Hansel, an 8-year-old neutered male German shepherd dog, was referred for persistent squinting and an inability to blink his right eye (OD).

**History**
Signs were present for 1 week. Hansel was otherwise normal, was current on vaccinations and heartworm and ectoparasite preventives, and had no pertinent medical history (eg, exposure to toxins, history of trauma). No blepharospasm was reported by the owner.

**Examination**
Physical examination revealed deviation of the nasal planum to the right and slight elevation of the right ear (*Figure 1*). Otoscopic examination was normal. Neurologic examination included evaluation of mentation, gait, postural reactions, spinal reflexes, tone, and muscle mass in all limbs; all were within normal limits. Evaluation of the cranial nerves revealed that the palpebral reflex and menace response were absent OD. A narrowed palpebral fissure OD was noted. Response to stimulation of the nasal mucosa was normal. All other cranial nerve reflexes were normal.
**Diagnostics**
CBC, serum chemistry panel, thoracic radiographs, and thyroid hormone testing (thyrotropin and free thyroxine by equilibrium dialysis) were normal. MRI of the head was normal.

**Diagnostic Considerations**
Anatomic diagnosis: Facial nucleus in the medulla or the facial nerve (cranial nerve VII) or hemifacial tetanus (HT) of the muscles of facial expression, including the obicularis oculi muscle (narrowed palpebral fissure) and levator nasolabialis (deviated nasal planum), or denervation atrophy (contracture) of the facial muscles. The lack of other neurologic deficits suggests the lesion did not involve the medulla.

Differential diagnoses: From the medulla, the facial nerve exits the cranial cavity via the internal acoustic meatus to enter the facial canal within the petrosal portion of the temporal bone. The facial nerve exits the facial canal via the stylomastoid foramen. Once extracranial, the facial nerve courses rostrally just ventral to the external ear canal where it branches. Causes to consider include disease of the middle ear, (eg, otitis media, which secondarily affects the facial nerve), or primary diseases of the facial nerve. Primary diseases include inflammation, neoplasia, aberrant blood vessel compressing the facial nerve, and trauma.

▲ At presentation, the palpebral fissure is narrowed on the right (arrow) as compared with the left. The nasal planum is deviated to the right (arrowhead). The right ear is positioned slightly more caudal on the head as compared with the left ear.

**ASK YOURSELF**
- What is the difference between ptosis and a narrowed palpebral fissure?
- What are the muscles and nerves that may cause a narrowed palpebral fissure?
- What is an appropriate differential list and diagnostic plan for a narrowed palpebral fissure?
On anesthetic induction for MRI, deviation of the nasal planum was not present (arrowhead). The dog’s closed eyelids make it difficult to appreciate the narrowed palpebral fissure. Note the near-symmetrical position of the ears.

In humans, HT is associated with microvascular compression of the facial nerve by aberrant vasculature.

**Diagnosis**
Canine idiopathic HT

**Discussion**
During general anesthesia for the MRI, the patient’s narrowed palpebral fissure, deviation of the nasal planum, and abnormal ear position resolved (Figures 2 and 3). On recovery from anesthesia, the abnormalities returned. This confirmed HT\(^1,2\) and excludes from consideration denervation atrophy (contracture), as relaxation of the muscles under anesthesia would not occur.

HT results in persistent contraction of the facial muscles innervated by the facial nerve. A narrowed palpebral fissure, deviation of the nasal planum toward the affected side, and a caudal position of the ear are seen. Under general anesthesia or with local anesthesia of the facial nerve, muscle activity is inhibited, muscle relaxation ensues, and the patient appears normal.\(^1\) In some cases, ipsilateral, hemifacial paralysis, which then resolves, may precede HT. Used synonymously, *hemifacial spasm* is a misnomer because muscle spasms are not present.

