

## Case Report

### Granulomatous posthitis caused by *Halicephalobus gingivalis* in association with penile squamous cell carcinoma in an equine: clinical and anatomopathological aspects

Jamile Macedo Garcia<sup>1</sup>  (<https://orcid.org/0009-0008-7737-6619>), Ticiania Brasil Ervedosa<sup>1</sup>  (<https://orcid.org/0000-0003-4148-4315>), Luciana Neves Torres<sup>1</sup>  (<https://orcid.org/0000-0003-0024-2213>), Luiz Augusto Santana Silva<sup>1</sup>  (<https://orcid.org/0000-0003-2457-7915>), Julio David Spagnolo<sup>2</sup>  (<https://orcid.org/0000-0002-0341-5039>), Carla Bargi Belli<sup>3</sup>  (<https://orcid.org/0000-0002-1256-3893>), José Luiz Catão-Dias<sup>1</sup>  (<https://orcid.org/0000-0003-2999-3395>), Lilian Rose Marques de Sá<sup>1\*</sup>  (<https://orcid.org/0000-0002-1909-1550>).

<sup>1</sup> Serviço de Patologia Animal, School of Veterinary Medicine and Animal Science, University of São Paulo, SP, Brazil

<sup>2</sup> Serviço de Cirurgia de Grandes Animais, School of Veterinary Medicine and Animal Science, University of São Paulo, SP, Brazil

<sup>3</sup> Departamento de Clínica Médica, School of Veterinary Medicine and Animal Science, University of São Paulo, SP, Brazil

\*Corresponding author: [liliansa@usp.br](mailto:liliansa@usp.br)

Submitted: January 21<sup>st</sup>, 2026. Accepted: May 28<sup>sh</sup>, 2026.

#### Abstract

Penile and preputial squamous cell carcinomas are among the most common tumors in horses, and inflammation of the external genitalia caused by *Halicephalobus gingivalis* is an important

27 differential diagnosis. *H. gingivalis* is a free-living nematode that causes fatal parasitic encephalitis  
28 in horses and humans and can eventually be diagnosed in the kidneys, lymph nodes, lungs, genital  
29 and ocular mucosa. The objective was to characterize clinical and pathological lesions caused by *H.*  
30 *gingivalis* infection in the prepuce with concomitant involvement of penile squamous cell carcinoma  
31 in an equine. A 15-year-old male Pampa horse with prepuce and penis ulcerated lesions had these  
32 surgically excised. Histopathological analysis revealed granulomatous posthitis with *H. gingivalis*  
33 intralesional and ulcerated penile squamous cell carcinoma. The animal had a satisfactory clinical  
34 and surgical evolution, and there was no recurrence of the lesions after a six-month follow-up period.  
35 Considerations regarding the route of infection, treatment, and zoonotic potential were highlighted,  
36 showing the importance of including this pathogen in the differential diagnosis of nodular lesions  
37 affecting the preputial and penile areas in horses.

38

39 **Keywords:** Nematode, diagnosis, pathology, zoonoses.

40

## 41 **Introduction**

42

43 *Halicephalobus gingivalis*, previously named *Micronema deletrix* or *Halicephalobus deletrix*,  
44 is a free-living nematode found primarily in soil and decaying organic matter (17, 28). This parasite  
45 has a worldwide distribution, with zoonotic potential (11), having been implicated in over 100 cases  
46 reported in horses, in addition to occasional cases in humans (18, 20, 30). There are also reports in  
47 donkeys (*Equus asinus*) (27), ponies (*Equus caballus*) (1, 3), zebra (*Equus grevyi*) (12), and cattle  
48 (*Bos taurus*) (7). Most cases are fatal due to meningoencephalitis (13, 18, 32). Halicephalobiasis  
49 predominantly affects the nervous system, although manifestations have also been observed in  
50 kidneys, nasal and oral cavities, lymph nodes, lungs, eyes, heart, blood vessels, testicles, liver,  
51 stomach, bones, spleen, and prepuce (1, 5-6, 18, 23, 25, 29-30).

