

Pteridium aquilinum (L.) Kuhn (Bracken Fern) and health hazards in animals

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Enzootic Bovine Haematuria (EBH) is a chronic disease of cattle in hilly regions and is characterized by the intermittent presence of blood in urine and tumours of mixed origin in the urinary bladder. EBH causes considerable economic losses due to decreased production and is a serious concern for farmers of hilly regions in India. The incidence of haematuria varies considerably in herds maintained under apparently similar conditions and even in the same herd from time to time. In some herds, only an occasional case occurs but in others, it is quite common to find 10 to 30% of animals affected clinically at the same time. EBH has been associated with chronic exposure to bracken fern (*Pteridium aquilinum*) in low doses in bovines of hilly areas

About the bracken Fern

Bracken fern (*Pteridium aquilinum*) is one of the most common weeds in our ecosystem and is a major animal health concern because of its special chemical constituents. Fern has thiaminase enzyme and other thermostable organic molecules of anti-thiamin character. It showed characteristic neurological symptoms in monogastric bracken fern-fed animals. Cattle graze bracken in the absence of conventional feed resources. The individual animals can develop a taste for the plant also. Young shoots and fronds are particularly preferred by the animals. Bracken fern is among the five most common plants in the world known to cause cancer naturally in animals. Enzootic bovine haematuria (EBH) is also associated with concurrent infection by Bovine Papillomavirus (BPV-2) which was demonstrated in bladder tumours of cattle exposed to bracken fern.

Distribution/ Epidemiology

In India, Bracken fern (*Pteridium* spp.) is present in and around grazing lands and forest areas throughout the Himalayan hills between 1,800 and 2,400 m above sea level. The disease is restricted to well-defined pockets despite the widespread distribution of the fern in the Himalayas and southern hills of the country. The possible reason for this could be the lack of carcinogenic



potential in the plants growing in different areas. Also, the variation in the disease pattern may be attributed to different environmental conditions and animal-rearing practices followed in the different regions. Fern is occasionally grazed by animals and in some areas, it is present as a contaminant in grasses stored for winter feeding. Bracken fern is reported to induce tumours in experimental animals also.

Pathophysiology of disease

Bracken fern toxicity appears to be cumulative and symptoms generally appear after animals are exposed for 1 to 3 months to a bracken-infested pasture. Occasionally, symptoms can be seen from 1 to 3 weeks even after the removal of animals from the source. During exposure, the total amount of bracken fern ingested may vary from 50 to 100% of the animal's body weight. The development of bladder tumours, on the other hand, requires exposure for a longer duration, ranging between 225 and 550 days depending on the availability of the bracken fern (0.5 to 2 kg/day). Prolonged exposure to this weed produces multiple tumours in the upper alimentary tract and urinary bladder in susceptible animals. These tumours lead to haemorrhages in the bladder mucosa. The disease is also associated with haematuria, leucopenia, anaemia, and reduced haemoglobin and was reproduced experimentally in bracken-fed cattle.

Toxicity

Bracken fern has several toxic components; ptaquiloside, a glycoside sesquiterpenoid is the major carcinogenic component and is capable of inducing clastogenesis in cell cultures. Ptaquiloside is also known to induce mutagenesis and carcinogenic cascade in experimental animals. Besides ptaquiloside, a large number of other compounds with diverse biological activities were isolated from bracken fern. Ptaquiloside content varies in the Pteridium samples collected from different regions of the world. Variation in the disease incidence in the hilly areas was linked largely to the variation in the ptaquiloside content of the fern from different areas. Ptaquiloside is excreted in urine where it preserves its carcinogenic potential and induces bladder tumours in cattle. Also, ptaquiloside is a potential risk to human health as it is secreted in milk and causes different types of tumours when administered to rats. Depending on exposure and amount ingested, the following three different clinical-pathological pictures mainly in cattle:

1. Haemorrhagic diathesis
2. BEH
3. Carcinomas of the upper digestive tract

Although, immune suppression is sufficient to initiate premalignant lesions, however, the mutagens present in bracken fern are responsible for the progression to neoplasia. Infection by Bovine Papillomavirus (BPV-2) was demonstrated in bladder tumours of cattle exposed to bracken fern. BPV-2, being capable of staying latent in some tissues including the urinary



bladder, was isolated from normal urothelium as well as bracken fern-induced spontaneous/experimental bladder tumours. BPV-2 genomic DNA was detected through PCR in urinary bladder tissue and urine of the majority of animals in the EBH endemic area. Upon cancer development, BPV-2 would seem to undergo significant changes, expressing itself. A similar synergism between *papillomavirus* and bracken fern was also postulated in bovine and human gastrointestinal tumours, associating sometimes BPV-4 and quercetin, a mutagenic flavonoid present in bracken fern.

