

Simultânea seneciose crônica e eurytrematose em uma vaca

Simultaneous chronic seneciosis and eurytrematosis in a cow

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Resumo

Descreve-se a intoxicação crônica por *Senecio brasiliensis* com concomitante pancreatite intersticial e periductal por *Eurytrema* spp em uma vaca que demonstrou emagrecimento progressivo como sua principal manifestação clínica. Na intoxicação crônica por *Senecio* spp observou-se hepatite tóxica caracterizada por fibrose periportal e em ponte, megalocitose e proliferação das células epiteliais dos ductos biliares. A infestação por *Eurytrema* spp induziu fibrose periductal e intersticial acentuada associada a formas interductais do trematódeo.

Palavras-chave: *Senecio* spp., *Eurytrema* spp., bovinos, parasitologia, patologia.

Abstract

Chronic intoxication associated with the ingestion of *Senecio brasiliensis* with concomitant interstitial and periductal pancreatitis induced by *Eurytrema* spp are described in a cow that demonstrated severe progressive emaciation as its principal clinical manifestation. In chronic seneciosis there was severe toxic hepatitis characterized by periportal and bridging fibrosis, megalocytosis, and proliferation of epithelial bile duct cells. Infestation by *Eurytrema* spp produced marked periductal and interstitial fibrosis associated with parasitic forms within interlobular pancreatic ducts.

Key words: *Senecio* spp., *Eurytrema* spp., bovine, parasitology, pathology.

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Introduction

In Brazil, plants from the genus *Senecio* spp are located principally within the States of São Paulo, Paraná, Santa Catarina, and Rio Grande do Sul (TOKARNIA; DÖBEREINER; PEIXOTO, 2000). Although 128 species have been described in Southern Brazil (BARROS et al., 1992), few are extremely toxic, with *S. brasiliensis* considered the most toxic to domestic animals (TOKARNIA; DÖBEREINER; PEIXOTO, 2000). Poisoning by *Senecio* spp is due to pyrrolizidine alkaloids found within the plant that are metabolized to chemical substances called pyrroles which are extremely toxic to the liver (KELLY, 1993).

Intoxication by *Senecio* spp is the principal cause of death in adult cattle within some Brazilian States (BARROS et al., 1992), and is responsible for serious economic loss to the local beef-cattle industry (RIET-CORREA; MEDEIROS, 2001). Clinically, cattle intoxicated by *Senecio* spp may demonstrate progressive emaciation, digestive and neurological alterations, icterus, and photodermatitis (BARROS et al., 1992; TOKARNIA; DÖBEREINER; PEIXOTO, 2000). Two distinct clinical manifestations of *Senecio* spp. poisoning are described: an acute or subacute form that is followed by death within a few days after ingestion of the plant; and a chronic manifestation with death occurring several weeks or months after initial contact with the plant (BARROS et al., 1992). Additionally, in the chronic form most animals demonstrate severe progressive emaciation; in areas where the disease is endemic, chronic intoxication may result in the continual lost of animals during prolonged periods (TOKARNIA; DÖBEREINER; PEIXOTO, 2000). Gross and microscopic alterations of both manifestations include severe and diffused hepatic fibrosis, marked hepatomegalocytosis, and hyperplasia of intrahepatic bile ducts (BARROS et al., 1992; KELLY, 1993; TOKARNIA; DÖBEREINER; PEIXOTO, 2000).

Eurytrematosis is caused by trematodes (*Eurytrema coelomaticum* and *Eurytrema pancreaticum*) that live principally in the pancreatic ducts and occasionally in the bile ducts of ruminants

and other animals (TRAVASSOS; FREITAS; KOHN, 1969; SOULSBY, 1982; JUBB, 1993). In Brazil, bovine eurytrematosis has been more related to *E. coelomaticum* than other species (TRAVASSOS; FREITAS; KOHN, 1969; MATTOS JR; VIANNA, 1987). Bovine eurytrematosis is considered endemic within the State of Paraná; the prevalence of infested animals varies with the geographical location, and may range from 10 to 50% (AZEVEDO et al., 1994).