52 Preputial and penile tumors are among the most common neoplasms in horses, with squamous  
53 cell carcinoma (SCC) being the most frequently diagnosed type (4). As these tumors enlarge, affected  
54 animals may exhibit copulatory difficulties and frequent penile protrusion (31). Cytology can be used  
55 as a preoperative diagnostic tool, but it is not entirely reliable due to the cytological characteristics of  
56 keratinocytes, which are similar across multiple lesion types, including non-neoplastic ones (31). The  
57 most recommended diagnostic technique is biopsy, as it allows for assessment of tumor architecture  
58 and the extent of tissue invasion (31). These tumors are histologically classified as well-differentiated  
59 (grade 1), moderately differentiated (grade 2), or poorly differentiated (grade 3) (31).

60 This report describes the clinical and pathological features of *Halicephalobus gingivalis* in the  
61 prepuce of an equine with concomitant involvement of penile SCC, and points out the first  
62 documented case in Brazil involving this anatomical site.

63

#### 64 **Case description**

65

66 A 15-year-old male Pampa horse was admitted to the Veterinary Teaching Hospital, School of  
67 Veterinary Medicine and Animal Science, University of São Paulo, presenting a nodular formation  
68 in the prepuce covered by pigmented mucosa, measuring 6.5 x 3.5 x 3.0 cm, and an ulcerated  
69 formation in the penis, measuring 6.5 x 6.0 x 2.5 cm (Fig. 1). According to the responsible, the animal  
70 was treated for 20 days with an oral antimicrobial based on sulfadiazine in association with  
71 trimethoprim, twice a day, and the lesions were washed with soap and water, with subsequent  
72 application of wound healing ointment twice a day. The formations exhibited contact with each other  
73 when the penis was retracted. No other clinical signs were observed.

74 Fine-needle aspiration cytology was performed from one of the lesions (preputial or penile).  
75 However, the anatomical origin of the sampled lesion was not specified in the submission records.  
76 The slides were stained using a rapid panoptic method and revealed a high cellularity, composed  
77 predominantly of polymorphonuclear cells, with fewer macrophages and keratinocytes exhibiting

78 occasional atypia. The background contained abundant cellular debris. The cytological findings were  
79 suggestive of a predominantly neutrophilic inflammatory process. However, the marked  
80 inflammatory component may have contributed to the observed keratinocyte atypia, precluding a  
81 clear distinction between reactive changes and neoplastic transformation. Given the uncertainty  
82 regarding the origin of the sample and the overlap between inflammatory and potential neoplastic  
83 features, the cytological evaluation was considered inconclusive for definitive diagnosis. On the same  
84 day, the horse underwent sedation and local anesthesia for surgical excision of the lesions.

85 Samples were fixed in 10% buffered formalin and submitted to the Animal Pathology Service  
86 at the same institution for histopathological examination. Macroscopically, the preputial formation  
87 was black, firm, and irregular. The cut surface was white, and the remaining features were similar to  
88 the external ones. The penile formation was firm, tanned, irregular, and ulcerated.

89 Representative fragments were routinely processed and stained with hematoxylin and eosin for  
90 examination under optical microscopy using an Eclipse, NiU light microscope (Nikon, Japan) by two  
91 pathologists (JMG, LRMS). The preputial samples exhibited a marked and diffuse infiltration of  
92 epithelioid macrophages, multinucleated giant cells, along with occasional lymphocytes, plasma  
93 cells, and rare neutrophils and eosinophils. There were a significant number of eggs (Fig. 2A), larvae  
94 (Fig. 2B), and adult female nematode parasites. The adult nematode measured between 250 to 460  
95  $\mu\text{m}$  in length, and displayed a rhabditoid esophagus divided into body, isthmus, and bulb (Fig. 2C),  
96 with a dorsiflexed ovary and ventroflexed uterus (Fig. 2D), sometimes presenting a developed egg  
97 measuring 40 to 55  $\mu\text{m}$ . The morphological diagnosis was granulomatous posthitis, focally extensive,  
98 associated with larvae, eggs, and adult females of a nematode parasite consistent with *Halicephalobus*  
99 *gingivalis*.

100 Regarding the penile formation, a diagnosis of malignant neoplastic proliferation of  
101 keratinocytes arranged in islands and anastomosed trabeculae, with invasive growth, formation of  
102 keratin pearls, and ulceration with neutrophilic exudation, whose diagnosis was ulcerated well  
103 differentiated penile SCC (Fig. 3).