Effect on animals' non-ruminant animals

Horses: They are mostly affected animals due to the presence of thiaminase in fern which splits the essential vitamin B1 resulting in decreased levels in blood. Typical signs will occur only when the bracken content of forage is at least 10 to 20% and consumption is at least 3 to 4 weeks. Symptoms of poisoning include weight loss, lethargy, anaemia, anorexia, colic, convulsion, staggering gait, recumbency, and loss of muscular control. In severe cases, tachycardia is preceded by convulsions, clonic spasms and opisthotonus. Rectal temperature may be high (40°C) or normal. Ruminants are practically resistant to thiamine deficiency since rumen microbe can synthesise it.

Swine: The reports are relatively rare, however, symptoms like dyspnoea, and recumbency are reported. Conditions like cardiac enlargement and mottling, congestive heart failure, degeneration of cardiac muscle, oedematous lung and enlarged gallbladder are common.

Ruminants: The diseases of ruminants are haemorrhagic syndrome (acute haemorrhagic disease), and upper alimentary carcinoma. The haemorrhage in the urinary bladder in cattle is an outcome of cancer development leading to haematuria.

Haemorrhagic syndrome (acute hemorrhagic disease): Common in weaned calves, but may also occur in older cattle and rarely in sheep. The affected animal showed weakness, anorexia, pyrexia (41° to 43°C) with pale mucosa, laboured breathing and multiple haemorrhages. Furthermore, sudden death is occasionally observed. Bone marrow depression due to acute toxicity. Haemorrhages are common in the nose, vagina, mouth and eyes. Oedema of the throat is also quite frequent. Post-mortem also reveals haemorrhages in the lungs, heart, stomach and intestines. Bone marrow showed hypoplasia, became fatty and colour changed to yellow.

Upper alimentary carcinoma: Different forms of carcinomas in the oral cavity, oesophagus and fore-stomach were reported from cattle. In the majority of the cases, malignant transformation occurs, if accompanied by BPV4 infection.

Diagnosis

With the recent advances in technology, new diagnostic tools facilitated the detection of two main etiological agents of the disease. A traditional method used to diagnose EBH was to



detect the presence of erythrocytes in urine samples. However, haematuria may sometimes be absent during the remission phase, hence leading to incorrect diagnosis. Due to the difficulty of diagnosis of BPV infection by virus isolation, various molecular techniques were developed and standardised which helped in rapid and accurate diagnosis of EBH. PCR, Real-time PCR, semi-nested PCR, in situ hybridization, Southern blotting etc. are some of the sensitive and commonly used molecular techniques in the diagnosis of this disease. Extensive studies confirmed that BPV-2 causes abortive infection in the bladder and the virus could not be demonstrated by TEM and infection is not transmissible but one can demonstrate BPV-2 DNA by PCR and other more sensitive molecular techniques.

Treatment and control

The prognosis of acute haemorrhagic disease is generally poor and most of the animals (> 80- 90%) die within 1 to 2 weeks after the onset of the symptoms. Treatment with the frequently reported antidote for fern toxicity, DL-butyl alcohol, is of limited use as it generally fails to stimulate the bone marrow in clinically advanced cases. Furthermore, its use as a therapeutic agent is prohibited in food-producing animals. In critically ill animals, blood or platelet transfusion can be effective but generally requires a large amount (2-4 litre) of blood making this approach less feasible. Antimicrobial agents can be used to prevent secondary infections. The infested pasture should be removed immediately and animals should be stall fed separately. Removal of animals from the primary source of bracken is the best way of preventing or at least limiting the duration of grazing. Rotational grazing on bracken-contaminated and non-contaminated pastures at regular intervals is a fair approach to prevent possible toxicity in animals. The use of herbicide application, cutting, rolling and burning can be adopted as a control measure but has its limitations. Although, multiple treatments with asyllum are necessary for the effective control of bracken, however, 100% control is difficult to achieve. No specific line of treatment is available for EBH, and therapy generally relies on the symptomatic treatment.