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Suspected Secondary Thiafentanil Intoxication in a Captive Mountain Lion (*Puma concolor*)

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ABSTRACT: Inadvertent ingestion of thiafentanil oxalate by a captive adult female mountain lion (*Puma concolor*) caused a prolonged clinical syndrome that included sedation and depression, muscle tension, and myopathy that was incompletely antagonized by naltrexone HCl. A serum chemistry profile revealed markedly elevated creatinine phosphokinase (CK; 490,450 IU/l), alanine aminotransferase (ALT; 1,896 IU/l), and aspartate aminotransferase (AST; 4,321 IU/l) 2 days after onset. The affected animal's condition gradually improved over the next 15 days in response to supportive therapy that included diazepam (5 mg as needed), Normasol R® (3 l/day), dexamethasone (tapering dose starting at 1 mg/kg), and ketoprofen (1 mg/kg). She eventually recovered completely. Based on these observations, carcasses of animals immobilized with thiafentanil should be marked and disposed of properly to preclude opportunities for secondary exposure and potential intoxication in scavenging species. In addition, caution is advised when using thiafentanil in animals that could be preyed upon before full metabolism of the drug.

Key words: A3080, intoxication, mountain lion, opioid, puma, *Puma concolor*, secondary poisoning, thiafentanil.

Thiafentanil oxalate (A-3080) (Wildlife Pharmaceuticals Inc., Fort Collins, Colorado, USA), a potent opioid anesthetic, has been used to immobilize a variety of wild ungulates including Rocky Mountain elk (*Cervus elaphus nelsoni*) (Stanley et al., 1988), impala (*Aepyceros melampus*) (Janssen et al., 1993), pronghorn (*Antilocapra americana*) (Kreeger et al., 2001), and mule deer (*Odocoileus hemionus*) (Wolfe et al., 2004). As with other synthetic opioids, narcotic effects of thiafentanil in these species can be completely antagonized by naltrexone HCl and closely related drugs. There are no published data available on the effect of thiafentanil in large carnivores, but as a general rule opioids are not recommended for use in felids (Wallach et al., 1967; Kreeger et al., 2002). Here, we report a case of inadvertent ingestion of thiafentanil by an adult mountain lion (*Puma concolor*) that caused severe and sustained depression, muscle tension, and myopathy, which only partially reversed with naltrexone HCl.

Since October 2001, three sibling, hand-raised mountain lions (one spayed female and two castrated males) were held at the Colorado Division of Wildlife's Foothills Wildlife Research Facility near Fort Collins, Colorado. All three were housed in a common outdoor enclosure and shared food and water sources. Since March 2002, their diet consisted almost entirely of carcasses of freshly culled and vehicle-killed mule deer and elk that were stored frozen at −20 C until fed as part of an ongoing study (L. L. Wolfe and M. W. Miller, unpubl. data) on chronic wasting disease (CWD; Williams and Young, 1980) susceptibility in mountain lions. Culled animals were usually either shot with a high-power rifle or darted with a tiletamine–zolazepam (250 mg) and xylazine (200 mg) mixture and given a lethal intravenous (IV) injection of KCl. Most of the individual deer and elk consumed by these mountain lions were naturally infected with CWD.

On 4 December 2003, the mountain lions were fed the carcass of a free-ranging male mule deer from which the gastrointestinal tract had been removed. The following day (day 1), about 18 hr after they received this carcass, a caretaker reported a suspected injury and unusual behavior in the female. On initial examination, the affected animal was alert and responsive but had hind limb ataxia, mydriasis, ptyalism, and was vocalizing in an unusual manner;

