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1 **Spondyloarthropathy in vertebrae of the aquatic Cretaceous snake *Lunaophis***
2 ***aquaticus*, and its first recognition in modern snakes**
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13

Abstract

14 Arthritis is documented for the first time in snakes. Ossification of the intervertebral
15 capsule and zygapophyseal joints resulting in segmental vertebral fusion was observed in
16 the aquatic Cretaceous snake *Lunaophis aquaticus*. Such pathologic alterations are
17 pathognomonic for the spondyloarthropathy form of inflammatory arthritis. The alterations
18 are easily distinguished from vertebral fractures because of the absence of collapse and
19 from osteomyelitis and neoplasia because of absence of destructive changes and reactive
20 new bone formation. A survey of 2144 snakes in recent collections, performed to identify
21 Holocene prevalence, revealed only two occurrences in extant snakes. The findings in *Bitis*
22 *gabonica* and *Elaphe taeniura* were indistinguishable from those noted in *Lunaophis*
23 *aquaticus* and identical to those previously recognized in modern varanids. The pathology
24 likely represents a form of reactive arthritis related to enteropathic infection. While the

25 disease probably did not affect general locomotion, its vertebral column position may have
26 compromised mating.

27 **Keywords** Spondyloarthropathy • Mesozoic • Marine snakes • South America • Venezuela

28

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37 collaboration.

38

39 **Introduction**

40 *Lunaophis aquaticus* is a representative of an early lineage of snakes that exploited tropical
41 marine pelagic environments of Cretaceous northern South America (Albino et al. 2016). It
42 is known by several precloacal vertebrae from sediments of the Cenomanian La Luna
43 Formation in the Andes of Venezuela. A short portion of articulated vertebral column of
44 this snake reveals an osseous pathology previously unreported in any snake.

45 Reported cases of snake postcranial osseous pathology have been limited to those of
46 traumatic, infectious and neoplastic (tumor) origin (Isaza et al. 2000; Rothschild et al.
47 2012). The report suggesting Paget's disease was diagnosed on the basis of disorganized
48 osseous architecture (Frye and Carney 1974). Although a viral cause (based on electron
49 microscopically recognized structures suggested of measles or respiratory syncytial virus in
50 humans) has been suggestive for Paget's disease (Altman and Singer 1980), the bone
51 alterations in Frye and Carney (1974) have been reinterpreted as representing bacterial
52 osteomyelitis (Rothschild and Martin 2006; Rothschild et al. 2012). The two are
53 morphologically distinguishable on the basis of gross morphology, but not histology.

54 In this study, we describe the occurrence of spondyloarthropathy in vertebrae of
55 *Lunaophis aquaticus*. Spondyloarthropathy is a form of arthritis in which the margins of
56 vertebrae are bridged through either the outer layers of intervertebral disks or joint capsules
57 (Resnick 2006; Rothschild and Martin 2006). This pathology has been previously
58 recognized in extant varanids and crocodylians (Rothschild 2008) and in the fossil record of
59 mosasaurs (Rothschild and Everhart 2015), but not for either fossil or Recent snakes
60 (Rothschild et al. 2012). We provide evidence supporting the diagnosis of this pathology in
61 *Lunaophis*, which constitutes the first instances of this kind of arthritis in snakes (both from

62 a phylogenetic and from a chronologic perspective). Additionally, we surveyed extant
63 snake collections to determine the occurrence and prevalence of the phenomenon.

64 **Materials and methods**

65 The pathologic fossil vertebrae investigated in this study are catalogued and stored at the
66 collection of the Museo de Ciencias Naturales de Caracas, Venezuela (MCNC). The
67 specimen was composed of the vertebral remains of a single individual, preserved in a
68 small block of black shale (MCNC-1827). All vertebrae are consistent in size,
69 corresponding to a 1.5 meters long snake. The remains include four isolated prelocal
70 vertebrae (MCNC-1827-A, MCNC-1827-B, MCNC-1827-C, MCNC-1827-D), an isolated
71 anterior vertebra (MCNC-1827-E), five mid- or posterior prelocal vertebrae (MCNC-
72 1827-F), and a poorly preserved vertebral fragment (MCNC-1827-G). The pathologic
73 vertebrae correspond to the segment MCNC-1827-F.

