

**UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL
FACULDADE DE VETERINÁRIA
PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS VETERINÁRIAS**

POLICONDRITE EM SUÍNOS DE CRECHE E CRESCIMENTO-TERMINAÇÃO

ANDERSON GRIS

PORTO ALEGRE

2022

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Dissertação apresentada como requisito parcial à obtenção do grau de Mestre em Ciências Veterinárias na área de Patologia Animal e Patologia Clínica.

Orientador: Prof. Dr. David Driemeier.

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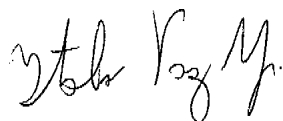
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RESUMO

Em animais, inflamações do tecido cartilaginoso (condrites) geralmente ocorrem devido à extensão de lesões em outros tecidos. Condrites primárias são raras e geralmente apresentam características semelhantes às observadas em humanos com uma condição autoimune denominada policondrite recidivante. O objetivo deste trabalho é caracterizar a apresentação clínico-patológica de um surto de policondrite em suínos. No mês de junho de 2021, foram realizadas visitas a quatro granjas suínas na cidade de Pinhalzinho (SC), nas quais foram obtidos dados clínicos, realizou-se coleta de sangue e avaliação clínica, seguida de necropsia dos suínos acometidos. Na fase de creche e crescimento-terminação aproximadamente 3 e 4% dos suínos, respectivamente, apresentavam otomatomas. Ainda, nas últimas fases, aproximadamente 60% dos suínos com lesão auricular apresentavam piora clínica caracterizada por dispnéia inspiratória e estridor respiratório que, por vezes, evoluía para óbito quando movimentados. Macroscopicamente, os leitões da creche apresentavam as orelhas aumentadas e, na superfície de corte, a cartilagem estava fragmentada, entremeada a material esbranquiçado e firme (fibrose), os quais separavam do tecido cutâneo, e formavam uma fenda, preenchida por fibrina e coágulos sanguíneos. Os suínos de crescimento-terminação apresentavam lesões auriculares semelhantes, porém, usualmente mais crônicas, e apresentavam também, as cartilagens laríngeas (epiglote e aritenoide) espessadas com oclusão parcial do lúmen laríngeo. Ao corte, essas cartilagens apresentavam-se fragmentadas. Microscopicamente, as cartilagens laríngeas e auriculares estavam circundadas por infiltrado inflamatório linfo-histiocitário com eventuais células gigantes multinucleadas tipo corpo estranho, além de perda da basofilia da matriz cartilaginosa na periferia. Essas cartilagens ainda estavam fragmentadas e intercaladas por fibrose, hemorragia e deposição de fibrina. Ainda, as cartilagens afetadas apresentavam evidência de fibras elásticas e perda da coloração na periferia da matriz cartilaginosa nas colorações de azul de toluidina e alciano. Os achados desses casos foram compatíveis com policondrite, que acomete as cartilagens laríngeas e auriculares, semelhante ao descrito em outras espécies animais e nos casos de policondrite recidivante em humanos. Não foi possível isolar um fator epidemiológico ou etiológico que justificasse o desencadeamento deste surto. Nos suínos aqui relatados, as lesões foram restritas às cartilagens elásticas (auricular, aritenoide e epiglote) e causaram prejuízos pela perda de desempenho zootécnico e pela morte de animais por insuficiência respiratória. Ao conhecimento dos autores, este é o primeiro relato de policondrite primária em suínos.

Palavras-chave: Cartilagem. Otomatoema. Laringe. Orelha.

ABSTRACT

In animals, inflammation of the cartilage tissue (chondritis) usually occurs due to the extent of damage to other tissues. Primary chondritis is rare and often has similar features to those seen in humans with an autoimmune condition called relapsing polychondritis. The aim of this work is to characterize the clinicopathological presentation of an outbreak of polychondritis in swine. In June 2021, visits were carried out to four swine farms in the city of Pinhalzinho (SC), in which clinical data were obtained, blood gathered, and clinical evaluation were performed, followed by necropsy of the affected pigs. In the nursery and growing-finishing phase approximately 3 and 4% of the pigs, respectively, had otohematomas. Also, in the last stages, approximately 60% of the pigs with auricular damage presented clinical worsening characterized by inspiratory dyspnea and respiratory stridor that sometimes died when moved. Grossly, the nursery piglets had enlarged ears and, on the cut surface, the cartilage was fragmented, interspersed with whitish and firm material (fibrosis), which separated from the skin tissue and formed a cleft, filled with fibrin and blood clots. Growing-finishing pigs had similar, but usually more chronic, auricular lesions, as well as thickened laryngeal cartilages (epiglottis and arytenoid), with partial occlusion of the laryngeal lumen. In the cut surface, these cartilages were fragmented. Microscopically, the laryngeal and auricular cartilages were surrounded by a lymphohistiocytic inflammatory infiltrate with occasional foreign body-type multinucleated giant cells, in addition to loss of basophilia of the cartilaginous matrix in the periphery. These cartilages were still fragmented and interspersed with fibrosis, hemorrhage, and fibrin deposition. Furthermore, the affected cartilages showed evidence of elastic fibers and loss of stain in the periphery of the cartilaginous matrix in the toluidine blue and alcian blue stains. The findings of these cases were compatible with polychondritis, which affects the laryngeal and auricular cartilages, similar to that described in other animal species and in human cases of relapsing polychondritis. It was not possible to isolate an epidemiological or etiological factor that justified the triggering of this outbreak. In the swine reported here, the lesions were restricted to the elastic cartilages (auricular, arytenoid and epiglottis) and caused losses due to loss of zootechnical performance and the death of animals due to respiratory failure. To the authors' knowledge, this is the first report of primary polychondritis in pigs.

