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Neurological signs following suspected exposure to stinging nettles in two dogs

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SUMMARY

Two gun dogs presented with a combination of neuromuscular and autonomic signs following suspected exposure to stinging nettles (*Urtica dioica*) in the UK. Both dogs developed first clinical signs on the same day and had been working in the same area where the presence of stinging nettles had been reported. Clinical signs included urticaria, tachypnoea, hypersalivation, bilateral miosis, ambulatory tetraparesis, muscle fasciculations and myokymia and generalised decreased hyporeflexia. Complete blood count and acetylcholinesterase activity were within normal limits apart from the elevated creatine kinase levels. One dog had three toxic episodes over a period of three weeks and the second case had a single toxic insult. Both dogs made a complete recovery after supportive care including intravenous fluid therapy, antihistamines, proton pump inhibitors, analgesics, antibiotics and steroidal eye-drops. There was no report of any permanent clinical signs as a result of the exposure.

BACKGROUND

The cases are submitted for its uniqueness in being the first reported cases of suspected nettle toxicity producing neurological signs in dogs in the UK, implying that *Urtica dioica* (common nettle) contact should be considered in the differential diagnosis of the described acute neurological signs in the USA and New Zealand, and in the UK.

CASE PRESENTATION

Case 1

A seven-year-old male neutered springer spaniel, hunting dog, weighing 18 kg, presented acutely with collapse, tachypnoea and generalised muscle fasciculations. Clinical signs started while he was hunting in a field. On physical examination, the dog showed marked hypersalivation, teeth chattering, hyperkinetic pulses, heart rate of 100 beats per minute, hyperaemic mucous membranes, preputial erythema and hyperthermia of 40.6°C (105.08°F). Neurological examination disclosed an alert mental status, generalised muscle fasciculations and ambulatory tetraparesis. No proprioceptive deficits were detected. Muscle tone was decreased in all four limbs, and patellar and withdrawal reflexes were decreased. Cranial nerve examination showed bilaterally decreased palpebral reflexes and miotic pupils with intact pupillary light reflexes. A generalised neuromuscular disease with autonomic involvement was suspected. Main differential diagnoses included toxic, metabolic and inflammatory diseases. Haematology and comprehensive biochemistry including electrolytes were unremarkable. The dog was bathed and started on an intravenous infusion of Ringer's lactate at a maintenance rate and received omeprazole (1 mg/kg (0.45 mg/lb), intravenous, every 24 hours) and chlorphenamine (10 mg/kg (4.5 mg/lb), intravenous, every eight hours). The dog developed a mild cough during the first day of hospitalisation. Neurological signs rapidly improved during the first hours after hospitalisation and had ceased by three days, and the dog was discharged.

The dog was presented again one week later for systemic and neurologic signs that were similar to its previous presentation after working in the same area that triggered the previous episode. Ophthalmological examination revealed mild early signs of bilateral episcleritis. Haematology and biochemistry including electrolytes were unremarkable except for increased creatine kinase (578 iu/l, reference range 75–375 iu/l). Urinalysis (dipstick and sediment) revealed haematuria and proteinuria. Acetylcholinesterase activity was evaluated to investigate possible organophosphate or carbamate toxicity, and was within normal limits (99 per cent). The dog received intravenous Ringer's lactate at maintenance rate, omeprazole (1 mg/kg (0.45 mg/lb), intravenous, every 24 hours) and chlorphenamine (10 mg/kg (4.5 mg/lb), intravenous, every eight hours). There was one episode of regurgitation and diarrhoea during the hospitalisation period. The dog was discharged with eye-drops containing prednisolone to treat the episcleritis and oral chlorphenamine (4 mg/kg (1.8 mg/lb), oral, every eight hours) for five days.

A third incident occurred within few days after having been working in a different field. The owner reported the presence of nettles and confirmed its presence on previous fields. The dog presented with the same clinical signs in addition to an erythematous scrotum, periocular and periauricular erythema, protrusion of third eyelids, photophobia, epiphora and mild disorientation. Blood tests did not show any significant abnormalities. Thoracic radiographs showed mild generalised bronchial pulmonary pattern. The dog responded well to conservative therapy including intravenous fluid therapy and antihistamines, and was discharged within three days with a one-week course of amoxicillin clavulanate (20 mg/kg (9 mg/lb), oral, every 12 hours) and instructions to avoid nettles. No further episodes were reported since then.