74 Snakes in the collections of the American Museum of Natural History (AMNH),
75 Carnegie Museum (CM), National Museum of Natural History (NMNH) and Texas
76 Memorial Museum (TMM) were examined by epi-illumination microscopy (Dino-lite,
77 AM7915MZT, Dunwell Tech, Inc, 19803 Hamilton Ave #200, Torrance CA 90502) for
78 vertebral bridging and fusion.

79 Spondyloarthropathy was recognized on the basis of intervertebral margin ossification
80 producing bridging/fusion of otherwise intact vertebrae (Resnick 2002; Rothschild and
81 Martin 2006), in the absence of vertebral compression characteristic of fractures and the
82 destructive bone changes with draining fibriscesses characteristic of osteomyelitis and mass
83 effect of neoplasia (Resnick 2002; Rothschild and Martin 2006; Rothschild et al. 2012).
84 Anterior longitudinal ligament ossification is a diagnostic characteristic of a phenomenon
85 referred to as diffuse idiopathic hyperostosis (DISH), when capsule fusion is not present

86 (Resnick 2002; Rothschild and Martin 2006). Its presence, however, does not rule out
87 spondyloarthropathy, which is also associated with such ligamentous ossification (Resnick
88 2002; Rothschild and Martin 2006). The presence of intact intervertebral spaces allowed
89 spondyloarthropathy to be distinguished from congenital block vertebrae (Burnham et al.
90 2013; Resnick 2002; Rothschild and Martin 2006; Rothschild et al. 2012).

91 **Geological setting**

92 The vertebrae of *Lunaophis aquaticus* were found exposed in a quarry of the Cementos
93 Andinos company, 10 km northeast of Monay city (9°36.57' 06"N, 70°24'14"W), Municipio
94 Candelaria, Trujillo State, Venezuela (Albino et al. 2017). The fossils come from strata
95 corresponding to the La Aguada Member of the La Luna Formation (Albino et al. 2017;
96 Guinot and Carrillo-Briceño 2018). A Cenomanian age for the La Aguada Member was
97 determined by planktonic foraminifera and ammonites (Renz 1959). Associated fauna from
98 the same strata as *Lunaophis* indicate a marine environment, and include bivalves, sharks
99 and bony fishes (Albino et al. 2016; Guinot and Carrillo-Briceño 2018).

100 **Results**

101 *Paleoecology of Lunaophis aquaticus*

102 Examination of the vertebral morphology reveals that *Lunaophis aquaticus* resembles
103 simoliophiids (Albino et al. 2016), the earliest sea-invaders in the evolution of snakes
104 (Hsiang et al. 2015). *Lunaophis* represents the first aquatic snake from the Cenomanian
105 found outside of the African and European Tethyan and Boreal Zones, which is where the
106 simoliophiids have been previously documented (Albino et al. 2016).

107 All simoliophiids display pachyostosis in which the centrum and neural arch are
108 swollen in all dimensions, increasing the mass of the vertebrae (Lee and Caldwell 1998;
109 Houssaye 2010; Rage et al. 2016). Pachyostosis is a non-pathological condition in these

110 vertebrates in which the bones experience a thickening, generally caused by extra layers of
111 lamellar bone (Houssaye 2009). It occurs in both terrestrial and, especially, aquatic or semi-
112 aquatic vertebrates. The pachyostosis in *Lunaophis* is less evident than in simoliophiids,
113 and is concentrated on the prezygapophyseal bodies and on the posterior part of the neural
114 arch, above the postzygapophyses (Fig. 1a).

115 In addition, the vertebrae of *Lunaophis* are characterized by the ventral position of the
116 paradiapophyses, which are closely spaced, project ventrally from the centrum, and bear
117 ventrally oriented surfaces (Fig. 1a). This morphology contrasts with the morphology of
118 terrestrial, arboreal and fossorial snakes, in which the paradiapophyses are well-separated
119 each other, not projected from the centrum and have lateroventrally-oriented surfaces
120 determining a lateralized articulation of the ribs with the vertebra (Fig. 1b). The
121 hypothetical ribs of *Lunaophis* would have been articulated with the paradiapophyses
122 ventrally to the vertebral centra (Fig. 1c). Thus, the body of this snake was strongly
123 compressed laterally, giving it an eel-like appearance as an adaptation for swimming.
124 Aquatic habits are supported by the size of the snake, presence of pachyostosis, and
125 depositional conditions of the La Aguada Member of the La Luna Formation.