Keywords: Cartilage. Otohematoma. Larynx. Ear.

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1. INTRODUÇÃO

O Brasil é o quarto maior produtor e exportador de carne suína do mundo, com um total de 4.436 milhões de toneladas de carne produzidas e exportação de 33% deste montante. Dentro do país, a região sul se destaca e concentra 70,91% da produção nacional (ABPA, 2021).

Para tornar possível tal capacidade produtiva, o sistema intensivo de criação foi adotado, no entanto, isso favorece o aparecimento de doenças (MAES *et al.* 2001). Sendo assim, medidas de controle como o correto dimensionamento de instalações e manejo adequado dos animais é necessário (SOBESTIANSKY *et al.* 2012).

Apesar dos manejos e cuidados adotados, óbitos de suínos durante as fases de produção são frequentes. É tido como toleráveis taxas de mortalidade de até 2,5% na creche e 1% na fase de terminação (SOBESTIANSKY *et al.* 2012). Na fase da terminação, as causas de morte são relacionadas principalmente a enfermidades que afetam o sistema respiratório, com destaque para as pneumonias com associações de vários agentes patogênicos, os quais são agrupados dentro do complexo de doenças respiratórias dos suínos (RECH *et al.* 2017; PIVA *et al.* 2020).

Esse complexo de doenças é composto por agentes infecciosos, os quais são de maior importância e são amplamente estudados (RECH *et al.* 2017; PIVA *et al.* 2020). No entanto, enfermidades com menor frequência, como as de origem nutricional, metabólica, tóxica, autoimune ou traumática são diagnosticadas em menor escala. Esses diagnósticos geralmente são mais desafiadores, o que necessita uma estrutura laboratorial especializada, além de um estudo epidemiológico detalhado (SOBESTIANSKY *et al.* 2012; DRITZ *et al.* 2019; SCHWERTZ *et al.* 2021).

A parte condutora do sistema respiratório é composta por narinas, cavidade nasal, seios paranasais, nasofaringe, laringe, traqueia e brônquios extra e intrapulmonares, os quais são revestidos por um epitélio colunar pseudoestratificado ciliado com células caliciformes (LIEBICH, 2019). Na área da veterinária, enfermidades que afetam o sistema condutor do trato respiratório são comumente observadas em cães e equinos; já em suínos, são menos frequentes (LOPEZ; SHANNON, 2017).

Quadros de condrite laríngea costumam estar relacionados a outros quadros primários, com acometimento da cartilagem por extensão (LÓPEZ; MARTINSON, 2017). No entanto, existem outras condições que acometem a cartilagem laríngea de forma primária, sem causar ulceração do epitélio (REINEKING *et al.* 2020). Independente da origem, primária ou secundária, em todos os casos, as lesões levam a aumento de volume do órgão, o que restringe a passagem do ar. Isso faz com que os animais desenvolvam um quadro de dificuldade

respiratória e de estridores (roncos) durante os movimentos respiratórios (BOLFA *et al.* 2020; REINEKING *et al.* 2020).

As condrites primárias não afetam somente a laringe, mas também outras cartilagens, presentes em articulações e pavilhão auricular, além de outros tecidos ricos em proteoglicanos como vasos sanguíneos e olhos. Quando afeta o pavilhão auricular, a condição é chamada condrite auricular, a qual é relatada em gatos, cães, bovinos e ratos (MCEWEN; BARSOUM, 1990; BABA *et al.* 2009; ADISSU *et al.* 2014; NOXON *et al.* 2021). Nessa condição, ocorre a transformação da cartilagem do pavilhão auricular, que normalmente é basofílica, em hipereosinofílica, além de ser circundada por infiltrado inflamatório composto por linfócitos, plasmócitos, macrófagos e células multinucleadas. Por vezes, essa cartilagem pode fragmentar-se e ser substituída por tecido conjuntivo fibroso, um processo crônico de reparação (NJAA, 2017).

Na medicina veterinária, a ocorrência de inflamação das cartilagens auriculares e laríngeas simultaneamente foi descrita somente em bovinos, a qual possui uma apresentação semelhante ao que se é observado em humanos com policondrite recidivante (BLEUL *et al.* 2011). Entretanto, quadros de condrites auriculares em ratos e gatos também apresentam achados semelhantes aos descritos na condição humana (MCEWEN; ARSOUM, 1990; BABA *et al.* 2009). Na policondrite recidivante em humanos, ocorre um distúrbio inflamatório que atinge as cartilagens elásticas ou hialinas do corpo. Essa enfermidade possui uma frequência de 3,5 casos a cada um milhão de pessoas, e acomete principalmente humanos adultos entre 40 e 50 anos (CUNNANE, 2017). A policondrite recidivante inicia com um quadro de inflamação e aumento de volume auricular, que pode afetar outras cartilagens simultaneamente, como as da laringe, traqueia, nariz, articulações, entre outras estruturas ricas em proteoglicanos, como olhos, coração, vasos sanguíneos e ouvido interno (BORGIA *et al.* 2018). Suspeita-se que essa enfermidade tenha origem autoimune, tendo como principais alvos o colágeno tipo II, uma proteína da matriz cartilaginosa denominada matrilina I ou a proteína oligomérica da matriz cartilaginosa (ARNAUD *et al.* 2014).