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in addition, she appeared frightened and somewhat agitated. Because of her agitation, vital signs were not assessed at that time. Based on the history and clinical signs, we suspected drug intoxication and removed the remainder of the carcass suspected to be the source of her intoxication. We initially presumed the reaction to be secondary to oral tiletamine-zolazepam (250 mg)-xylazine (200 mg) exposure because that drug combination was used for most deer that were chemically immobilized before euthanasia. However, upon reviewing mule deer capture records after the initial clinical examination, we determined that the deer in question had been immobilized on 30 October 2003 with 10 mg of thiafentanil oxalate and 100 mg of xylazine HCl delivered via dart injection in the hind leg, and the deer was killed <10 min after immobilization with IV KCl. Because the deer was euthanized shortly after immobilization, we surmised that drug residue may have remained at the dart site. The carcass had been stored frozen since euthanasia, and then thawed at approximately 20 C for about 1 day before it was fed to the mountain lions in late afternoon. Because the feeders did not observe the lions consuming the carcass, we do not know the actual time interval between when the female fed on this carcass and when clinical signs were first noticed.

Clinical evaluation of the affected female about 4 hr after signs were first observed revealed that the foregoing signs were still apparent, and that her condition had not improved. The affected animal was given subcutaneous (SC) injections of 100 mg of naltrexone HCl (Wildlife Pharmaceuticals) and 5 mg of yohimbine HCl (Wildlife Pharmaceuticals). Within 6 min her pupil size was normal, drooling cleared, and coordination had improved significantly. Based on these clinical improvements, no other treatments (e.g., emetics, activated charcoal, or supportive care) were given at that time.

Aside from slight apprehension presumably caused by the behavior of the affected female, neither of the males showed any unusual behavior or other clinical signs of intoxication. Although these lions were housed together, they usually fed individually, and the female was often the dominant feeder. We therefore suspect that the female may have consumed the portion of the carcass with the dart site before the males fed and consequently was exposed to the highest drug residue.

The next day (day 2), the affected female was again vocalizing, agitated, biting at the chain-link wire of the enclosure, and nonambulatory. On physical examination, vital signs were normal. Lower motor reflexes also appeared normal, but generalized muscle tone was increased. We initiated supportive care using intramuscular (IM) injections of diazapam (5 mg) as needed to relieve anxiety and agitation (five injections were given over 24 hr), 3 l/day of fluid (Normasol R®, Abbot Laboratories, North Chicago, Illinois, USA) SC for 9 days, and tapering-dose SC dexamethasone (1 mg/kg on days 1–3; 0.5 mg/kg on days 4–6; 0.2 mg/kg on days 7–8) (Vedco Inc., Saint Joseph, Missouri, USA). Naltrexone (100 mg) was given SC every 24 hr on days 2 through 4 to prevent or treat delayed opioid uptake or recycling; however, unlike the first injection, we saw no immediate response. Because clinical signs were not consistent with xylazine toxicity, yohimbine was not repeated. The affected female was moved to an indoor enclosure. We collected blood via cephalic venipuncture for complete serum chemistry profile and complete blood count (CBC) performed at the Colorado State University Diagnostic Laboratory (Fort Collins, Colorado). We discontinued diazepam once anxiety was relieved. Despite treatment, the animal was anorexic and unable to stand.

Supportive care was continued for 8 days. Recovery was gradual but progressive. On day 4, after 3 days of continued supportive care, the affected mountain lion was able to sit up and stand with assistance, and was eating. By day 8 she was

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able to walk unassisted, but still showed noticeable stiffness in the hind limbs and fatigued after a few steps. Dexamethasone administration was discontinued on day 8, but the affected animal appeared to become painful. Consequently, we treated with ketoprofen (1 mg/kg SC, daily) (Fort Dodge Animal Health, Fort Dodge, Iowa, USA) for 5 days to provide analgesia. On day 9 we repeated blood chemistry profile and CBC to monitor progress. By day 15, she was able to walk almost normally and jump onto low platforms.