104 After the excision, the surgical site was washed with saline solution twice a day, followed by  
105 the application of topical antimicrobial agents. The animal had a satisfactory clinical and surgical  
106 recovery, with no recurrence of the parasite or the tumor after six-month of follow-up

107

## 108 **Discussion**

109

110 Here, the concomitant involvement of preputial halicephalobiasis and penile SCC in an equine  
111 was completely described. To our knowledge, this would be the first reported case in the literature.  
112 There are three other reports of this parasite in the prepuce of horses (6, 16, 21), this being the fourth  
113 described in the world and the first in Brazil.

114 Lesions associated with *H. gingivalis* can vary widely depending on the affected organs and the  
115 extent of involvement (5, 23, 29). Horses with parasitic posthitis previously described showed solely  
116 preputial formations, without systemic or neurological symptoms. In contrast, the animal in this report  
117 exhibited a concomitant neoplastic process in the penis. Previous reports described lesions caused by  
118 *H. gingivalis* as multiple nodules ranging from 0.5 to 8.0 cm in size, whereas this case demonstrated  
119 a single ulcerated lesion (6, 16, 21).

120 The clinical and pathological diagnosis of halicephalobiasis in horses is a challenge. In cases  
121 with cutaneous and/or mucosal nodular lesions, the granulomatous process should be considered  
122 among the potential differentials, such as habronemosis, pythiosis, atypical mycobacteriosis, foreign  
123 body reactions, and neoplasms, such as SCC (28). Diagnostic methods for nodular lesions include  
124 cytology, histopathological examination of incisional or excisional biopsies, and molecular tests (28).  
125 In the present case, a presumptive diagnosis of neoplasia was initially considered, and cytological  
126 evaluation was performed prior to surgical excision. However, an important limitation was that the  
127 anatomical origin of the cytological sample was not recorded, preventing the determination of  
128 whether the material originated from the penile neoplastic lesion or from the adjacent preputial lesion  
129 associated with parasitic infection. Cytologically, the sample was characterized by a marked

130 polymorphonuclear inflammatory infiltrate with cellular debris and keratinocytes displaying  
131 occasional atypia. Although these findings were suggestive of an inflammatory process, it is well  
132 recognized that intense inflammation may induce reactive epithelial atypia, complicating the  
133 differentiation from neoplastic changes. Consequently, the overlapping cytological features,  
134 combined with the uncertainty regarding the lesion sampled, limited the diagnostic value of cytology  
135 in this case and precluded definitive interpretation. Cytodiagnosis was not used in any reported case  
136 to demonstrate the inflammatory process or the intralesional parasite in similar cases (6, 16, 21). The  
137 definitive diagnosis was the histopathological examination of the nodular tissue fragment, confirming  
138 parasitic granulomatous posthitis and penile SCC. Histopathology remains the primary diagnostic  
139 tool applicable in clinical settings capable of identifying *H. gingivalis*, despite its predominantly post-  
140 mortem diagnosis by other authors (15, 18, 24, 32).

141         The morphological aspects of the parasites were used to determine the agent, considering  
142 rhabditiform esophagus, dorsiflexed ovary, and slender tail for identifying *H. gingivalis* in  
143 histological sections (2, 6). Only eggs, larvae, and adult females were observed in the inflammatory  
144 process, which suggests that the parasite reproduces asexually by parthenogenesis, as stated before  
145 (2).

146         The main differential diagnoses of *H. gingivalis* in equine skin are two rhabditids, *Cephalobus*  
147 sp. and *Strongyloides westerii* (6). Both can be differentiated from *H. gingivalis* by morphology (28).  
148 *Cephalobus* sp. has differences in the posterior end and esophagus, which has a greater proportion of  
149 body to isthmus (28). *Strongyloides westerii*, on the other hand, does not present eggs in the middle  
150 of the inflammatory process, since only larvae penetrate the skin (28).

151         We postulate that the proximity between the preputial and penile lesions facilitated the  
152 development of the parasitic infection, as tumor-associated penile exposure may have increased  
153 contact between the preputial mucosa and the ground. Although the routes of infection remain  
154 unclear, previous reports suggest that the parasite penetrates through damaged mucosa (2, 6, 22). It

155 should also be considered that mucosal lesions may not be clinically apparent, which could explain  
156 cases in which lacerations are not observed (18, 24).

