Helium crisis getting you down?

Zero-Helium (ZHM) 1.5T high-field MRI could be the answer

Did you know that helium is a finite resource?

The world's first veterinary-specific small animal MRI is helium-free, giving you improved access to advanced diagnostics.

As part of Q-Care, our unique solution reduces financial, environmental and supply-chain risks.

We speak vet at hallmarq.net

Hallmarq
Advanced Veterinary Imaging

Best in Biz Awards 2022 WINNER

Case Report
J Vet Intern Med 2012;26:1227–1231

Bilateral Sciatic Neuropathy in Dogs Caused by Spontaneous Muscular and Intraneural Hemorrhage

S. Ródenas, M. Pumarola, R.R. Gopegui, and S. Añor

Peripheral neuropathies secondary to hemostatic disorders are well recognized in human medicine, and they are usually secondary to hemophilia or to anticoagulant therapy.[1] Here, we report peripheral neuropathies secondary to bleeding disorders in dogs.

Case 1

A 9-year-old, intact male German Shepherd was evaluated for nonambulatory paraparesis and severe anemia of 3 days duration. The dog had a history of minor trauma with a fence while running a few days before onset of clinical signs. Two days before admission, a complete blood cell count (CBC) performed by the referring veterinarian revealed a nonregenerative anemia (PCV 13%, reference interval [RI] 37–55%; reticulocytes 2.3%, RI 1–3%). The dog was treated with amoxicillin/clavulanic acid[a] (10 mg/kg IV q12h) and prednisone[b] (1 mg/kg IV q12h), with no improvement. On presentation to the hospital, physical examination revealed a lethargic mental status, tachycardia (180 beats/min), prolonged capillary refill time, and pale oral mucous membranes. A soft subcutaneous swelling affecting mainly the biceps femoris, semitendinosus, and semimembranosus muscles, worse in the left pelvic limb, was detected on palpation. Neurologic examination revealed nonambulatory paraparesis with absent postural reactions in the pelvic limbs. Postural reactions and reflexes were normal in both thoracic limbs. The patellar reflex was normal but the withdrawal, gastrocnemius, and cranial tibial reflexes were all decreased. Reduced muscle tone was also noted in both pelvic limbs. Mild hyperesthesia was elicited upon palpation of the caudal lumbar area. Pain sensation was present in the medial aspect of both pelvic limbs, yet appeared markedly reduced to absent in the cranial, lateral, and caudal aspect of both pelvic limbs below the stifle. The perineal reflex was normal. On the basis of the neurologic findings, a bilateral peripheral sciatic neuropathy was considered most likely, but a focal spinal cord lesion or a lesion affecting the L7 nerve roots in the spinal canal was also considered.

Abbreviations:

APTT	activated partial thromboplastin time
CBC	complete blood cell count
CPK	creatine phosphofructokinase
MR	magnetic resonance
PT	prothrombin time
RBC	red blood cells
RI	reference interval
TT	thrombin time
vWF	von Willebrand factor
vWD	von Willebrand disease

CBC disclosed severe regenerative anemia (PCV 11%; reticulocyte count 183,600, RI 0–60,000), neutrophilic leukocytosis (50.6 $\times$ $10^3/\mu L$, RI 6–17 $\times$ $10^3/\mu L$) with a left shift (band neutrophils 3.04 $\times$ $10^3/\mu L$, RI 0–0.3 $\times$ $10^3/\mu L$), and mild thrombocytopenia (108 $\times$ $10^3/\mu L$, RI 200–500 $\times$ $10^3/\mu L$). Serum biochemistry results were all within reference limits except for slightly decreased serum protein concentration (5 g/dL, RI 5.4–7.1 g/dL). A blood coagulation profile revealed normal prothrombin time (PT), normal activated partial thromboplastin time (APTT), and increased fibrinogen concentration (626 mg/dL, RI 200–400 mg/dL). Results of thoracic radiographs and abdominal ultrasound were normal. On the basis of the history, physical and neurologic examinations, and CBC findings, an acute expanding hematoma affecting both pelvic limbs and a regenerative anemia secondary to a hemostatic disorder were considered most likely. Emergency treatment included fluid therapy using lactated Ringer's solution[c] (1 mL/kg/h IV) supplemented with potassium chloride[d] (20 mEq/L), cephazoline[e] (20 mg/kg IV q8h), vitamin K[f] (1 mg/kg SQ q24h), prednisone (2 mg/kg IV q24h), and ranitidine[g] (2 mg/kg IV q12h). In addition, a transfusion of 1 unit of fresh frozen plasma and 1 unit of packed red blood cells (RBCs) was given. Physical examination on day 2 revealed tachycardia (150 beats/min) and pale oral mucous membranes. The PCV was 13% and serum total protein concentration was 5.5 mg/dL. On day 4, the mass in the right pelvic limb had resolved and the one in the left pelvic limb had considerably decreased in size, but the neurologic deficits in the pelvic limbs persisted. CBC revealed a regenerative anemia (PCV 20%, reticulocytes 65.760) and neutrophilic leukocytosis (98.2 $\times$ $10^3/\mu L$) with 1.1 $\times$ $10^3/\mu L$ band neutrophils. Serum biochemistry abnormalities included increased alanine aminotransferase (123 U/L, RI 21–102 U/L), creatine