Serial serum chemistry profiles demonstrated marked changes in muscle-associated enzymes early in the clinical course. Abnormalities in the serum chemistry profile on day 2 included extremely elevated creatinine phosphokinase (CK) (observed, 490,450 IU/l; normal, 442 IU/l; Wack, 2003), elevated alanine aminotransferase (ALT) (observed, 1,896 IU/l; normal, 44 IU/l; Wack, 2003), and aspartate aminotransferase (AST) (observed, 4,321 IU/l; normal, 36 IU/l; Wack, 2003). By day 9, both ALT and AST levels had returned to normal ranges, and CK had decreased to 1,212 IU/l. When revaluated 5 months later, all serum chemistry values for the affected animal were within normal limits.

Based on changes in serum chemistry profiles, we attributed most of the observed clinical problems and prolonged recovery to severe muscle damage caused by sustained, thiafentanil-induced muscle rigidity. Elevation in serum CK concentration reflects both occurrence and relative severity of myopathy (Ishak, 2004). Although elevations in the aminotransferases ALT and AST can arise from either skeletal muscle or liver damage, the ratio of AST:ALT concentrations and elevated CK suggested that the most likely cause of serum chemistry abnormalities was skeletal muscle damage (Ishak, 2004). The precise mechanism causing the observed muscle rigidity and subsequent myopathy is unclear. Elevations in blood urea nitrogen (observed, 73 mg/dl; normal, 29 mg/dl; Wack, 2003) and slight elevations in creatinine (observed, 3.2 mg/dl; normal, 2.4 mg/dl; Wack, 2003) indicated minimal renal changes. Capture (or exertional) myopathy (CM) also presents as hind limb weakness and ataxia as well as markedly elevated CK levels (Spraker, 1982). We ruled out CM per se as the cause of the observed problems because there was no history of exertion or handling in the affected animal. However, chronic muscle tension stimulated by thiafentanil may have led to similar physiological processes as occur in CM, resulting in myopathy and elevated muscle-associated enzymes. Supportive fluid therapy may have prevented myoglobin-associated renal damage, as occurs in CM (Spraker, 1982).

The unusual clinical syndrome that we observed shared clinical signs of two potentially important diseases of captive felids: feline spongiform encephalopathy (FSE) and rabies. Feline spongiform encephalopathy is a prion disease affecting both domestic and nondomestic, captive felids, including mountain lions, that had presumably consumed carcasses or products from cattle infected with bovine spongiform encephalopathy (BSE) (Gruffydd-Jones and Pearson, 1991; Wyatt et al., 1991; Willoughby et al., 1992; Kirkwood and Cunningham, 1994; Ryder et al., 2001). Common clinical findings of FSE include an abnormal gait characterized by ataxia, hypermetria, and dysmetria (Wyatt et al., 1991). In addition, both domestic and captive wild cats with FSE were described as showing abnormal behavior that included hyperaesthesia, muscle fasciculation, and hypersalivation (Gruffydd-Jones and Pearson, 1991; Wyatt et al., 1991; Willoughby et al., 1992; Kirkwood and Cunningham, 1994; Ryder et al., 2001). Because the affected cat in this report had been consuming deer and elk naturally infected with CWD, we initially considered FSE as a differential diagnosis even though onset seemed too acute. Signs of rabies in wild felids also include many of the same clinical signs, as well as aggression (Rupprecht et al., 2001). Rabies

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was unlikely in this case because the affected animal had been vaccinated (Rabvac®, Fort Dodge Laboratories, Fort Dodge, Iowa, USA) and because exposure to terrestrial rabies in Colorado was improbable (Colorado Department of Public Health and Environment, 2003). Both FSE and rabies were ruled out based on response to therapy, clinical pathology findings, and ultimately, on full recovery of the affected animal.

The clinical syndrome described here does not appear to be attributable to generalized drug susceptibility in mountain lions; the three individuals in this report have fed upon numerous carcasses of deer immobilized with tiletamine-zolazepam-xylazine, both before and after the intoxication incident, without apparent adverse effects. This case of suspected secondary opioid intoxication emphasizes the importance of proper marking and disposal of animals captured with chemical immobilization agents to prevent inadvertent exposure of predatory or scavenging species, including human beings.

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