Nos equinos, uma condição comum que afeta a parte condutora do sistema respiratório é a hemiplegia laríngea, também conhecida como síndrome do cavalo roncador, a qual é relatada principalmente em cavalos de corrida e associado a exercício extenuante. Além disso, a lesão observada é uma axonopatia distal, a qual resulta da desmielinização e consequente falha na inervação dos músculos da laringe, desenvolvendo-se, assim, a síndrome clínica da hemiplegia laríngea (CLERCQ *et al.* 2018).

Ainda, em equinos, menos comumente são relatados casos de condrite aritenoide, a qual é uma condição que se desenvolve através de um processo inflamatório progressivo que afeta a cartilagem aritenoide da laringe, o que leva ao seu espessamento com consequente estenose do lúmen e restrição do fluxo do ar (BOLFA *et al.* 2020). A patogênese dessa condição ainda não é totalmente conhecida, mas relaciona-se inicialmente com uma lesão traumática da mucosa laríngea, que acontece normalmente quando o animal está com a respiração acelerada. Esta lesão do epitélio favorece a introdução de bactérias ou vírus, os quais desencadeiam uma resposta inflamatória que atinge a cartilagem laríngea por extensão (DUCHARME; CHEETHAM, 2014; BOLFA *et al.* 2020).

Em ovinos, há relatos de uma condrite aritenoide semelhante àquela descrita em equinos. No entanto, a patogênese também não é bem esclarecida, mas os autores citam ser necessário um evento inicial traumático, seguido de uma infecção bacteriana secundária, a qual leva ao agravamento da lesão (REINEKING *et al.* 2020). As enfermidades que afetam a laringe muitas vezes estão relacionadas a agentes que afetam o trato respiratório e digestório, visto que a sua localização anatômica favorece a colonização e o desenvolvimento das lesões (SANTOS; GUEDES, 2016). Um dos principais exemplos relatados é a necrobacilose causada por *Fusobacterium necrophorum* (BONOW *et al.* 2020). Em suínos, todavia, doenças que afetam a laringe não são comumente reportadas, além disso, quadros de condrite laríngea primária não são descritos na literatura. Portanto, o objetivo deste trabalho é caracterizar a apresentação clínico-patológica de um surto de policondrite em suínos em fase de creche e crescimento-terminação.

2. ARTIGO

Neste item é apresentado o artigo intitulado “*Polychondritis in nursery and growing-finishing pigs*” o qual foi redigido sob as normas da revista “*Veterinary Pathology*” para ser submetido em breve.

1 **Polychondritis in nursery and growing-finishing pigs**

2

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16

17 **ABSTRACT**

18 The aim of this work was to characterize the clinic-pathological presentation of an
19 outbreak of polychondritis in pigs. In June 2021, visits were made to four swine farms
20 in the city of Pinhalzinho (SC), Brazil, where clinical history was obtained, blood
21 gathered, clinical evaluation and *post-mortem* examination were performed. The pigs
22 had 3-4% of otohematoma, which started in the nursery and extended to the
23 growing-finishing phase. Animals that got worse presented a respiratory condition of
24 respiratory stridor and, after intense movement, evolved to respiratory distress and
25 death. Grossly, nursery piglets had enlarged ears, and in the cut surface, the

26 cartilage was fragmented intermingled with whitish fibrous material, and
27 accumulation of blood clots. At growing-finishing phase, in addition to the similar
28 auricular lesion, pigs presented thickened epiglottis and arytenoid cartilages, which
29 partially occluded the laryngeal lumen. In the cut surface, the laryngeal cartilage had
30 lesions similar to the auricular cartilage. Microscopically, the laryngeal and auricular
31 cartilages showed hypereosinophilic matrix, in addition to lymphohistiocytic
32 inflammatory infiltrate and occasional multinucleated giant cells. These cartilages
33 were still fragmented and interspersed with fibrosis. These findings were compatible
34 with polychondritis, already described in humans and some animal species. It was
35 not possible to determine the factor that triggered the condition. The lesions were
36 confined to the elastic cartilages in pigs and caused increased mortality due to acute
37 respiratory distress in finishing pigs. To the authors' knowledge, this is the first report
38 of polychondritis in swine.

39 **Keywords:** respiratory stridor, otophematoma, cartilage, ear, larynx.

40

41 Chondritis are inflammations that affect the cartilaginous tissue. Laryngeal
42 chondritis are reported in cattle, horse, and sheep, which can be caused by trauma
43 followed by bacterial or viral infection that led to ulceration of the epithelium and
44 influx of inflammatory cells to the cartilage.^{5,15} In sheep, laryngeal chondritis without
45 ulceration is rarely described and the etiology is unknown.²¹

46 Another presentation of chondritis reported in rats,¹⁶ cats,³ cattle,¹ and dogs¹⁸
47 is called auricular chondritis. In this disease, the auricular cartilage presents loss of
48 basophilia, and is surrounded by an infiltrate of lymphocytes, plasma cells,
49 macrophages, and multinucleated giant cells. Sometimes this cartilage can fragment
50 and be replaced by fibrous tissue.¹⁷

51 In humans, a condition called relapsing polychondritis is recognized. This
52 disease is characterized by inflammation and increased ear volume, which can affect
53 other cartilages simultaneously, such as larynx, trachea, nose, ear, and joints. In
54 addition, it can affect other proteoglycans rich structures, such as eyes, heart and
55 blood vessels.⁶ This disorder is believed to have an autoimmune origin, and type II
56 collagen, matrilin I or cartilage oligomeric matrix protein are pointed as the main
57 targets of the immune system.² These cases of polychondritis are reported, in
58 humans, and in some animal species, however, in pigs, are not described. The aim
59 of this work was to characterize the clinic-pathological presentation of an outbreak of
60 polychondritis in pigs.