157 Despite the presence of ulceration in the neoplastic tissue, intralesional parasites were not  
158 identified in this area. This finding may be explained by the particular characteristics of the tumor  
159 microenvironment (TME) (14). Neoplastic tissue, especially in advanced and ulcerated lesions, is  
160 frequently associated with hypoxia, necrosis, and abnormal vascularization with reduced blood flow  
161 (14, 34), which may influence the establishment and persistence of infectious agents. Additionally,  
162 the TME represents a specialized and dynamically regulated niche characterized by altered immune  
163 responses and cytokine signaling (14, 33). These conditions may variably influence parasite survival  
164 and may not support typical host-parasite interactions within tumor tissue. Alternatively, parasite  
165 distribution may be focal and therefore not represented in the examined sections. Therefore, the  
166 absence of parasites in the neoplastic tissue does not preclude the proposed route of infection but  
167 underscores the complexity of host-parasite-tissue interactions in such cases.

168 The treatment based only on the surgical procedure was sufficient to control the disease in the  
169 animal, which has not presented recurrence or systemic clinical manifestations. In the literature, in  
170 the few cases of success in the treatment of halicephalobiasis, protocols based on ivermectin were  
171 used, which may or may not be associated with other medications or surgical procedures (6, 16). In  
172 cases of parasite infection of the brain, mortality rates reach 100%, even in animals treated with  
173 anthelmintics (3, 8, 10, 13, 25), since the drug does not cross the blood-brain barrier in satisfactory  
174 concentrations, and due to the low sensitivity of *H. gingivalis* to available medications (9, 26).

175 In humans, rare cases of *H. gingivalis* infection have been reported, all resulting in fatal parasitic  
176 meningoencephalitis (1, 15, 19). None of these cases had a documented history of direct contact with  
177 infected horses. However, one case reported disease development following contact with horse feces  
178 (1). Although rare, halicephalobiasis is recognized as an occupational disease with zoonotic potential,  
179 highlighting the critical role of veterinarians in controlling and preventing human infections (1).

180

181 **Data Availability**

182 All the original contributions presented in this study are included in the article/supplementary  
183 material. Further inquiries can be directed to the corresponding author.

184

185 **Author Contributions**

186 **Jamile M. Garcia:** Investigation, Data Curation, Visualization, Writing – Original Draft.

187 **Ticiana B. Ervedosa:** Investigation, Writing – Review & Editing. **Luciana N. Torres:** Investigation,

188 Visualization, Writing – Review & Editing. **Luiz A. S. Silva:** Investigation, Writing – Review &

189 Editing. **Julio D. Spagnolo:** Resources, Writing – Review & Editing. **Carla B. Belli:** Resources,

190 Writing – Review & Editing. **José L. Catão-Dias:** Visualization, Supervision, Writing – Review &

191 Editing. **Lilian R. M. de Sá:** Conceptualization, Visualization, Supervision, Writing – Review &

192 Editing.

193

194 **Conflict of Interest**

195 The authors declare no competing interests.

196

197 **Generative AI Use Statement**

198 The authors did not use generative artificial intelligence tools or technologies in creating or  
199 editing any part of this manuscript.

200

201 **Funding**

202 This research received no specific grant from any funding agency in the public, commercial,  
203 or not-for-profit sectors.