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Case 2

A two-year-old female spayed labrador retriever, hunting dog, weighing 21 kg, presented for acute collapse, hypersalivation, shivering and tachypnoea. This dog presented the same day of the first episode of the dog described in case 1 and after working in the same area. Physical examination showed hyperaemic mucous membranes and hyperkinetic pulses with a heart rate of 120 beats per minute. The remainder of the examination was unremarkable. Neurological examination disclosed an alert mental status, myokymia in all four limbs and ambulatory tetraparesis with an increased muscle tone in all limbs (online supplementary video 1). Proprioception was considered normal. Patellar and withdrawal reflexes were decreased in all four limbs. Palpebral reflex was decreased bilaterally. A generalised neuromuscular disease was suspected. After verifying that the dog had been working on the same area as case 1, a toxic insult was mainly suspected for both cases. Haematology and biochemistry showed mild increase in creatine kinase (566 iu/l, reference range 75–375 iu/l). Acetylcholinesterase activity was measured (160 per cent) and results were not consistent with organophosphate-carbamate toxicity. The dog was hospitalised and received only intravenous infusion of Ringer's lactate at a maintenance rate. Progressive improvement was observed and within two days the dog did not show any neurological signs and she was discharged. No further complications have been reported since.

DISCUSSION

Urtica species is a genus of plants in the family of Urticaceae. *Urtica* species are found worldwide, and *U dioica* (stinging nettle, common nettle) is the most common species found in the British Isles.[1] The stems and leaves are covered by stinging hairs, also called trichomes, which act like hypodermic needles. Chemical toxic substances found in the trichomes include histamine, acetylcholine and 5-hydroxytryptamine (serotonin).[1–3] However, it has been suggested that additional substances may be present.[4] Besides, *U dioica* has been widely reported to have various pharmacological activities such as immunomodulatory, anti-inflammatory, antioxidant or diuretic effects due to the numerous constituents identified in nettle herb (leaves and roots).[4 5]

Physical contact with stinging nettle often results in a non-immunologic-induced contact urticarial or irritant dermatitis.[6] Despite toxic effects are usually local and dermatological, systemic signs can occur. Few reports of *Urtica* species toxicity have been documented in humans, dogs and horses.[7 8] Clinical signs of nettle toxicity in humans are variable and include tingling of the hands, feet and tongue, unsteadiness, fatigue, dyspnoea, abdominal cramps, tremors, hypersalivation and hypothermia.[9] The neurological features of nettle toxicity in veterinary medicine literature have been reported to be variable. The limited cases of nettle systemic toxicity in dogs, which have occurred outside of Europe, have involved species which are not native in the UK (*U ferox* and *U chamaedryoides*). Muscular weakness (either affecting pelvic limbs or all four limbs) and muscle fasciculations have been mentioned in dogs.[7] Disorientation, hypersalivation and tetraplegia caused by *U ferox* exposure in New Zealand were reported in a dog.[10] In the USA, *U chamaedryoides* caused vomiting, clawing at the face and ataxia in a group of dogs.[11] However, complete neurological examinations were not described in these reports. Several case reports of suspected neurological toxicity due to exposure to *U dioica* have been described in UK.[12–14] *U dioica* toxicity has been described in three horses in Newmarket, UK.[14] The horses showed an acute onset of ataxia, weakness and urticarial reaction. One filly had ataxia and weakness of all four limbs and bradycardia. Interestingly, the author of that report stated that nettle poisoning was a well-recognised problem in the area, especially in summer and autumn, which coincides with the same region and time of the year (October) in our two patients.

Case 1 showed fasciculations and case 2 showed myokymia. Fasciculations are defined as brief spontaneous contractions affecting small number of muscle fibres, while myokymia is defined as continuous involuntary muscle twitching that gives the appearance of vermiform movements of the skin. Both are currently classified as peripheral nerve excitability disorders, and myokymia is suggested to account for a more severe manifestation of motor nerve hyperexcitability.[15] In dogs, myokymia is reported most commonly associated to neuromyotonia and spinocerebellar ataxia, and is described mainly in Jack Russell terriers as a hereditary disease.[16 17] Focal myokymia has also been reported secondary to intracranial neoplasia or inflammatory disease, and induced by radiotherapy in a dog.[18] In humans, toxic myokymia has been described after snake envenomation.[19] Although it has been suggested that toxic causes of tremors in veterinary medicine could be reclassified as peripheral nerve hyperexcitability disorders given their irregular frequency, to the author's knowledge, actual myokymia due to toxic disease has not been previously reported in dogs.[15]