61

62 **MATERIALS AND METHODS**

63 Technical visits were performed at four pig farms with the responsible
64 veterinarian and farm employees: one nursery and three growing-finishing farms.
65 Data were obtained regarding the occurrence of an atypical disease, including sex,
66 age, and clinical signs of the affected pigs, in addition to epidemiological data. The
67 affected pigs were clinically evaluated and some with poor prognosis were selected
68 for *post-mortem* examination. Fragments of thoracic and abdominal organs,
69 cartilages (larynx, trachea, ear, and nose), joints (costochondral and
70 metacarpophalangeal), and tissues rich in proteoglycans (eye and aorta) were
71 collected and fixed in 10% formalin solution. Afterwards, the laryngeal cartilages
72 were mapped, and fragments of the epiglottis, thyroid, cricoid, and arytenoid
73 cartilages were trimmed. All collected organs were routinely processed for histology
74 and were stained with hematoxylin and eosin (H&E). Also, the histological sections
75 that contained ear and laryngeal cartilages from affected and control pigs were

76 subjected to toluidine blue, alcian blue (pH 2.5), Masson's trichrome, Verhoeff's
77 elastic stains and picrosirius red, being this last evaluated under optical and polarized
78 light microscopy. The control tissues used in histochemical techniques were collected
79 from pigs of farms without any relation to those affected by this condition.

80

81 **RESULTS**

82 A cooperative of animal production composed by 300 integrated pig farms,
83 located in Pinhalzinho (SC), Brazil (26°51'18.5"S; 52°59'16.1"W), reported that
84 approximately 5% of its farms (5 nurseries and 10 growing-finishing) detected about 3-
85 4% of ear changes, described as otohematomas, in addition to an atypical respiratory
86 condition mainly characterized by respiratory stridor. Visits were performed in four
87 farms: one was a nursery and three were growing-finishing farms. These farms were
88 technified, with automatized feeding *ad libitum*, and the animals were vaccinated
89 against porcine circovirus type 2, influenza A virus (autogenous) and *Mycoplasma*
90 *hyopneumoniae*. Additionally, the swine were located in batches with flooring consisted
91 of solid concrete and slat concrete, with a capacity of one pig each square meter.

92 The problem had been going on from August 2020 until June 2021, when the
93 visits were conducted, however were reported that the number of animals affected by
94 the condition had reduced. The affected batches were composed by pigs from
95 different origins and genetics. Besides that, all pigs received the feed made by the
96 same factory, which was from the own cooperative. There was a report of changes in
97 the premix used in the feed during the period of the outbreak.

98 At the nursery, it was observed that about 3% of the piglets (approximately
99 60/2100), 60 days old, had clinical signs, which were first noticed 10 days before the
100 visit. At this stage, no increase in mortality was reported; ear changes were more

101 prominent, and respiratory signs were rare. The ear lesions were either unilateral or
102 bilateral, initially characterized by reddish discoloration and mild increased in volume;
103 afterwards, it assumed a slightly domed and smooth surface. In other cases, the pigs
104 had reduced size ears, wrinkled surface, and firm consistency (known as “*cauliflower*
105 *ear*”). Some of the piglets with severe lesions also showed underdevelopment.

106 In the three growing-finishing farms, the pigs were between 125 and 140 days
107 old, and about 4% of them (approximately 20/500 each farm) were affected. In this
108 phase, an increase in mortality was reported, with accumulated rates between 2 and
109 3% in the visited farms. The usual mortality rates in the previous batches in those
110 farms were around 0.5%.

111 Affected growing-finishing pigs had lower weight gain and ear changes
112 characterized by ears reduced in size and with wrinkled surface. From these pigs
113 with ear lesions, about 60% of them still had moderate inspiratory dyspnea,
114 accompanied by an audible noise, mainly on inspiration (respiratory stridor),
115 sometimes associated with coughing. According to reports, the pigs arrived in the
116 farms with initial ear lesions, which worsened during this phase and were later
117 accompanied by respiratory signs. When the affected pigs were moved, dyspnea
118 became severe, the animals adopted an orthopneic position and progressed to
119 death.

120 Two nursery pigs and five growing-finishing pigs were necropsied. In the
121 macroscopic evaluation of both pigs from the nursery, the ears were enlarged,
122 hyperemic, with a domed and smooth surface. Upon cutting, the auricular cartilage
123 was fragmented, separated by whitish material, and intermingled with an
124 accumulation of blood clots, and whitish fibrillar material (otohematoma).

125 The growing-finishing pigs presented auricular lesions characterized by the
126 ear reduced in size, with wrinkled surface, that in the cut surface, the auricular
127 cartilage was fragmented, interspersed by whitish material, and delimited a cleft filled
128 of blood clots, and whitish fibrillar material.

129 In the five necropsied growing-finishing pigs, it was also observed that the
130 larynx presented a reduction in the luminal diameter, due to a severe thickening of
131 the epiglottis and arytenoid, in variable intensity among the animals. Upon cutting,
132 the epiglottic and arytenoid cartilages were fragmented and interspersed with a firm
133 whitish material.