Infestations of *Eurytrema* spp in bovines induces chronic interstitial pancreatitis with subsequent ductal obstruction (JUBB, 1993), which often leads to condemnation of the organ by the Federal Inspection Service during routine inspection (MATTOS JR; VIANNA, 1987; HEADLEY, 2000). Massive infestation by *Eurytrema* spp has been related to dietary disturbances (FOX et al., 1981). However, in most cases of chronic parasitic pancreatitis the acinar pancreas (Islets of Langerhans) is markedly spared (JUBB, 1993). Even though clinical manifestations of chronic parasitic pancreatitis are non-specific; in most cases, there is progressive weight loss (MATTOS JR; VIANNA, 1987). Therefore, it has been postulated that sudden cachexia, debility, associated with marked absence of diarrhea, anemia, and cardio-respiratory difficulties are the principal clinical manifestations of bovine eurytrematosis (CORREA et al., 1984). Three distinct histopathological manifestations have been associated with bovine eurytrematosis (YAMAMURA, 1989; BELÉM et al., 1994), suggesting a direct relationship between the degree of parasitism and the damage observed in the affected organ (BELÉM et al., 1994).

This paper describes the occurrence of simultaneous chronic intoxication by *S. brasiliensis* and parasitism by *Eurytrema* spp in a cow, and offers brief differential diagnosis for common diseases of cattle that presents emaciation as part of its clinical manifestation.

Case Report

The animal in question was a four-year-old, mixed-breed cow that was found dead by its owner. He related that the animal was severely emaciated, anorexic, and that treatment with antibiotics was unsuccessful. A visit to the location where the animal was maintained revealed several clumps of *Senecio brasiliensis*; there were also few severely emaciated cattle on the farm. The owner was not aware of the toxic effects of this plant and indicated that the plant was disseminated within his farm, but he eradicated most by stumping. He also related that there is constant year-around lost of animals severely emaciated.

At necropsy, there was marked dehydration, moderate ocular jaundice, moderate hydroperitoneum, and severe lost of body mass. Significant gross alterations were restricted to the liver and pancreas. The pancreas was extremely large, firm, with various different-sized (0.3 – 1.5 cm diameter) darkened nodular areas disseminated throughout the organ (Figure 1); these nodular areas were surrounded by whitish proliferative connective tissue. The sectioned pancreas revealed a severe disseminated infestation of brown, thin leaf-like flukes packed within the interlobular pancreatic ducts (Figure 2); the size of all ductal walls was markedly increased. The liver was markedly atrophic, firm and yellowish in color. Selected tissues (liver, pancreas, kidney, lung, and brain) were fixed in 10% formalin solution and routinely processed for histopathological evaluation.

Microscopically, the pancreas revealed severe, diffused, chronic parasitic pancreatitis associated with interlobular pancreatic flukes consistent with *Eurytrema* spp (Figure 2). The walls of all interlobular ducts were severely proliferated resulting in compressive atrophy and loss of adjacent pancreatic parenchyma. In almost all sections of the pancreas examined, there was marked absence of entire pancreatic lobes; those found demonstrated normal or mild atrophy of Islets of Langerhans (endocrine pancreas). In these few areas of reminiscent pancreatic tissue within the damaged organ, there was severe necrosis, proliferation, or atrophy of the acinar lobes (exocrine pancreas). In some areas of severe periductal proliferation of connective tissue, few pancreatic acinars were observed; these were either extremely dilated or markedly atrophic and surrounded by a mild to severe mononuclear infiltrate associated with eggs of the trematode. Liver alterations revealed severe chronic hepatitis (Figure 3). There was marked proliferation of periportal and interlobular connective tissue, resulting in severe bridging fibrosis, atrophy of adjacent hepatic parenchyma, and the forming of tiny islands of hepatocytes. Associated with this severe proliferation of connective tissue there was discrete, multifocal bile stasis, discrete megalocytosis, moderate foci of mid-zonal hepatocellular degeneration, and moderate congestion of hepatic sinusoids. Other significant histopathological alterations were observed in the kidneys, and were characterized as tubular toxic nephrosis, in which there was severe multifocal, coagulative necrosis of tubular epithelial cells associated with tubular loss of protein.