From the Department of Animal Medicine and Surgery, Veterinary School, Autonomous University of Barcelona, Barcelona, Spain (Ródenas, Pumarola, Gopegui, Añor). *This work was presented at the ESVN-ECVN 20th Annual Symposium; Berna, Switzerland, September 2007.*

Corresponding author: S. Añor, Patologia General i Médica, Facultat de Veterinària, Universitat Autònoma de Barcelona, 08193 Bellaterra (Barcelona), Spain; e-mail: sonia.anor@uab.es.

Submitted March 8, 2012; Revised April 13, 2012; Accepted May 22, 2012.

Copyright © 2012 by the American College of Veterinary Internal Medicine

10.1111/j.1939-1676.2012.00962.x

phosphofructokinase (CPK) (8,991 U/L, RI 10–150 U/L), and alkaline phosphatase (597 U/L, RI 20–156 U/L). Serum total protein concentration was within normal limits (5.6 g/dL), but electrophoresis revealed mild hypoalbuminemia (2.29 g/dL, RI 2.6–3.3 g/dL) and increased α1 (0.84 g/dL, RI 0.2–0.5 g/dL) and α2 (1.8 g/dL, RI 0.3–1.1 g/dL) globulin fractions. Repeat coagulation profile revealed persistent hyperfibrinogenemia (560 mg/dL). Magnetic resonance (MR) imaging of the lumbar spine (L1-S1) was performed using a 0.2-Tesla magnet.[h] T1 weighted (pre and post contrast) and T2 weighted images were acquired in dorsal, sagittal, and transverse planes. The only abnormality seen on the MR images was a degenerated and mildly protruded disk at the L7-S1 intervertebral space, which could not explain the neurologic status of the animal. On day 8, a new CBC revealed mild regenerative anemia only (PCV 26%; reticulocytes 77,400). A coagulation profile, including D-dimers concentration, was also performed. Results of this revealed a mild increase in thrombin time (TT) (19.9 seconds, RI 14–18 seconds) and increased D-dimers concentration (>1,000 ng/mL, RI < 250 ng/mL). In addition, von Willebrand factor (vWF) activity and factor VIII concentration were determined to rule out the most common hemostatic diseases affecting German Shepherds in Europe, vWD and hemophilia. Results of vWF activity (214%, RI 70–100%) and concentration of factor VIII (89%, RI 80–140%) were not consistent with these diseases. Nine days after presentation, because of lack of neurologic improvement and poor prognosis, the owners elected to humanely euthanize the animal.