134 In the histopathological examination of the ears of all pigs (7/7), it was
135 observed, the cartilage fragmented, and surrounded by marked inflammatory infiltrate
136 of lymphocytes, plasma cells, macrophages, and occasional multinucleated foreign-
137 body giant cells, which usually formed small adjacent nodules. In these areas, there
138 were also moderate peripheral loss of basophilia of the cartilage matrix.

139 Formation of clefts was frequently observed separating the auricular cartilage
140 from the adjacent tissue. In these clefts, there was accumulation of inflammatory
141 cells similar to those described, in addition to a fibrillar eosinophilic material (fibrin)
142 and blood (otohematoma). Besides that, the auricular cartilage had been fragmented
143 in other areas, which were characterized by the formation of cartilage islands of
144 varied sizes, filled with a slightly basophilic matrix, hypertrophic and hyperplastic
145 chondrocytes. In other cases, in addition to the inflammatory exudate, moderate
146 proliferation of fibrovascular connective tissue was also observed. The proliferation of
147 fibrous connective tissue, frequency of cartilage islands formation, and number of
148 multinucleated giant cells were more evident in growing and finishing pigs.

149 In the laryngeal cartilages of pigs from the nursery, there were no microscopic
150 lesions. However, in the larynx of growing-finishing pigs, it was observed that the
151 epiglottic and arytenoid cartilages had lesions similar to those described in the ears,
152 characterized by a lymphoplasmacytic and granulomatous inflammatory infiltrate,
153 which surrounded an eosinophilic and usually fragmented cartilage, interspersed by
154 proliferation of fibrovascular tissue. Multifocal erosion or ulceration of the luminal
155 epithelium (3/5) were also observed.

156 In the histological sections of both cartilage lesion sites of all cases, in the
157 toluidine blue and alcian blue stains, it was evidenced that the ear and laryngeal
158 cartilages presented strong labelling of the cartilaginous matrix in the center.
159 However, in the periphery, where there was the inflammatory reaction, this staining
160 was mild or absent. In Masson's trichrome staining of these same areas, there were
161 formation of adjacent islands with a bluish cartilaginous matrix. The Verhoeff's elastic
162 stain resulted that in the affected cartilages (ear, arytenoid and epiglottis), there was
163 elastin fibers staining, characterizing these sites as elastic cartilages. Into the
164 remaining elastic cartilages, there was intense evidence of elastin fibers interspersing
165 the chondrocytes, while on the edges of the affected cartilages, there is a decrease
166 and/or loss of evidence of these fibers. Also, in areas of fibrosis there was complete
167 loss of elastin fibers. In the other cartilages of larynx (cricoid and thyroid), the
168 labelling of elastin fibers was not observed, so these cartilages were characterized as
169 hyaline. Also, in the picosirius red, the cartilage matrix there was not a
170 predominance of any type of collagen, being evidenced both immature and mature
171 fibrous connective tissue.

172 Other body cartilages, represented by trachea, bronchi, larynx (thyroid and
173 cricoid cartilage), nose, joints (costochondral and metacarpophalangeal), and other

174 sites such as aorta and eye were also evaluated, however, no lesions were
175 evidenced microscopically.

176

177 **DISCUSSION**

178 The diagnosis of polychondritis in the pigs was performed through the
179 association of clinical, macroscopic, and microscopic findings, which indicated
180 lesions in the laryngeal (epiglottis and arytenoid) and auricular cartilages. There are
181 few reports of lesions restricted to the ear cartilage, in distinct species, such as cats,³
182 dogs,¹⁸ cattle,¹ and rats.¹⁶ These reports and the pigs of this outbreak have some
183 aspects that are similar with relapsing polychondritis of humans.^{11,17}

184 Relapsing polychondritis in humans is treated as an autoimmune disease, as it
185 has a variable period of inflammation, followed by spontaneous remission,
186 autoantibodies, and is occasionally associated with other autoimmune diseases.^{2,6} In
187 the pigs reported here, differences in the clinical progression and morphological
188 aspects of the lesions found in the same animal may be related to an intermittent
189 behavior, similar to which occurs in relapsing polychondritis in humans.

190 In humans, there are criteria to confirm the diagnosis of relapsing
191 polychondritis, such as the presentation of symptoms of inflammation confirmed by
192 biopsy in two or more cartilage sites.⁶ In the present study, the pigs from the nursery
193 only presented lesions in the ear cartilages, which were considered the initial site of
194 the condition. However, growing-finishing pigs had lesions in two or more different
195 cartilages, which supports the similarity of the condition discussed here with the
196 relapsing polychondritis in humans.

197 The triggering event of relapsing polychondritis in humans is not yet
198 understood, though some aspects thought to be involved include a genetic

199 susceptibility (HLA-DR4 gene expression), structural similarity with infectious agents,
200 in addition to mechanical or chemical aggression.² The etiology of cases of laryngeal
201 chondritis in horses is suggested to be triggered by trauma and secondary viral or
202 bacterial infection.⁵ In auricular chondritis cases described in animals, an association
203 with genetic is reported in cattle,⁴ and with ear tags in rats.¹³ In our cases, the
204 affected herd were composed of several genetic lines, that are also used by
205 numerous other producers in the country, which have not been experienced the
206 same problem. However, a genetic origin cannot be ruled out, as no analyzes were
207 performed. The affected pigs did not use ear tags and did not receive tattoos. They
208 only received the notch, which is a procedure widely used in Brazil to identify the
209 swine farm of origin, so this was not considered the associated factor to trigger the
210 condition described here.

