seen if the dog is maintained on its existing diet and this supplemented with anti-oxidants. It is possible that Hills b/d™ is effective because it has a low glycaemic index. Starchy/sugary treats may aggravate the condition and should be avoided. Other diets with a low glycaemic index may be effective.

The seizures should be treated symptomatically - in some cases this can be difficult since some dogs do not respond to traditional anti-epileptic drugs like phenobarbitone. The author typically starts with potassium bromide at 30-40mg/kg once daily. A serum bromide concentration should be assessed 8-16 weeks after initiating the drug (since it takes 4 months to achieve steady state levels of bromide so ideally blood samples should be taken at 16 weeks) aiming for a concentration of ~ 1000mg/l (or 15 mmol/l) - 2000mg/l / (or 25mmol/l). Higher serum concentrations are acceptable if there are no adverse effects such as sedation, ataxia.

If this serum concentration of bromide has been achieved and the number of seizures is still unacceptable then phenobarbitone at 3mg/kg every 12 hours should be added to the regime. Phenobarbitone should also be considered if there are clusters of seizures. A serum phenobarbitone concentration should be assessed 2 weeks after initiating the drug.

If the seizures are still not adequately controlled when the phenobarbitone serum concentration is =25mg/l (120µmol/l) then switching to unlicensed anti-epileptic drug should be considered. The author typically chooses Levetiracetam (Keppra) at a dose of 10-20mg/kg twice to three times daily. Coincidentally with starting the levetiracetam the phenobarbitone is slowly withdrawn (providing the seizure frequency does not increase). Anecdotally levetiracetam is more effective than phenobarbitone or bromide for controlling the myoclonus (jerking) so you might consider using this drug earlier if the myoclonus is disabling.

Some dogs have a problem walking in sunlight and some owners have found that the jerking significantly improves if the dog wears sunglasses (DOGGLES).

Follow up

Lafora disease is not generally fatal in the dog however the myoclonus and seizures may worsen with time and older dogs may become blind and ataxic compelling the owner to request euthanasia. The beagle has a different genetic mutation and a more severe form of the disease. In particular the epilepsy may be drug resistant in this breed. The human form of the disease is also more serious with affected children developing dementia and status epilepticus; most do not survive beyond their second decade.

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