At necropsy, the main gross changes were found in the pelvic limbs and lumbar area. The subcutaneous and interstitial tissues in the pelvic limbs were edematous and filled with multiple focal or diffuse large hemorrhages. Furthermore, muscle fascicles of the proximal pelvic limbs showed tumefaction, laceration, and rupture of fibrils. Both sciatic nerves had a reddish discoloration. Multiple reddish areas were also visualized in all abdominal viscera, but were more prominent in the kidneys, which showed multiple hemorrhagic foci of approximately 0.5-cm diameter. A large (5 × 7 cm) pale zone was present in the splenic parenchyma. Microscopically, large amounts of erythrocytes mixed with an abundant inflammatory infiltrate formed by neutrophils and mononuclear cells were found in the pelvic limb muscles. These showed numerous fragmented fibers with coagulative necrosis, marked edema, and a mild inflammatory infiltrate (Fig 1A). Numerous hemorrhages were observed in the endoneurium of both sciatic nerves, surrounding vessels, and nerve fascicles (Fig 1B,C). The hemorrhages were intermixed with fragmented axons and myelin sheaths. In addition, numerous digestion chambers indicative of Wallerian degeneration were also observed (Fig 1D). An abundant mixed inflammatory infiltrate was present in the epineurium. In addition, large interstitial hemorrhages mixed with inflammatory cells were observed in the kidneys, a large necrotic area with thrombi occluding the lumen of some vessels was observed in the spleen, and extramedullary hematopoiesis was detected in both the spleen and liver. The histopathologic findings were consistent with necrosis and hemorrhage with hematoma formation within pelvic limb muscles, intraneural hemorrhages in the sciatic nerves, focal splenic necrosis, and multiple renal hematomas.

Case 2

A 5-year-old intact male German Shepherd was referred for a 3-day history of acute, nonprogressive, nonambulatory paraparesis and development of a subcutaneous fluid accumulation in both pelvic limbs that extended ventrally to the abdomen and thorax. The owners did not report any traumatic event. Physical examination abnormalities included pale oral mucous membranes and a soft subcutaneous swelling affecting both pelvic limbs entirely and extending ventrally to the thorax. Neurologic examination revealed nonambulatory paraparesis, absent postural reactions in both pelvic limbs, and decreased withdrawal and gastrocnemius reflexes bilaterally. Pain sensation was absent in the cranial, caudal, and lateral aspect of both pelvic limbs below the middle of the femur. Pain sensation was normal in the medial aspect of the left pelvic limb and decreased in the medial aspect of the right pelvic limb. The patellar and perineal reflexes were normal. Neurologic deficits were consistent with a bilateral sciatic peripheral neuropathy. CBC disclosed a regenerative anemia (PCV 13%; reticulocyte count 151,000), mild thrombocytopenia ($155 \times 10^3/\mu L$), and neutrophilic leukocytosis ($31 \times 10^3/\mu L$) with $25.6 \times 10^3/\mu L$ mature neutrophils. Serum biochemistry abnormalities included decreased serum total protein concentration (4.89 g/dL), and increased CPK (6,734 UI/L). Serum protein electrophoresis revealed mild hypoalbuminemia (2.36 g/dL). The only abnormality found in the coagulation profile was mild hyperfibrinogenemia (546.4 mg/dL). Results of vWF activity and concentration of factor VIII were within normal limits. Thoracic radiographs and abdominal ultrasound did not reveal any abnormalities. The dog was transfused 1 unit of fresh frozen plasma and 1 unit of packed RBCs. Fluid therapy with lactated Ringer's solution (1 mL/kg/h IV) supplemented with potassium chloride (20 mEq/L) was initiated. Cephazoline (20 mg/kg IV q8h), prednisone (2 mg/kg IV q24h), and ranitidine (2 mg/kg IV q12h) were also administered. Four days after the initial presentation the dog was humanely euthanized because of persistent neurologic dysfunction. At necropsy, gross findings included diffuse subcutaneous edema, as well as large hemorrhages and hematomas affecting the left pelvic limb, abdominal and thoracic muscles, and, to a lesser degree, the right pelvic limb muscles. All the viscerae had a reddish discoloration and petechial hemorrhages were observed in the pancreas, kidneys, and lungs. Both sciatic nerves appeared reddish. Histopathologically, there were diffuse hemorrhages affecting all muscles of the pelvic limbs, which had large

19391676, 2012, 5, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/j.1939-1676.2012.00962.x by Consorci De Serveis Universitaris De Catalunya, Wiley Online Library on [18/05/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