211 A common factor to all farms was that the feed provided to the pigs was the
212 same, being manufactured by the cooperative itself. However, nutritional components
213 have not been described in the literature as possible triggers for polychondritis.^{2,5}
214 Moreover, the cooperative nutritionists reviewed the formulations and did not find
215 possible foreign elements in the feed. However, we cannot totally exclude the
216 possibility of an alimentary association, as the incidence of new cases decreased
217 after the premix was changed and later the problem disappeared.

218 Substances that are described as triggering factors for skin hypersensitivity in
219 humans are metals as nickel, aluminum, beryllium, chromium, cobalt, copper, gold,
220 iridium, mercury, palladium, platinum, rhodium and titanium.²⁵ Despite it, levels of
221 these metals were not researched in the feed or cartilaginous tissue. So, we cannot
222 totally rule out the possibility of hypersensitivity in our cases. Additionally, in human
223 cases of hypersensitivity there are histopathological lesions mostly characterized by

224 varied degree of perivascular inflammatory infiltrates, in which predominates
225 eosinophils.¹⁰ However, in our cases, the lesions pattern was characterized by a
226 lymphohistiocytic inflammatory infiltrate surrounding the cartilaginous tissue, which
227 differs from the pattern of hypersensitivity.

228 Otohematomas are injuries commonly reported in human athletes, being related
229 to traumatic causes, with consequent hemorrhage in the space between the
230 epidermis and the auricular cartilage.¹² In veterinary medicine, otohematomas are
231 mainly reported in dogs¹⁹ and swine,⁹ which are also frequently associated with
232 trauma and some intercurrent condition, predisposing to self-trauma. However, cases
233 of polychondritis in domestic animals and humans are not associated with
234 otohematoma in the literature.^{1,3,8,16,18} In the pigs of this study, otohematomas were
235 frequently observed in the nursery, and progressed to a chronic form in the growing-
236 finishing phase. These may have developed by self-trauma, irritation and pain
237 induced by the inflammatory process, in addition to the formation of the cleft between
238 the cartilage and adjacent tissue, which allows the accumulation of fluid.

239 Humans affected by relapsing polychondritis commonly present lesions in the
240 ears, nose, larynx, trachea, bronchi, peripheral articular cartilages, eye, and
241 cardiovascular system, being affected individually or in different combinations.⁶ The
242 simultaneous involvement of auricular cartilages and the respiratory system is
243 reported in half of the human cases,⁷ and only in one outbreak in cattle.⁴ Involvement
244 of respiratory tract, especially the larynx and tracheobronchial tree, has a worse
245 prognosis in humans, as it can lead to laryngotracheal stenosis.^{6,24} In this work,
246 clinical respiratory signs of respiratory stridor, and lesions in upper respiratory tract,
247 were observed only in growing-finishing pigs, which presented a poor general

248 condition, with weight loss and sometimes died with respiratory distress, mainly
249 during managements.

250 In the sampled pigs, the lesions were restricted to the auricular cartilages and to
251 two of the laryngeal cartilages (epiglottis and arytenoid). The common feature of
252 these cartilages is that they are all elastic cartilages, as seen on the Verhoeff's elastic
253 stain.¹⁴ The other types of cartilage present in the body (hyaline and fibroelastic) did
254 not show macroscopic or microscopic lesions in the animals evaluated in this
255 outbreak. Thus, it is suggested that the antigen that may triggered the immune
256 mediated reaction is present only in the elastic cartilage.

257 Toluidine blue and alcian blue stains have affinity for proteoglycans and
258 glycosaminoglycans present in extracellular matrix of cartilage.²²⁻²³ Thus, based on
259 the loss of staining at the edges of chondrocyte islands, it is suggested that chronic
260 inflammation of cartilage tissue led to loss of extracellular matrix components,
261 corroborating with which is described in horses.⁵ In Masson's trichrome stain, the
262 remain healthy cartilage matrix was stained red, and adjacent to it there were islands
263 with the matrix stained in blue, which were considered as regeneration or newly
264 formed collagen.²⁰

265 Therefore it is conclude that pigs can be affected by a polychondritis that affects
266 the elastic cartilages in various parts of the body, especially ears and larynx
267 (epiglottis and arytenoid). These condition occurred with a high incidence of
268 otohematomas in the herd, in addition to respiratory distress, mainly characterized by
269 respiratory stridor, besides emaciation and death of severely affected pigs. Under the
270 conditions of this study, it was not possible to identify a triggering factor that led to
271 the occurrence of the condition in these farms. To the authors' knowledge, this is the
272 first reported of polychondritis in pigs.

273

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286 REFERENCES

287 1. Adissu HA, Baird JD, Wood GA. A case of bilateral auricular chondritis in a heifer.

288 *Case Rep Vet Med.* 2014;1-4.

289 2. Arnaud L, Mathian A, Haroche J, Gorochov G, Amoura Z. Pathogenesis of

290 relapsing polychondritis: a 2013 update. *Autoimmun Rev.* 2014;**13**(2):90-5.

291 3. Baba T, Shimizu A, Ohmuro T, et al. Auricular chondritis associated with systemic

292 joint and cartilage inflammation in a cat. *J Vet Med Sci.* 2009;**71**(1):79-82.

293 4. Bleul U, Stranzinger G, Sydler T. Polychondritis: Eine neue Erkrankung beim

294 Braunvieh?. *Schweizer Archiv für Tierheilkunde.* 2011;**153**(11):526-529.

295 5. Bolfa P, Cercone M, Dennis MM, Conan A, Grevemeyer B, Ducharme NG. Clinical

296 and pathological features in horses with advanced arytenoid chondritis. *Vet Pathol.*

297 2021;**58**(1):91-102.