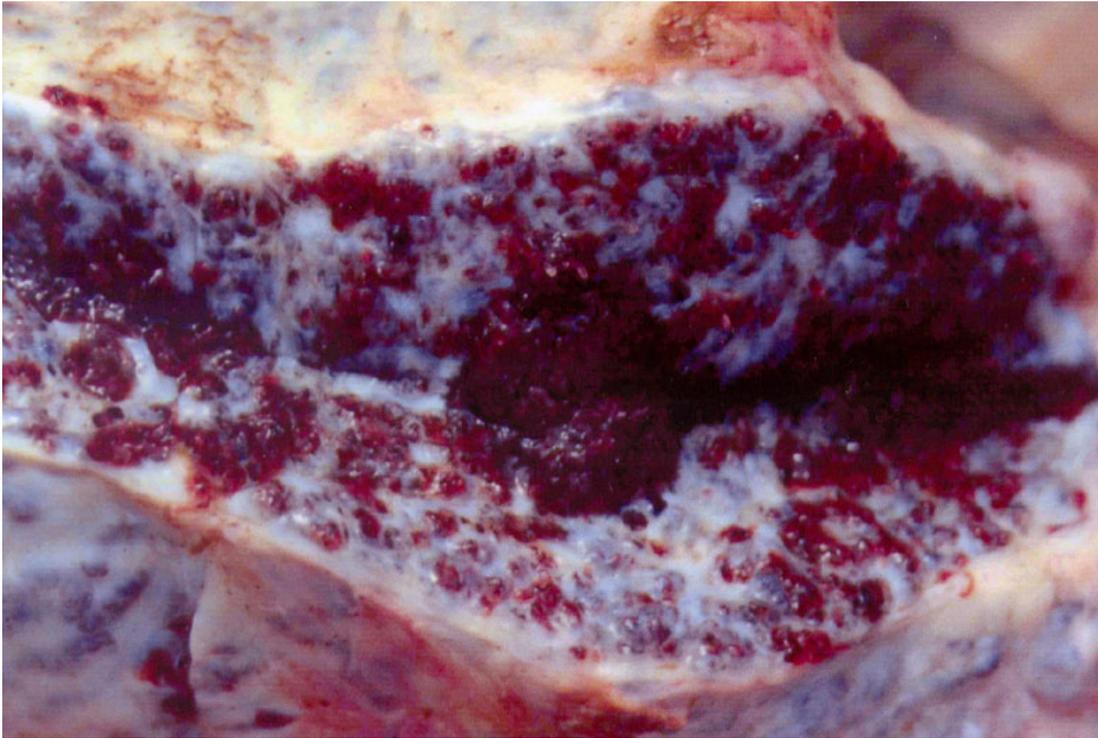


Figure 1. Sectioned pancreas; gross manifestation of chronic bovine eurytrematosis. There are numerous tiny, brown, leaf-like flukes closely packed within interlobular pancreatic ducts and severe proliferation of connective tissue.