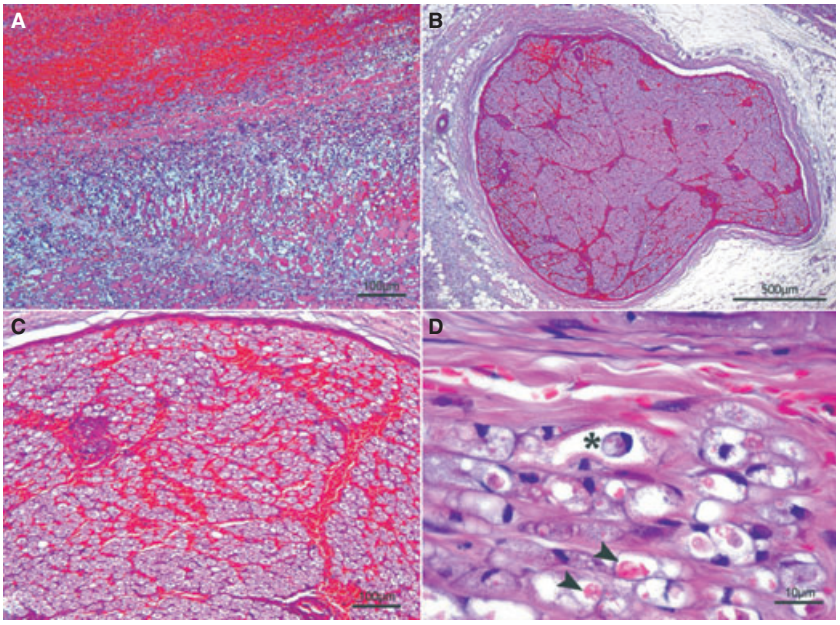

Fig 1. (**A**) Photomicrograph of the semitendinosus muscle in case 1 showing the presence of hemorrhage and abundant inflammatory cells infiltrating muscle fiber fascicles. Hematoxilin and eosin. Bar = 100 μm. (**B**) Transverse view of the affected sciatic nerve. Note the presence of the hemorrhages in the endoneurium. Hematoxilin and eosin. Bar = 500 μm. (**C**) Detail of Figure 1B Intraneural hemorrhages surrounding vessels and nerve fascicles. Hematoxilin and eosin. Bar = 100 μm. (**D**) Photomicrograph of a transverse section of the affected sciatic nerve. Note the presence of altered fibers causing myelin fragmentation (arrow heads) and digestion chambers (asterisk). Hematoxilin and eosin. Bar = 10 μm.

amounts of atrophied fibers. Numerous epineural and endoneural hemorrhages were observed in both sciatic nerves (Fig 2). The vessel wall of endoneural small arterioles showed segmental fibrinoid necrosis (Fig 3) of the media and a transmural mixed inflammatory infiltrate (lymphocytes and macrophages, neutrophils undergoing leukocytoclasis in the necrotic areas, and few eosinophils and plasma cells). Adjacent nerve fibers showed axonal fragmentation, myelin sheath dilatation, and digestion chambers indicative of Wallerian degeneration. Purulent inflammatory cells from the vessel walls infiltrated the endoneurium. Alteration of the normal histologic architecture of different organs (skeletal muscles, pancreas, liver, and brain) was observed associated with perivascular hemorrhages or edema, and pyknotic smooth muscle fibers in the vessel wall of medium-sized arteries. The histopathologic findings were consistent with muscular hemorrhages, hematoma formation, intraneural hemorrhages, and intraneural and systemic necrotizing vasculitis.

The initial differential diagnoses that could explain spontaneous bleeding in the dogs of this report included vWD, inherited or acquired coagulation

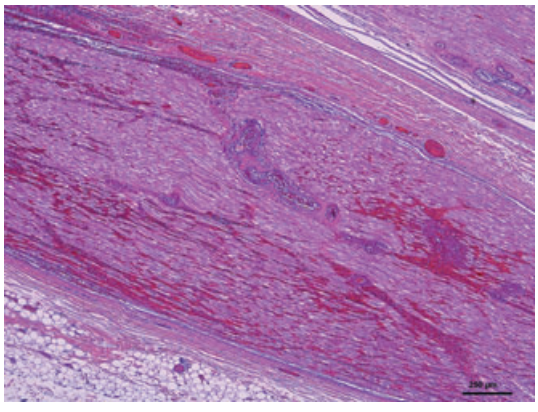

Fig 2. Sagittal view of one of the affected sciatic nerves in case 2. Note the presence of numerous hemorrhages in the epineurium and the endoneurium. Hematoxilin and eosin. Bar = 250 μm.