204

205 **References**

206

- 207 1. Akagami M, Shibahara T, Yoshiga T, Tanaka N, Yaguchi Y, Onuki T, Kondo T, Yamanaka T,  
208 Kubo M. Granulomatous nephritis and meningoencephalomyelitis caused by *Halicephalobus*  
209 *gingivalis* in a pony gelding. *J Vet Med Sci.* 2007;11:1187-90. doi: 10.1292/jvms.69.1187.
- 210 2. Anderson RC, Linder KE, Peregrine AS. *Halicephalobus gingivalis* (Stefanski, 1954) from a  
211 fatal infection in a horse in Ontario, Canada with comments on the validity of *H. deletrix* and a  
212 review of the genus. *Parasite.* 1998;5:255-61. doi: 10.1051/parasite/1998053255.
- 213 3. Baker E, Geick A, Hines M, Gerhold R, Cordero-Aponte C. Case report: *Halicephalobus*  
214 *gingivalis* in a Tennessee pony. *Vet Parasitol Reg Stud Reports.* 2023;39:100843. doi:  
215 10.1016/j.vprsr.2023.100843.
- 216 4. Bianchi MV, Boos GS, Mello LS, Vargas TP, Sonne L, Driemeier D, Pavarini SP. A  
217 retrospective evaluation of equine cutaneous lesions diagnosed in southern Brazil. *Acta Sci Vet.*  
218 2016;44:1-7. doi: 10.22456/1679-9216.81154.
- 219 5. Cavasani JPS, Silva WDM, Pavelegini LAD, Colodel EM, Furlan FH. Granulomatous disease  
220 associated with *Halicephalobus* sp. in a horse. *Braz J Vet Pathol.* 2025;18(Suppl 1):e018S105.  
221 doi: 10.24070/bjvp.1983-0246.018S105.
- 222 6. Dunn DG, Gardiner CH, Dralle KR, Thilsted JP. Nodular granulomatous posthitis caused by  
223 *Halicephalobus* (syn. *Micronema*) sp. in a horse. *Vet Pathol.* 1993;30:207-8. doi:  
224 10.1177/030098589303000215.
- 225 7. Enemark HL, Hansen MS, Jensen TK, Larsen G, Al-Sabi MNS. An outbreak of bovine  
226 meningoencephalomyelitis with identification of *Halicephalobus gingivalis*. *Vet Parasitol.*  
227 2016;218:82-6. doi: 10.1016/j.vetpar.2016.01.014.
- 228 8. Ferguson R, van Dreumel T, Keystone JS, Manning A, Malatestinic A, Caswell JL, Peregrine  
229 AS. Unsuccessful treatment of a horse with mandibular granulomatous osteomyelitis due to  
230 *Halicephalobus gingivalis*. *Can Vet J.* 2008;49:1099-103.

- 231 9. Fonderie P, Bert W, Hendrickx F, Huthoofd W, Moens T. Anthelmintic tolerance in free-living  
232 and facultative parasitic isolates of *Halicephalobus* (Panagrolaimidae). *Parasitology*.  
233 2012;139:1301-8. doi: 10.1017/S0031182012000558.
- 234 10. Henneke C, Jespersen A, Jacobsen S, Nielsen MK, McEvoy F, Jensen HE. The distribution  
235 pattern of *Halicephalobus gingivalis* in a horse is suggestive of a haematogenous spread of the  
236 nematode. *Acta Vet Scand*. 2014;56:56. doi: 10.1186/s13028-014-0056-0.
- 237 11. Hoostraten J, Young WG. Meningoencephalomyelitis due to the saprophagous nematode  
238 *Micronema deletrix*. *Can J Neurol Sci*. 1974;2(2):121-6. doi: 10.1017/s0317167100020102
- 239 12. Isaza R, Schiller CA, Stover J, Smith PJ, Greiner EC. *Halicephalobus gingivalis* (Nematoda)  
240 infection in a Grevy's zebra (*Equus grevyi*). *J Zoo Wildl Med*. 2000;31(1):77-81. doi:  
241 10.1638/1042-7260(2000)031[0077:HGNIA]2.0.CO;2.
- 242 13. Kinde H, Mathews M, Ash L, Leger JS. *Halicephalobus gingivalis* (*H. deletrix*) infection in  
243 two horses in southern California. *J Vet Diagn Invest*. 2000;12:162-5. doi:  
244 10.1177/104063870001200213.
- 245 14. Li Z, Li J, Bai X, Huang X, Wang Q. Tumor microenvironment as a complex milieu driving  
246 cancer progression: a mini review. *Clin Transl Oncol*. 2025;27:1943–1952. doi:  
247 10.1007/s12094-024-03697-w.
- 248 15. Lim CK, Crawford A, Moore CV, Gasser RB, Nelson R, Koehler A, Bradbury RS, Speare R,  
249 Dhattrak D, Weldhagen GF. First human case of fatal *Halicephalobus gingivalis*  
250 meningoencephalitis in Australia. *J Clin Microbiol*. 2015;53(5):1768-74. doi:  
251 10.1128/JCM.00032-15.
- 252 16. Muller S, Grzybowski M, Sager H, Bornand V, Brehm W. A nodular granulomatous posthitis  
253 caused by *Halicephalobus* sp. in a horse. *Vet Dermatol*. 2008;19(1):44-8. doi: 10.1111/j.1365-  
254 3164.2007.00643.x.
- 255 17. Nadler SA, Carreno RA, Adams BJ, Kinde H, Baldwin JG, Mundo-Ocampo M. Molecular  
256 phylogenetics and diagnosis of soil and clinical isolates of *Halicephalobus gingivalis*