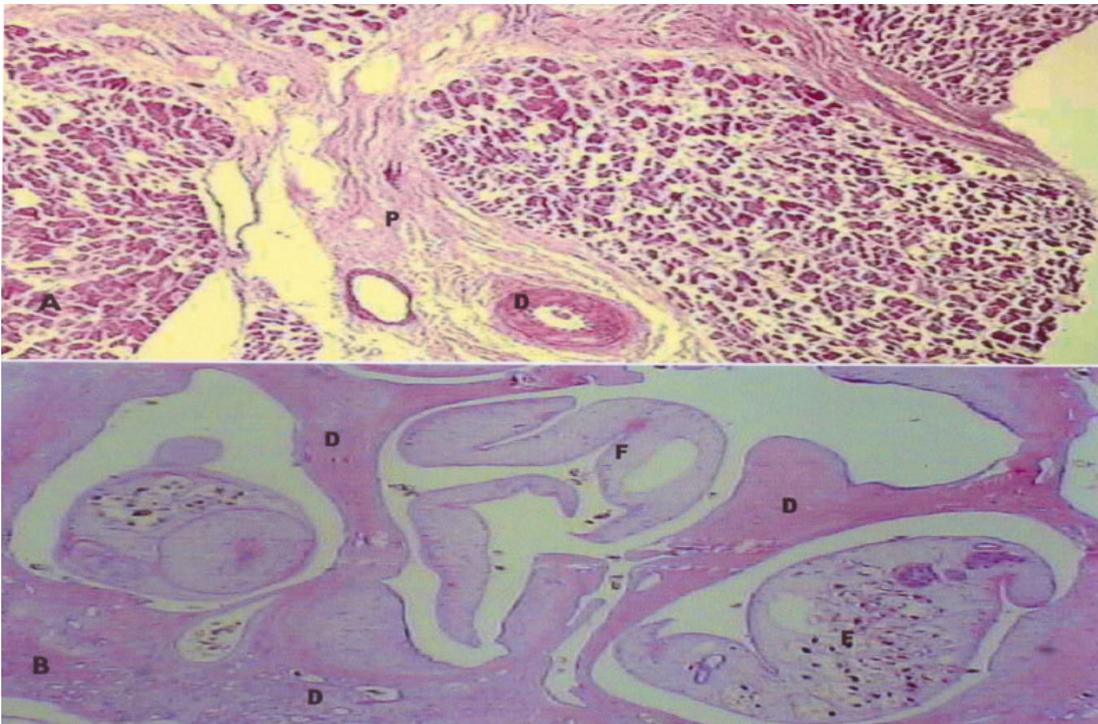


Figure 2. Pancreas; composed photomicrograph (A, HE, Obj. 4x; B HE, Obj. 20x) of chronic bovine eurytrematosis. Observe marked proliferation (P) of fibrous tissue around interlobular pancreatic ducts in A; and examples of the fluke (F) within interlobular ducts (D) in B.