126 *Spondyloarthropathy in vertebrae of Lunaophis and extant snakes*

127 Spondyloarthropathy was recognized in MCNC-1827-F (Fig. 2a, b) on the basis of osseous
128 fusion of the capsule surrounding intervertebral spaces (Resnick 2002; Rothschild and
129 Martin 2006), while normal vertebral shape and configuration were retained. Examination
130 of 2144 modern snakes revealed only one additional affected snake, the viperid *Bitis*
131 *gabonica* CM145474S (Fig. 2c, d). Fusion of posterior (facet) joints is also present in
132 *Lunaophis aquaticus* MCNC-1827-F (Fig. 2c). This is distinguished from congenital
133 vertebral pathology which represents segmentation defects, predominantly failure of

134 segmentation or failure of development of one of the segments (e.g., hemivertebra or block
135 vertebrae) that normally combine to form a normal vertebra (Burnham et al. 2013).

136 Fusion through the outer layers of the capsule joining vertebral centra (Fig. 2) is
137 pathognomonic (definitive) for spondyloarthropathy (Resnick 2002; Rothschild and Martin
138 2006; Rothschild et al. 2012). It is accompanied by ligamentous ossification. Vertebral
139 body shape and configuration appear otherwise unaltered.

140 **Discussion**

141 These observations represent the first recognition of the inflammatory arthritis condition,
142 spondyloarthropathy, in fossil snakes, and establish the geological depth of this disease.
143 This condition is apparently rare in snakes, as there is only one recent case, other than that
144 discovered in *Bitis gabonica* in the current study, noted to date. Marcus (1981) initially
145 reported an anomaly affecting the extant snake *Elaphe taeniura* as osteoperiostitis, but
146 Rothschild et al. (2012) suggest it would correspond to spondyloarthropathy, which is
147 confirmed here.

148 Differential diagnosis: Lack of vertebral disruption and draining sinuses rules out
149 osteomyelitis (Jacobson 2007; Resnick 2002; Rothschild and Martin 2006). Maintenance
150 of vertebral body shape and intervertebral spaces is incompatible with fracture or segmental
151 defect evidencing congenital origin of the pathology. Presence of capsular calcification
152 dismisses DISH as a diagnostic consideration. The associated ligamentous ossification in
153 *Lunaophis aquaticus* MCNC-1827-F represents the enthesial reaction commonly found in
154 individuals with spondyloarthropathy.

155 Spondyloarthropathy is a classification consisting of several diseases (Resnick 2002;
156 Rothschild and Martin 2006): 1) A primary arthritis (ankylosing spondylitis). 2) A
157 dermatologically-related disorder, psoriatic arthritis. 3) Arthritis associated with

158 inflammatory bowel diseases, ulcerative colitis and Crohn's disease. 4) A reactive arthritis
159 (previously referred to as Reiter's syndrome). 5) An undifferentiated form, not assignable
160 to the first four categories. Ankylosing spondylitis generally starts in what would be the
161 pelvic region and results in vertebral fusion proceeding uniformly in a cephalad (cranial)
162 direction (Resnick 2002; Rothschild and Martin 2006). If the precloacal fused *Lunaophis*
163 *aquaticus* vertebrae represent the most posterior portion of that segment, early ankylosing
164 spondylitis or inflammatory bowel disease could be considered as the specific variety of
165 spondyloarthropathy. Reactive arthritis, psoriatic arthritis and the undifferentiated form of
166 spondyloarthropathy are not so limited in vertebral column distribution (Resnick 2002;
167 Rothschild and Martin 2006). While psoriasis is characterized by erythematous skin
168 reaction with scale shedding, this is quite different from snake dysecdysis, with residual
169 tissue from normal skin shedding, and the hyperkeratosis that can complicate vitamin A
170 deficiency (Marcus 1981). Skin disease in the form of psoriasis has not been recognized in
171 snakes. However, reactive arthritis is worthy of consideration. The term "reactive" refers to
172 the bone alterations that can take place subsequent to what is generally referred to as food
173 poisoning by such organisms as enteropathic (intestinal wall invading) *Escherichia coli*,
174 *Salmonella*, *Shigella*, *Campylobacter* and *Yersinia* bacteria (Rothschild and Martin 2006).
175 The originating infection has generally resolved, but is followed by an immunologic
176 reaction producing the pathology. Such intestinal infections have been reported in snakes
177 (Jacobson 2007) and gastritis has been related to parasitic infection (Brownstein et al.
178 1977), which can cause inflammatory bowel disease in humans (Nime et al. 1976).
179 Reactive arthritis and ankylosing spondylitis are the most likely varieties of
180 spondyloarthropathy responsible for the vertebral alterations in *Lunaophis aquaticus*
181 MCNC-1827-F.