- 257 (Nematoda: Cephalobina: Panagrolaimoidea), an opportunistic pathogen of horses. *Int J*  
258 *Parasitol.* 2003;33:1115-25. doi: 10.1016/s0020-7519(03)00134-6.
- 259 18. Noiva R, Ruivo P, Carvalho LM, Fonseca C, Fevereiro M, Carvalho P, Orge L, Monteiro M,  
260 Peleteiro MC. First description of a fatal equine infection with *Halicephalobus gingivalis* in  
261 Portugal: relevance for public health. *Vet Med Sci.* 2019;5(2):222-9. doi: 10.1002/vms3.142.
- 262 19. Ondrejka SL, Procop GW, Lai KK, Prayson RA. Fatal parasitic meningoencephalomyelitis  
263 caused by *Halicephalobus deletrix*. *Arch Pathol Lab Med.* 2010;134(4):625-9. doi:  
264 10.5858/134.4.625.
- 265 20. Onyiche TE, Okute TO, Oseni OS, Okoro DO, Biu AA, Mbaya AW. Parasitic and zoonotic  
266 meningoencephalitis in humans and equids: current knowledge and the role of *Halicephalobus*  
267 *gingivalis*. *Parasite Epidemiol Control.* 2018;3:36-42. doi: 10.1016/j.parepi.2017.12.002.
- 268 21. Payán J, Soto R, Romero J, Flórez G. Granulomas en el prepucio de un equino causados por  
269 *Micronema*. *Rev ICA.* 1979;14(4):283-9.
- 270 22. Pearce SG, Bouré LP, Taylor JA, Peregrine AS. Treatment of a granuloma caused by  
271 *Halicephalobus gingivalis* in a horse. *J Am Vet Med Assoc.* 2001;219(12):1735-8. doi:  
272 10.2460/javma.2001.219.1735.
- 273 23. Pillai VV, Mudd LJ, Sola MF. Disseminated *Halicephalobus gingivalis* infection in a horse. *J*  
274 *Vet Diagn Invest.* 2023;35(2):173-7. doi: 10.1177/10406387221141698.
- 275 24. Pintore MD, Cerutti F, D'Angelo A, Corona C, Gazzuola P, Masoero L, Colombo C, Bona R,  
276 Cantile C, Peletto S, Casalone C, Iulini B. Isolation and molecular characterisation of  
277 *Halicephalobus gingivalis* in the brain of a horse in Piedmont, Italy. *Parasit Vectors.*  
278 2017;10:135. doi: 10.1186/s13071-017-2070-3.
- 279 25. Rames DS, Miller DK, Barthel R, Craig TM, Dziezyc J, Helman RG, Mealey R. Ocular  
280 *Halicephalobus* (syn. *Micronema*) *deletrix* in a horse. *Vet Pathol.* 1995;32(5):540-2. doi:  
281 10.1177/030098589503200514.