Differences of concentration of toxins contained in the different *Urtica* species and individual susceptibility to these toxins may account for the variances of clinical signs observed between reported cases.[7] Excess of acetylcholine receptor stimulation produces nicotinic, muscarinic and central nervous system signs. Hypersalivation described in both dogs and miosis observed in case 1 could be explained by muscarinic receptor overstimulation, whereas involuntary movements and neuromuscular weakness could represent excess of nicotinic activity. These signs are observed most frequently in cases of organophosphate and carbamate toxicity, in which acetylcholinesterase is inhibited, allowing acetylcholine to accumulate synapses resulting in excessive cholinergic stimulation. However, acetylcholinesterase activity measurements were not consistent with organophosphate-carbamate toxicity in our cases. The cough and retching observed could be explained by bronchospasm, which can be caused by both acetylcholine and serotonin excess. Further signs that could be attributed to serotonin excess in the two cases reported include tachypnoea, increased muscle tone, teeth chattering, face rubbing and hyperthermia. Similar signs have been reported in dogs due to increased central nervous system serotonin neurotransmission after selective serotonin reuptake inhibitor overdose or 5-hydroxytryptophan toxicosis, which have been compared with serotonin syndrome in humans.[20] It has also been described that an unidentified neurotoxin of *U ferox* produces loss of myelinated axons and electrophysiological signs of axonopathy in a model of rats.[21] However, this has not been demonstrated in other *Urtica* species. Moreover, the rapid improvement of neuromuscular signs in our cases is not consistent with an axonal damage.

Main differential diagnoses for an acute onset of neuromuscular signs in dogs include botulism, fulminant myasthenia gravis and acute idiopathic polyradiculoneuritis. A toxic aetiology rather than an inflammatory disease was suspected since both cases presented with similar signs on the same day and after being in the same area. Dogs presenting with botulism frequently show cranial nerve dysfunction (eg, facial nerve paralysis) and autonomic signs associated with decreased cholinergic function leading to rapid flaccid tetraplegia which was absent in our two cases. Rapid improvement after a few

hours was also not consistent with myasthenia or idiopathic polyradiculoneuritis.

Haematology and biochemistry were unremarkable in both cases, apart from the increase of creatine kinase, which was mildly elevated. This could reflect neuromuscular disease, fasciculations or be a consequence of increased exercise on the day of presentation. Urinalysis in case 1 revealed haematuria and proteinuria. In a previous report of a dog with nettle toxicosis, urine dipstick was positive for erythrocytes/haemoglobin and it was hypothesised that muscle fasciculations could lead to myopathy and myoglobinuria.[10] Rapid improvement of neuromuscular weakness in both cases precluded the need of an electrophysiological study. In addition, abnormalities may not be detectable initially following the initiation of clinical signs.[22]

The first step in treating nettle exposure is often skin decontamination. Depending on the severity of the clinical signs, serotonin antagonists, atropine or antihistamines should be considered. Chlorphenamine has been reported to contribute to the serotonin syndrome in humans, however no worsening of clinical signs was observed when this drug was administered in case 1.[23] In the case involving *U ferox* in a dog, the recovery time was reported to be two weeks, and full recovery was reported after 36 hours in the dogs affected in the USA.[10 11] Both cases in this report made a full recovery within 72 hours.

Unfortunately, we cannot endorse that other neurotoxins or other *Urtica* species were present in the fields where these two dogs worked, as nettles were not evaluated by a botanist. The clinical signs, history provided, localisation, reiteration and witness of the owner regarding the nettle contact support the possibility of nettle toxicity in our two patients. However, the authors cannot exclude the presence of another toxic substance since the nettles are common and spread in UK. In addition, no further tests to screen for toxics were performed. Therefore, these cases highlight the potential clinical signs that can result from stinging nettles (*U dioica*) and the need for veterinarians to include them in their differential diagnosis of cases presenting acutely with neuromuscular signs, especially in areas where this plant is present.

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