182 It is unclear that involvement of such a limited portion of the vertebral column would
183 have impaired movement or ability to capture prey. It may, however, have impeded the
184 physical act of mating. This form of arthritis may be quite painful and thus could have
185 impacted the snake's quality of life.

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239 **Figure captions**

240 Figure 1. **a** Pachyostosis (pch) in isolated precloacal vertebra of *Lunaophis aquaticus*

241 MCNC-1827-A (anterior, lateral and dorsal views). **b** Trunk vertebrae and articulated

242 ribs of terrestrial *Boa constrictor occidentalis*. **c** Trunk vertebrae and hypothetical

243 articulated ribs of aquatic *Lunaophis aquaticus*.

244 Figure 2. **a** Ventral view of *Lunaophis aquaticus* MCNC-1827-F vertebrae, fusion of

245 vertebrae through intervertebral capsule. **b** Left lateral view of *Lunaophis aquaticus*

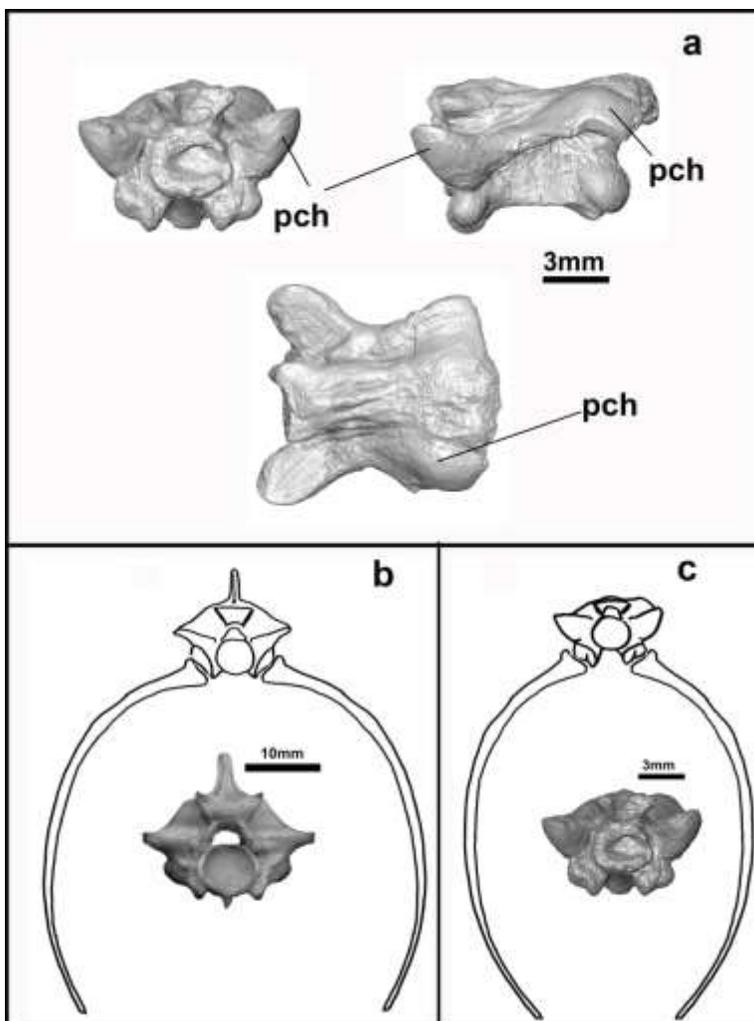
246 MCNC-1827-F vertebrae, continuous fusion of longitudinal ligament. **c** Ventral view