- 282 26. Schinkel AH. P-glycoprotein, a gatekeeper in the blood-brain barrier. *Adv Drug Deliv Rev.*  
283 1999;36:179-94. doi: 10.1016/s0169-409x(98)00085-4.
- 284 27. Schmitz DG, Chaffin MK. What is your diagnosis? *Halicephalobus gingivalis*. *J Am Vet Med*  
285 *Assoc.* 2004;225:1667-8. doi: 10.2460/javma.2004.225.1667.
- 286 28. Scott DW, Miller WH Jr. *Equine dermatology*. 2nd ed. Philadelphia: Elsevier; 2011. p. 90-1,  
287 248-9.
- 288 29. Sousa TM, Toma HS, Lima AP, Lacreata Junior ACC, Nunes MM, Silva APC, Wouters D,  
289 Albuquerque AS, Varaschin MS, Raymundo DJ, Toma CDM, Batista FA. Pathological fracture  
290 induced by *Halicephalobus gingivalis* (Nematoda: Rhabditida) in a horse limb. *Parasites Hosts*  
291 *Dis.* 2024;62(1):131–138. doi: 10.3347/PHD.23066.
- 292 30. Taulescu MA, Ionică AM, Diugan E, Pavaloiu A, Cora R, Amorim I, Catoi C, Roccabianca P.  
293 First report of fatal systemic *Halicephalobus gingivalis* infection in two Lipizzaner horses from  
294 Romania: clinical, pathological, and molecular characterization. *Parasitol Res.* 2016;115:1097-  
295 103. doi: 10.1007/s00436-015-4839-7.
- 296 31. Van den Top JGB, Ensink JM, Barneveld A, van Weeren PR. Penile and preputial squamous  
297 cell carcinoma in the horse and proposal of a classification system. *Equine Vet Educ.*  
298 2011;23(12):636-48. doi: 10.1111/j.2042-3292.2010.00216.x.
- 299 32. Vasconcelos RO, Lemos KR, Moraes JRE, Borges VP. *Halicephalobus gingivalis* (*H. deletrix*)  
300 in the brain of a horse. *Cienc Rural.* 2007;37(4):1185-7. doi: 10.1590/S0103-  
301 84782007000400047.
- 302 33. Wei XY, Feng HJ, Zhu YY, Guo SJ, Wang H, Li M, Mei Q. The immune microenvironment  
303 of pathogen-associated cancers and current clinical therapeutics. *Mol Cancer.* 2025;24:232. doi:  
304 10.1186/s12943-025-02448-x.
- 305 34. Xie Y, Wang J, Wang Y, Wen Y, Pu Y, Wang B. Parasite-enhanced immunotherapy:  
306 transforming the “cold” tumors to “hot” battlefields. *Cell Commun Signal.* 2024;22:448. doi:  
307 10.1186/s12964-024-01822-4.