In humans, HT is associated with microvascular compression of the facial nerve by aberrant vasculature. Treatment options (eg, botulinum toxin injections into the affected muscles, surgical microvascular decompression) exist.\(^3\) HT has been reported in 2 dogs secondary to a
brain lesion. In the authors’ experience, HT in dogs mostly occurs secondary to an irritative lesion of the facial nerve. Irritative lesions likely cause excessive activity (depolarization) of the nerve rather than a lack of function.

Diagnostics are aimed at identifying a metabolic disorder or structural lesion of the nerve or its nucleus in the medulla. An otoscopic examination should be performed to evaluate for abnormalities in the external ear canal because the facial nerve runs just ventral to it. A diagnostic evaluation consisting of CBC, serum chemistry panel, urinalysis, and thyroid hormone testing should help identify metabolic causes associated with nerve dysfunction. Finally, MRI of the head is used to evaluate the medulla and the course of the facial nerve. If an underlying cause is not identified, HT is assumed secondary to an irritative lesion. In such cases, supportive treatment aimed at muscle relaxation or empiric therapy for otitis media is not necessary.

Treatment

Given the normal results of the diagnostic testing and presumptive diagnosis, treatment was not pursued. Although the underlying cause is still not fully understood, it appears to remain a benign condition. Owners should be warned that the signs can remain indefinitely.

DID YOU ANSWER?

- Ptosis is the drooping or sagging of a body part, which here refers to a drooping superior eyelid. A narrowed palpebral fissure can result from ptosis, but it may also result from continual contraction of the muscles of the eyelids, blepharospasm, or enophthalmos.

- The orbicularis oculi muscle, innervated by the facial nerve, closes the palpebral fissure. Because of its small size in dogs, denervation rarely causes ptosis. However, denervation atrophy (contracture) of the orbicularis oculi muscle narrows the palpebral fissure. Likewise, continual contraction is observed with HT from an irritative lesion of the facial nerve. Alternatively, tetanus of the facial muscle may be part of generalized tetanus secondary to the toxin elaborated by Clostridium tetani.

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References

Adverse Reactions
NexGard can be administered with or without food. Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes to ensure that part of the dose is not lost or refushed. If it is suspected that any of the dose has been lost or if vomiting occurs within two hours of administration, re-treat with another full dose. If a dose is missed, administer NexGard and resume a monthly dosing schedule.

Avoid Treatment and Consultation: Treatment with NexGard may begin at any time of the year (see Effectiveness).

Contraindications: There are no known contraindications for the use of NexGard.

Warnings: NexGard is for dogs only. Keep this and all drugs out of the reach of children. In case of accidental ingestion, contact a veterinarian immediately.

Adverse Reactions:
NexGard is not effective against fleas on the day of dosing. It may take up to 48 hours for fleas to lose their ability to jump. The occurrence of underdosing was generally self-limiting and of short duration and tended to decrease with subsequent doses in both groups. The incidence of adverse reactions observed during the study, and of two of these dogs experienced anorexia with the first dose but not subsequent doses.

Table 1: Dogs With Adverse Reactions.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Body Weight (lbs)</th>
<th>N</th>
<th>% (in N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afoxolaner</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.4 to 3.0</td>
<td>8</td>
<td>17</td>
<td>4.1</td>
</tr>
<tr>
<td>3.0 to 6.0</td>
<td>13</td>
<td>100</td>
<td>12.5</td>
</tr>
<tr>
<td>4.0 to 10.0</td>
<td>12</td>
<td>100</td>
<td>12.5</td>
</tr>
<tr>
<td>10.0 to 25.0</td>
<td>11</td>
<td>100</td>
<td>9.1</td>
</tr>
<tr>
<td>25.0 to 50.0</td>
<td>25</td>
<td>100</td>
<td>10.0</td>
</tr>
<tr>
<td>Over 50.0</td>
<td>7</td>
<td>100</td>
<td>7.1</td>
</tr>
</tbody>
</table>

For example, in a well-controlled laboratory study, NexGard was given to eight to 12-week-old Beagle puppies at one level. At subsequent evaluations post-infestation, fleas from dogs in the control group were essentially unable to produce any eggs (0-1 eggs) while fleas from dogs in the NexGard treated group continued to produce eggs (1-141 eggs).