247 of *Bitis gabonica* CM145474S vertebrae. **d** Lateroventral view of *Bitis gabonica*

248 CM145474S vertebrae, fusion of both zygapophyseal joints and intervertebral capsule;

249 pd, paradiapophysis; pr, prezygapophysis; pz, postzygapophysis; vc, vertebral centrum;

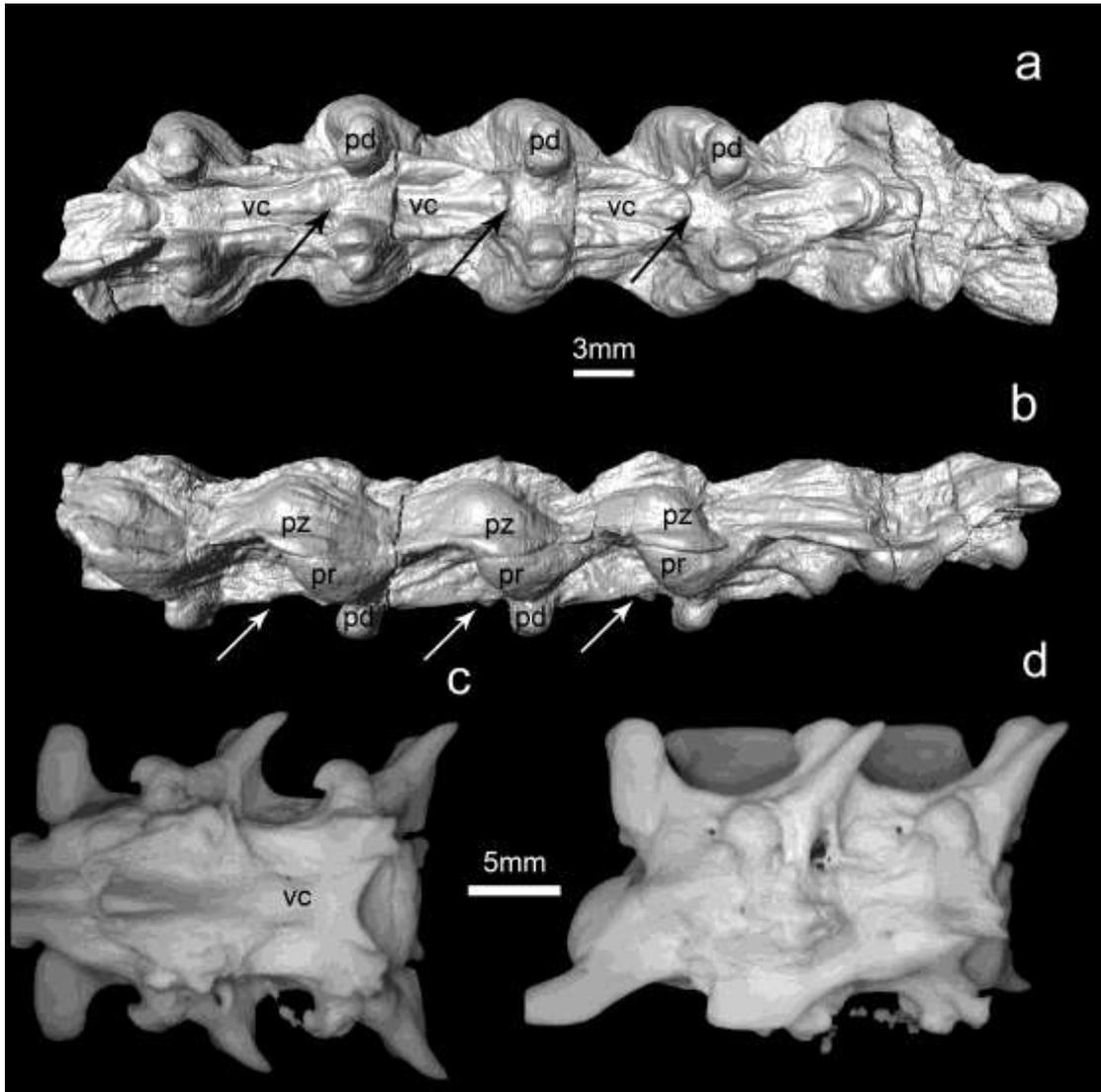
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