- 298 6. Borgia F, Giuffrida R, Guarneri F, Cannavò SP. Relapsing Polychondritis: An
299 Updated Review. *Biomedicines*. 2018;**6**(3):84-98.
- 300 7. Cantarini L, Vitale A, Brizi MG, et al. Diagnosis and classification of relapsing
301 polychondritis. *J Autoimmun*. 2014;**48-49**(1):53-59.
- 302 8. Damiani JM, Levine HL. Relapsing polychondritis report of ten cases.
303 *Laryngoscope*. 1979;**89**(6):929-946.
- 304 9. Drolet R, Hélie P, D'Allaire S. Pathology of ear hematomas in swine. *J Vet Diagn*
305 *Invest*. 2016;**28**(3):244-248.
- 306 10. Fung MA. The clinical and histopathologic spectrum of “dermal hypersensitivity
307 reactions,” a nonspecific histologic diagnosis that is not very useful in clinical
308 practice, and the concept of a “dermal hypersensitivity reaction pattern”. *J Am Acad*
309 *Dermatol*. 2002;**47**(6):898-907.
- 310 11. Gerber B, Crottaz M, von Tscharnier C, Schärer V. Feline relapsing
311 polychondritis: two cases and a review of the literature. *J Feline Med Surg*.
312 2002;**4**(4):189-194.
- 313 12. Kim Y, Choi JW, Park YH. Management of an inappropriately treated case of
314 auricular hematoma. *J Audiol Otol*. 2021;**25**(2):115–118.
- 315 13. Kitagaki M, Hirota M. Auricular chondritis caused by metal ear tagging in
316 C57BL/6 mice. *Vet Pathol*. 2007;**44**(4):458-66.
- 317 14. Liebich H. Connective and supportive tissues (textus connectivus). In: Liebich H,
318 ed. *Veterinary Histology of Domestic Mammals and Birds: Textbook and Colour*
319 *Atlas*. 5th ed. Sheffield, UK: Publishing; 2019: 62-90.
- 320 15. López A, Martinson SA. Respiratory System, Mediastinum, and Pleurae. In:
321 Zachary JF, ed. *Pathologic Basis of veterinary disease*. 6th ed. St. Louis, USA:
322 Elsevier; 2017:471-560.

- 323 16. McEwen BJ, Barsoum NJ. Auricular chondritis in Wistar rats. *Lab Anim.*
324 1990;**24**(3):280-283.
- 325 17. Njaa BL. The ear. In: Zachary JF, ed. *Pathologic Basis of veterinary disease*. 6th
326 ed. St. Louis, USA: Elsevier; 2017:1223-1264.
- 327 18. Noxon JO, Berger DJ, Ackermann MA, Petersen JR, Smith JD. Diagnosis and
328 clinical management of auricular chondritis in a dog presenting for evaluation of
329 severe pain. *Vet Dermatol.* 2021;**32**(2):200-e51.
- 330 19. Pachaly JR, Quessada AM, Belettini ST, et al. Treating otohematomas in dogs
331 with intra-lesional corticotherapy. *Acta Scient Vet.* 2021;**49**(2021):1785.
- 332 20. Ponce MC, Zorzi AR, Miranda JB, Amstalden EMI. Proposal for a new
333 histological scoring system for cartilage repair. *Clinics.* 2018;**73**:e562.
- 334 21. Reineking W, Punsmann TM, Wagener MG, et al. Laryngeal chondritis as a
335 differential for upper airway diseases in German sheep. *Acta Vet Scand.*
336 2020;**62**(2020):1-6.
- 337 22. Rutgers M, van Pelt MJP, Dhert WJA, Creemers LB, Saris DBF. Evaluation of
338 histological scoring systems for tissue-engineered, repaired, and osteoarthritic
339 cartilage. *Osteoarthritis and Cartilage.* 2010;**18**(1):12-23.
- 340 23. Schmitz N, Lavery S, Kraus VB, Aigner T. Basic methods in histopathology of
341 joint tissues. *Osteoarthritis and Cartilage.* 2010;**18**(Suplem. 3):113-16.
- 342 24. Taslı H, Birkent H, Gerek M. Three cases of relapsing polychondritis with isolated
343 laryngotracheal stenosis. *Turk Arch Otorhinolaryngol.* 2017;**55**(2):77–82.
- 344 25. Wang Y, Dai Shaodong. Structural basis of metal hypersensitivity. *Immunol Res.*
345 2013; **55**(0):83–90.

3. CONSIDERAÇÕES FINAIS

Nos limites deste estudo, pôde-se considerar que a policondrite descrita nos suínos afetou as cartilagens elásticas da orelha e da laringe, a qual favoreceu o desenvolvimento de uma doença clínica respiratória na fase da terminação. Quando os animais eram manejados, geravam dificuldade respiratória e em algumas situações a morte dos suínos. Além disso, estes apresentavam menor desempenho zootécnico, emagrecimento e otohematomas.

Várias das características clínicas, macroscópicas e microscópicas são semelhantes a policondrite recidivante descrita em humanos; assim, suspeita-se que a condição aqui descrita tenha uma etiopatogênese similar. Ainda, não foi possível identificar algum fator que possa estar relacionado e desencadeado a doença clínica nesses suínos. No conhecimento dos autores, este é o primeiro relato de policondrite simultânea em laringe e pavilhão auricular na espécie suína.