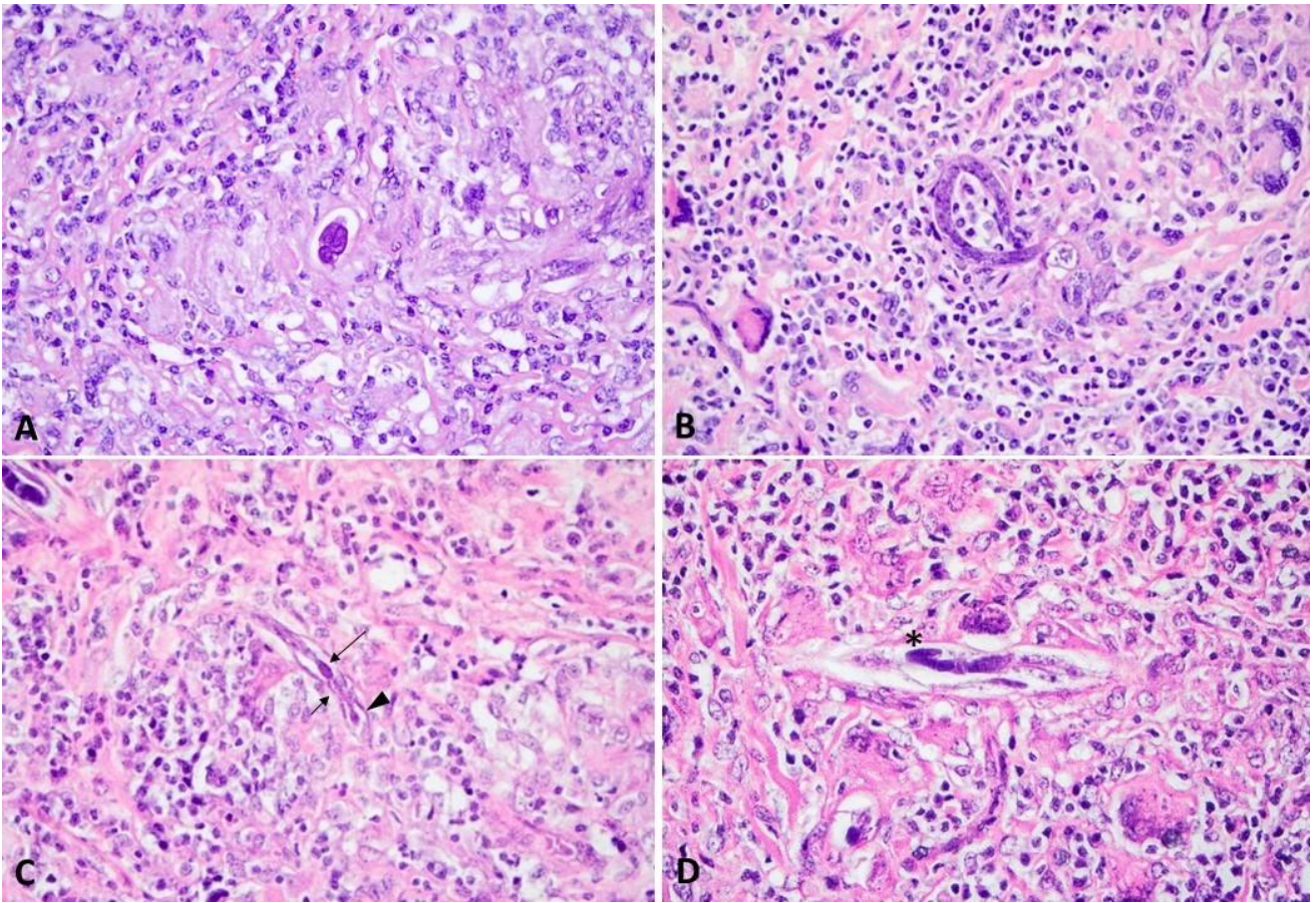




309

310 **Figure 1:** Equine, prepuce and penis. Nodular ulcerated formations in the prepuce (white arrow) and  
311 penis (asterisk) during clinical examination.

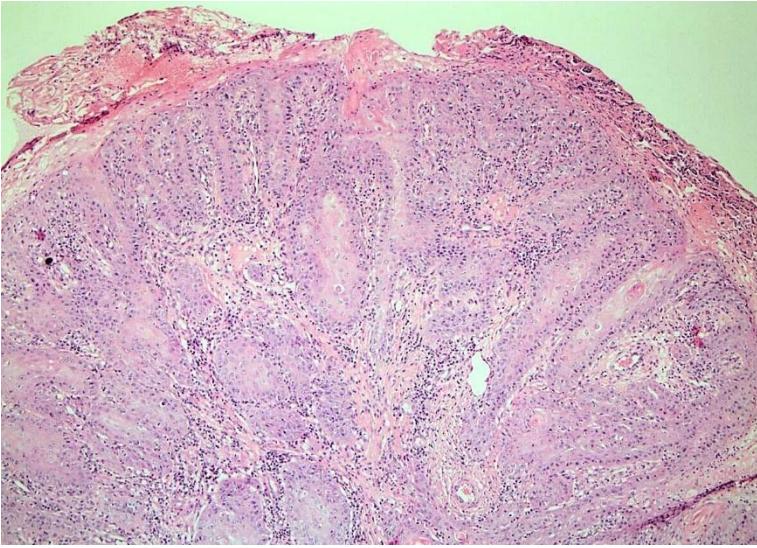
312



313

314 **Figure 2:** Equine, prepuce. Granulomatous posthitis with nematode parasites intralesional. Note the  
315 marked inflammation, mainly characterized by epithelioid macrophages and multinucleated giant cells,  
316 and cuts of egg (A), larvae (B), and adult females (C) with esophagus divided into body (arrowhead),  
317 isthmus (short arrow), and bulb (long arrow), (D) dorsiflexed ovary (asterisk) and ventroflexed uterus.  
318 Hematoxylin and eosin, 400x.

319



320

321 **Figure 3:** Equine, penis. Ulcerated squamous cell carcinoma well differentiated (grade 1).

322 Hematoxylin and eosin, 100x.