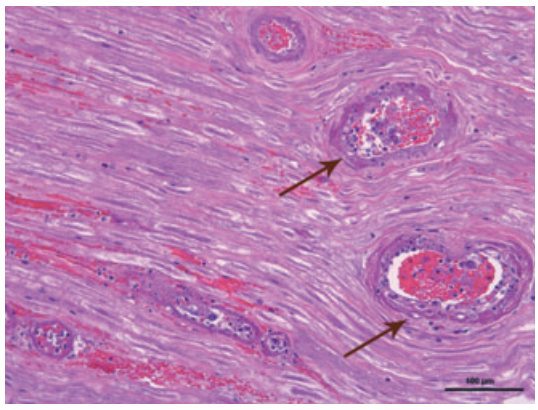

Fig 3. Transverse view of the sciatic nerve in case 2. Note several affected vessels in the endoneurium showing segmental fibrinoid necrosis and infiltration by mixed inflammatory cells (arrows). Hematoxilin and eosin. Bar = 100 μm.

19391676, 2012, 5, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/j.1939-1676.2012.00962.x by Consorci De Serveis Universitaris De Catalunya, Wiley Online Library on [18/05/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

disorders, platelet disorders, and vasculopathies. Thrombocytopenia and inherited or acquired coagulation disorders were considered unlikely on the basis of the results of CBCs and clotting profiles (normal APTT and PT). The vWF activity in these dogs was within reference ranges, thus vWD was excluded as the cause of bleeding. Diseases that affect vessel walls, such as vasculitis, were ruled out by means of lab work and necropsy findings in the first dog. In the second dog, the presence of necrotizing vasculitis associated with hemorrhages in the sciatic nerves, and the histologic signs of systemic vasculitis raise the question whether the bleeding was secondary to a vasculopathy. Because changes indicating vasculitis were only observed in the endoneurial vessels of the sciatic nerve, we assume that these were secondary to the increased intraneural pressure attributable to hemorrhages together with the presence of inflammatory cells in the endoneurium. Peripheral nerve vasculitides are well classified in humans beings and can be confined to the peripheral nerves or can be generalized with peripheral nerve involvement.[2] Case 2, should be included in the group of generalized vasculitis with peripheral nerve involvement.[2,3] The presence of massive bleeding in the second dog lead to the thought that the predisposing cause of the hemorrhages was most likely a secondary rather than a primary hemostatic disorder such as a thrombopathy or vasculopathy.[4] However, a primary unknown vessel disorder causing these hemorrhages could not be ruled out. Acquired thrombopathies were ruled out on the basis of the history, blood tests, and normal abdominal ultrasound and thoracic radiographs.

Whether the bleeding and hematoma formation in these dogs were a result of trauma or were caused by an unknown platelet dysfunction or vascular disorder is uncertain. However, trauma associated with an unknown thrombopathy or vascular disorder was considered the most likely cause of bleeding in the first case because of the lack of ante and postmortem findings indicative of a predisposing cause. CNS signs secondary to traumatic and nontraumatic bleeding have been described in veterinary medicine.[5–8] In contrast, peripheral nerve injuries caused by hemorrhages or hematomas have not been described in dogs to the authors' knowledge. Over the last few years, several articles describing neuropathies secondary to bleeding disorders in human beings have been published.[9–11] In these descriptions, the most common causes of neuropathy and muscular bleeding are hemophilia and anticoagulant therapy.[9,12,13] However, despite most muscular hemorrhages being described in patients with hemostatic disorders, spontaneous hemorrhages have also been reported in patients with normal coagulation.[14] The most common cause of neuropathies caused by bleeding disorders is nerve compression caused by intramuscular hemorrhage.[9] After intramuscular bleeding, polymorphonuclear cells accumulate, mononuclear phagocytosis begins and fibrous repair tissue is formed.[12] The usual mechanism of nerve injury is a result of compression or traction of the nerve caused by the hemorrhagic mass.[12,15] The degree and extent of nerve damage are related to the rate at which compression develops and to the duration of compression.[9] Although less common, intraneural hemorrhage has also been reported in human beings.[16–18] Intraneural hematomas may occur spontaneously secondary to bleeding disorders or after nerve traction injuries with rupture of the nutrient vessels.[13] In the dogs of this report, bilateral compression of both sciatic nerves was suspected on the basis of the presence of a hemorrhagic swelling in both pelvic limbs and the results of the neurologic examination.

In conclusion, this is a report of a peripheral neuropathy secondary to intramuscular bleeding in dogs. Another unique feature of the cases reported here is the presence of concurrent intraneural hemorrhage. Thus, intraneural hemorrhage should be included in the differential diagnosis of dogs with focal peripheral neuropathies of acute onset.