To report suspected adverse reactions, for technical assistance or to obtain a copy of the MSDS, contact (1-888-367-4231) OR visit www.nexgard.com. For additional information about adverse drug experience reporting for animal drugs, contact FAX at 1-888-437-1717 or visit http://www.fda.gov/AnimalVeterinary/SafetyHealth/AdverseDrugExperienceReporting.

Toxicity:
NexGard is a member of the isoxazoline family of compounds, which is known to inhibit the enzyme cyclic AMP-dependent protein kinase A, producing its antiparasitic effects. The toxicology of afoxolaner in dogs is primarily dose-dependent. Clinical signs are generally self-limiting and of short duration. In a well-controlled laboratory study, NexGard was administered orally to 8 to 9-week-old Beagle puppies at one level. Additional information about adverse drug experience reporting for animal drugs, contact FAX at 1-888-437-1717 or visit http://www.fda.gov/AnimalVeterinary/SafetyHealth/AdverseDrugExperienceReporting.

Effectiveness:
In a well-controlled laboratory study, NexGard was given to eight to 12-week-old Beagle puppies at one level. At subsequent evaluations post-infestation, fleas from dogs in the control group were essentially unable to produce any eggs (0-1 eggs) while fleas from dogs in the NexGard treated group continued to produce eggs (1-141 eggs).

In a 28-day field study conducted in households with existing flea infestations of varying severity, the effectiveness of NexGard against fleas on the Day 30, 60 and 90 was evaluated with baseline was 98.0%, 98.7% and 98.9%, respectively. Collectively, the data from these three studies show that NexGard is effective against fleas at the prescribed dose.

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Animal Safety:
In a range of safety study, safety of NexGard was assessed by oral dosing to 8- to 9-week-old Beagle puppies at 1, 3 and 5 times the maximum exposure dose (3.0 mg/kg) for three treatments every 28 days, followed by three treatments every 14 days, for a total of 22 treatments. Dogs in the control group were sham-dosed. There were no clinically-relevant effects related to treatment on physical examination, body weight, food consumption, clinical pathology (hematology, clinical chemistry, or coagulation profile), gait, gross pathologic, histopathology or organ weights. Injections occurred throughout the study, with a similar incidence in the treated and control groups, including one dog in the 5x group that vomited four hours after treatment.

Storage Information:
Store at or below 30°C (86°F) with excursions permitted up to 40°C (104°F).

How Supplied:
NexGard is available in four sizes of beef-flavored, soft chewables for oral administration to dogs and puppies according to their weight. Each chewable is formulated to provide a minimum afoxolaner dosage of 1.14 mg/lb (2.5 mg/kg). NexGard has the chemical composition: 4-[(3R)-3-chloro-4-oxo-6-phenylhexyl]-2,5-thiophene-3-carboxamide (I4, 5-thiophene-3-carbonyl)-4-oxo-2-(trifluoromethyl)aniline (I5).

Composition:
NexGard contains afoxolaner, a highly selective, irreversible, and post-synaptic transfer of chloride ions across cell membranes. Prolonged afoxolaner-induced hyperexcitation results in uncontrolled activity of the central nervous system and death of insects and acarines. The selective toxicity of afoxolaner between insects and mammals may be attributed to the differential sensitivity of the insects and acarines to ABA receptors versus mammalian GABA receptors.

安全性:
在一项临床研究中，NexGard在第10天给药后，与对照组相比，治疗组在第21天、第28天和第35天对伊蚊的清除率分别达到99.6%，99.4%和99.2%。本研究中未观察到治疗组的不良反应或毒性。

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How Supplied:
NexGard is available in four sizes of beef-flavored soft chewables: 11.3, 28.3, 88.0 or 156.0 mg afoxolaner. Each chewable size is available in color-coded packages of 1, 3 or 6 flavored chewables.

NADA 141-406, Approved by FDA
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CliniciansBrief.com, June 2016
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