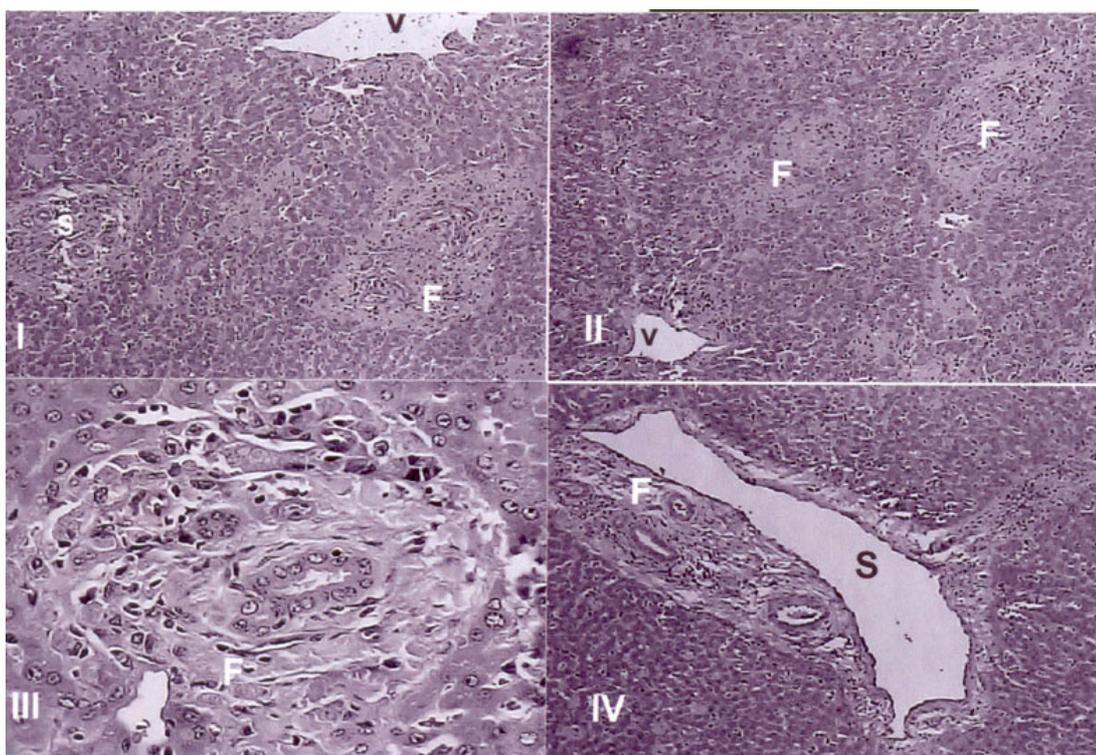


Figure 3. Liver; composed photomicrograph of chronic bovine seneciosis (III & IV: HE, Obj. 20x). There is marked fibrosis (F) distributed throughout the entire hepatic parenchyma, around the central lobular vein (V) and the periportal space (S), resulting in severe loss and atrophy of hepatic tissues (I & II: HE, Obj. 4x). Observe marked periportal fibrosis (F) with proliferation of bile ducts (III: HE, Obj. 20x), and severe fibrosis (F) at the periportal space (S) and the hepatic parenchyma (IV: Obj. 8x).

Discussion

The epidemiological information obtained associated with the gross and histopathological lesions observed in this cow are consistent with simultaneous chronic pancreatic parasitism by *Eurytrema* spp and chronic intoxication by *Senecio brasiliensis* as previously described (MATTOS JR; VIANNA, 1987; YAMAMURA, 1989; BARROS et al., 1992; JUBB, 1993; BELÉM et al., 1994; HEADLEY, 2000; TOKARNIA; DÖBEREINER; PEIXOTO, 2000). Although mortality has been associated with eurytrematosis (CORREA et al., 1984; GRAYDON et al., 1992), this is not a common manifestation of this disease; so we believe that in this case death should be related to severe hepatic dysfunction associated with renal damage due to chronic pyrrolizidine alkaloids intoxication (KELLY, 1993). Although these two chronic bovine alterations were observed in this animal in association with marked

progressive emaciation, there is no significant evidence to indicate that the diseases are interrelated or dependent.

Even though chronic intoxication by *Senecio* spp and eurytrematosis in cattle could be characterized clinically by progressive emaciation (CORREA et al., 1984; BARROS et al., 1992; GRAYDON et al., 1992; JUBB, 1993; KELLY, 1993), as was observed in this case, gross and histopathological findings of these diseases are markedly different, so this clinical manifestation must be considered as nonspecific for both diseases. Therefore, a definite *in vivo* diagnosis requires the realization of liver biopsies associated with specific biochemical evaluation for bovine seneciosis (BARROS; CASTILHOS; SANTOS, 1987), and cervical intradermal reactions to characterize bovine eurytrematosis (BELÉM et al., 1996); pathological observations of the dead animal are characteristic of each disease.

Hepatic encephalopathy, a relatively common histopathological nervous manifestation of chronic bovine seneciosis (BARROS et al., 1992), was not observed in this animal. In bovine seneciosis, this nervous manifestation has been related to the inability of the impaired liver to effectively transform ammonia absorbed from the intestine into urea, resulting in hyperammonemia and subsequent white matter loss to the central nervous system (KELLY, 1993). Other extra-hepatic alterations associated with bovine seneciosis observed in this case were hydroperitoneum and renal failure.

In this case of massive infestation by *Eurytrema* spp there was severe periductal fibrosis and subsequent marked destruction of the exocrine pancreas due to compressive atrophy, while the endocrine pancreas was remarkably spared. These pancreatic lesions described in this report correspond to the Third Stage histopathological manifestation of bovine eurytrematosis (YAMAMURA, 1989; BELÉM et al., 1994). Although massive infestation by *Eurytrema* spp has been related to dietary disturbances (FOX et al., 1981), and a reduction in the production of insulin (MATTOS JR; VIANNA, 1987), this animal demonstrated no morphological evidence to substantiate a decline in the production of insulin, since the endocrine pancreas (Islets of Langerhans) were preserved. Similar pathological observations have been described (JUBB, 1993; HEADLEY, 2000). Atrophy of the pancreatic islets, as occurred in this case, is a direct consequence of chronic interstitial pancreatitis (JUBB, 1993). Additionally, this author has indicated that the islets are more resistant to compressive atrophy than acinar tissue, reducing the possibility of producing diabetes mellitus as a secondary complication of chronic pancreatitis. This may indicate that there is no definite clinical, pathological, or physiological correlation between chronic pancreatitis due to bovine eurytrematosis and decreased insulin production.