Footnotes

[a] Augmentine inyectable, GlaxoSmithKline, SA, Madrid, Spain
[b] Urbason 40 mg, Aventis Pharma, SA, Madrid, Spain
[c] Lactato de ringer Braun, B. Braun Medical, SA, Rubí, Barcelona, Spain
[d] Cloruro potásico 14.9%, B. Braun Medical
[e] Kurgan 1 g, Normon, SA, Madrid, Spain
[f] Konakion 10 mg, Roche farma, SA, Madrid, Spain
[g] Zantac injectable, GlaxoSmithKline
[h] Vet-MR, Esaote, SpA, Genoa, Italy

References

1. Saraf SK, Singh OP, Singh VP. Peripheral nerve complications in haemophilia. J Assoc Physicians India 2003;51:167–169.

2. Davies L, Spies JM, Pollard JD, et al. Vasculitis confined to the peripheral nerves. Brain 1996;119:1441–1448.

3. Kissel JT, Collins MP. Peripheral nerve vasculitis. In: Younger DS, ed. Motor Disorders, 1st ed. Philadelphia, PA: Lippincott, Williams & Wilkins; 1999:243–246.

4. Brooks M. Coagulopathies and thrombosis. In: Ettinger SJ, Feldman EC, eds. Textbook of Veterinary Internal Medicine, 5th ed. Philadelphia, PA: WB Saunders; 2000:1829–1841.

5. Applewhite AA, Wilkens BE, McDonald DE, et al. Potential central nervous system complications of von Willebrand's disease. J Am Anim Hosp Assoc 1999;35:423–429.

6. Thompson MS, Kreeger JM. Acute paraplegia in a puppy with hemophilia A. J Am Anim Hosp Assoc 1999;35:36–37.

7. Muhle AC, Kircher P, Fazer R, et al. Intracranial haemorrhage in an eight-week-old puppy. Vet Rec 2004;154:338–339.

8. Okada M, Koie H, Kitagawa M, et al. MRI findings of haematomyelia in a dog with spontaneous systemic haemorrhage. Aust Vet J 2006;84:332–335.

9. Katz SG, Nelson IW, Atkins RM, et al. Peripheral nerve lesions in hemophilia. J Bone Joint Surg Am 1991;73:1016–1019.

10. Parmer SS, Carpenter JP, Fairman RM, et al. Femoral neuropathy following retroperitoneal hemorrhage: Case series and review of the literature. Ann Vasc Surg 2006;20:536–540.

19391676, 2012, 5, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/j.1939-1676.2012.00962.x by Consorci De Serveis Universitaris De Catalunya, Wiley Online Library on [18/05/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

11. Ehrmann L, Lechner K, Mamoli B, et al. Peripheral nerve lesions in haemophilia. J Neur 1981;225:175–182.

12. Balkan C, Kavakli K, Karapinar D. Iliopsoas haemorrhage in patients with haemophilia: Results from one centre. Haemophilia 2005;11:463–467.

13. Rayan GM, Pitha JV, Wisdom P, et al. Histologic and electrophysiologic changes following subepineurial hematoma induction in rat sciatic nerve. Clin Orthop Relat Res 1988;229:257–264.

14. Marquardt G, Barduzal S, Leheta F, et al. Spontaneous haematoma of the iliac psoas muscle: A case report and review of the literature. Arch Orthop Trauma Surg 2002;122:109–111.

15. Vijayakumar R, Nesathurai S, Abbott KM, et al. Ulnar neuropathy resulting from diffuse intramuscular hemorrhage. Arch Phys Med Rehabil 2000;81:1127–1130.

16. Kokkinakis M, Hinsche A, Rajeev A. Spontaneous intraneural haematoma causing acute neuropathy of the median nerve. J Hand Surg 2009;34:280.

17. Cordingley FT, Crawford GPM. Ulnar nerve palsy in a haemophiliac due to intraneural haemorrhage. Br Med J 1984;289:18–19.

18. Poppi M, Staffa G, Martinelli P, et al. Neuropathy caused by spontaneous intraneural hemorrhage. Neurosurgery 1991;28:292–295.

19391676, 2012, 5, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/j.1939-1676.2012.00962.x by Consorci De Serveis Universitaris De Catalunya, Wiley Online Library on [18/05/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License