REFERÊNCIAS

- ADISSU, H.A.; BAIRD, J.D.; WOOD, G.A. A case of bilateral auricular chondritis in a heifer. **Case Reports in Veterinary Medicine**. v. 2014, p.1-4, 2014.
- ARNAUD, L. *et al.* Pathogenesis of relapsing polychondritis: a 2013 update. **Autoimmunity Reviews**.13, v.2, p.90-95, 2014.
- ASSOCIAÇÃO BRASILEIRA DE PROTEÍNA ANIMAL (ABPA). Relatório Anual 2020. **Associação Brasileira De Proteína Animal**. 2021. Disponível em: https://abpa-br.org/wp-content/uploads/2021/04/ABPA_Relatorio_Anual_2021_web.pdf
- BABA, T. *et al.* Auricular chondritis associated with systemic joint and cartilage inflammation in a cat. **The Journal of Veterinary Medical Science**. v.71, n.1, p.79-82, 2009
- BLEUL, U; STRANZINGER, G; SYDLER, T. Polychondritis: Eine neue Erkrankung beim Braunvieh? **Schweizer Archiv für Tierheilkunde**. v.153, n.11, p.526-529, 2011.
- BOLFA, P. *et al.* Clinical and pathological features in horses with advanced arytenoid chondritis. **Veterinary Pathology**. v.58, n.1, p.91-102. 2021.
- BONOW, M.O. *et al.* Arytenoid chondritis in two calves. **Ciência Rural**. v. 50, n. 6, p.1-5, 2020.
- BORGIA, F. *et al.* Relapsing Polychondritis: An Updated Review. **Biomedicines**. v.6, n.3, p.84-98, 2018.
- CLERCQ, E.D.; ROSSIGNOL, F.; MARTENS, A. Laryngeal hemiplegia in the horse: an update. **Vlaams Diergeneeskundig Tijdschrift**. v.87, n.5, p.283-294, 2018.
- CUNNANE, G. Relapsing Polychondritis. In: FIRESTEIN, G.S., *et al.* (Eds) **Kelley and Firestein's Textbook of Rheumatology**. Vol 2, 10 th ed. Philadelphia: Elsevier, 2017. p. 1788-1796.
- DRITZ, S.S. *et al.* Nutrient Deficiencies and Excess. In: Zimmerman, J.J. (Ed) **Diseases of swine**. 11th ed. Hoboken: Wiley-Blackwell, 2019. p-1043-1054.
- DUCHARME, N.G.; CHEETHAM, J. Abnormalities of the upper airway. In: HINCHCLIFF, K.W.; KANEPS, A.J.; GEOR, R.J. (Eds) **Equine Sports Medicine and Surgery E-Book: Basic and Clinical Sciences of the Equine Athlete**. 2nd ed. New York: Saunders, 2013. p. 572–575.
- LIEBICH H. Respiratory System (apparatus respiratorius). In: LIEBICH H. (ed) **Veterinary Histology of Domestic Mammals and Birds: Textbook and Colour Atlas**. 5th ed. Sheffield: Publishing, 2019. p. 239-257.
- LOPEZ, A.; SHANNON S.A. Respiratory System, Mediastinum, and Pleurae. In: ZACHARY, J.F. (ed) **Pathologic basis of veterinary disease**. 6 th ed. St. Louis: Elsevier, 2017. p. 471-560.

MAES, D. *et al.* A retrospective study of mortality in grow-finish pigs in a multi-site production system. **Journal Swine Health Production.** v.9, n. 6, p.267-273, 2001.

MCEWEN, B.J.; BARSOUM, N.J. Auricular chondritis in Wistar rats. **Laboratory Animals.** v.24, n. 3, p.280-283, 1990.

NJAA, B.L. The ear. In: ZACHARY J.F. (Ed) **Pathologic Basis of veterinary disease.** 6 th ed. St. Louis: Elsevier, 2017. p. 1223-1264.

NOXON J.O. *et al.* Diagnosis and clinical management of auricular chondritis in a dog presenting for evaluation of severe pain. **Veterinary Dermatology.** v.32, n.2, p.200-251, 2021.

PIVA, M.M. *et al.* Causes of death in growing finishing pigs in two technified farms in southern Brazil. **Pesquisa Veterinária Brasileira.** v.40, n.10, p.758-775, 2020.

RECH R.R. *et al.* Porcine respiratory disease complex after the introduction of H1N1/2009 influenza virus in Brazil. **Zoonoses Public Health.** v.65, p.155–161, 2018.

REINEKING W. *et al.* Laryngeal chondritis as a differential for upper airway diseases in German sheep. **Acta Veterinaria Scandinavica.** v.62, n.12, p.1-6, 2020.

SANTOS, R.L.; GUEDES, R.M.C. Sistema respiratório. In: SANTOS R.L.; ALESSI, A.C. (Eds) **Patologia veterinária.** 2nd ed. Rio de Janeiro: Roca, 2016. p. 14-97.

SCHWERTZ, C.I. *et al.* Causes of death of sows in three Brazilian pig farms. **Pesquisa Veterinária Brasileira.**, v. 41, e06857. 2021.

SOBESTIANSKY, J. *et al.* Classificação das doenças, In: SOBESTIANSKY, J.; BARCELLOS D. (Eds) **Doenças dos suínos.** 2 nd ed. Goiânia: Cãnone Editorial, 2012. p. 15-20.