Although there are descriptions of hypertrophy and atrophy (SANTOS, 1989; GRAYDON et al., 1992), of the pancreas due to eurytrematosis, both

alterations described should be considered as compressive atrophy, as was observed in this case. This is because in the so-called hypertrophic (proliferative) form of eurytrematosis there is an increase in the size of the pancreas due to interstitial fibrous proliferation without a corresponding increase of normal pancreatic parenchyma. As a result, proliferating fibrous connective tissue would then induce secondary destruction of the adjacent glandular parenchyma by compressive atrophy, with preservation of the Islets of Langerhans. Therefore, we suggest that chronic proliferative pancreatitis induced by *Eurytrema* spp should be related to secondary severe compressive atrophy of the pancreatic parenchyma, terminal obliteration, and obstruction of the pancreatic ducts associated with interductal forms of the trematode.

In various Brazilian States, there are other relatively common diseases that affect cattle and which maybe easily confused clinically (due to severe and progressive emaciation), with seneciosis or eurytrematosis in cattle. These include enzootic bovine calcosinosis that is endemic within the State of Mato Grosso do Sul, intoxication by bracken fern (*Pteridium aquilinum*), and bovine tuberculosis.

Enzootic bovine calcosinosis and intoxication by bracken fern are two diseases that are also considered responsible for severe economic loss to the local beef industry (RIET-CORREA; MEDEIROS, 2001). Enzootic bovine calcosinosis is a chronic debilitating seasonal disease induced by the active metabolite of vitamin D (1,25 (OH)₂ D₃; calcitriol), that is found within the calcinogenic plant *Solanum malacoxylon* (TOKARNIA; DÖBEREINER; PEIXOTO, 2000; SOARES; RIET-CORREA, 2003) Clinically there is progressive emaciation, rigid walking movements, and marked retraction of the abdomen (TOKARNIA; DÖBEREINER; PEIXOTO, 2000). Grossly, there is severe mineralization of the cardiovascular system and soft tissues (principally the lungs), which on microscopic evaluation corresponds to calcification of soft tissues and the elastic fibers of affected blood

vessels (SOARES; RIET-CORREA, 2003). These lesions do not occur in either bovine seneciosis or eurytrematosis.

Intoxication by bracken fern (*Pteridium aquilinum*) produces three distinct clinical-pathological manifestations in cattle: enzootic hematuria, carcinoma of the upper digestive tract, and acute hemorrhagic syndrome (TOKARNIA; DÖBEREINER; PEIXOTO, 2000). The first two clinical syndromes of this intoxication presents severe weight loss as part of their clinical manifestations, and may be confused with chronic seneciosis or eurytrematosis, in the absence of other clinical signs that are more specific for these diseases.

Bovine tuberculosis is caused by *Mycobacterium bovis* (TIMONEY et al., 1992; JONES; HUNT; KING, 1997; RADOSTITS et al., 2002). Clinically bovine tuberculosis is characterized by chronic progressive emaciation without other significant clinical manifestations (RADOSTITS et al., 2002). In most cases of bovine tuberculosis there is involvement of the bronchial, mediastinal, submaxillary and retropharyngeal lymph nodes (TIMONEY et al., 1992). However, disseminated pleural and peritoneal (TIMONEY et al., 1992; JONES; HUNT; KING, 1997), cutaneous (RADOSTITS et al., 2002), and systemic (HEADLEY, 2002) manifestations of bovine tuberculosis have also been described. This disease is characterized by various different sized, superficial or deeply located, firm or hard tubercles bulging from mucous or serous surfaces (SMITH, 1990; JONES; HUNT; KING, 1997); sectioned tubercles are yellowish, caseous, solid and dry necrotic center that is normally calcified (JONES; HUNT; KING, 1997). Microscopically, there is a collection of epithelioid and giant cells surrounded by a layer of fibroblasts and lymphocytes, having the center of the granuloma necrotic and calcified (JONES; HUNT; KING, 1997); acid-fast (red) bacteria identified by the Ziehl-Neelsen method within typical tubercles are diagnostic for tuberculosis (TIMONEY et al., 1992; JONES; HUNT; KING, 1997).

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