

ENZOOTIC BOVINE HAEMATURIA: CLINICAL AND PATHOMORPHOLOGICAL STUDIES

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Abstract

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Clinical and pathomorphological features of spontaneous enzootic bovine haematuria in seven cattle were studied. In early stage no constitutional disturbance could be seen, but with the lapse of time discharge of blood-tinged urine, anaemia and lymphopenia became evident. In advanced stages of disease, the animals became hide-bound. Urinary bladder was the main site of lesions though liver (biliary hyperplasia), ureters and kidneys were also involved. The wall of urinary bladder was thickened, hyperaemic and oedematous. The pathological lesions of significance in urinary bladder were chronic cystitis, papilloma, squamous cell metaplasia, transitional cell carcinoma and adenocarcinoma. Pathomorphology of these lesions has been described and the aetiology discussed briefly.

Haematuria, cattle, neoplastic growth, bracken fern.

Enzootic bovine haematuria (EBH) is an age-old problem and occurs in different parts of the world. The first case in India was reported by Rangaswami in 1922 from the Nilgiri hills in Tamil Nadu (Nandi 1969). The epizootiological survey carried out recently has shown its prevalence in different districts of Arunachal Pradesh, Sikkim, Nagaland, West Bengal, Uttar Pradesh, Himachal Pradesh, Jammu and Kashmir, Kerala, Karnatak and Tamil Nadu (Prasad and Singh 1982). Considering the wide prevalence, obscure etiology and diverse panorama of lesions (inflammatory, hyperplastic, metaplastic and neoplastic) of the disease, the present communication describes the clinical signs/symptoms and pathomorphological alterations occurring in spontaneous cases.

Materials and Methods

A total of seven aged (7-10 years) haematuric cattle (4 cows and 3 bullocks) were purchased from Sundarkhal (an enzootic

pocket), Mukteswar, U. P. These were suffering from haematuria for periods varying from six months to one year. The general body condition of these animals was poor. Maintenance rations were provided to them and they were allowed to die their natural death. Clinical signs/symptoms exhibited by these animals and haemogram were recorded regularly. Detailed necropsy was conducted after death. The gross lesions were recorded and morbid materials were processed by conventional methods to study the histopathological changes.

Results

Clinical signs/symptoms

Clinically, no other constitutional disturbance could be seen apart from haematuric symptoms. The colour intensity of the urine increased and the body condition started deteriorating with the advancement of the illness. Initially, the discharge of the bloody urine was intermittent but with the lapse of time it became a regular and constant feature in all the animals. The haemogram gave an indication of anaemia and lymphopenia with compensatory neutrophilia but the total leukocyte count remained within the normal range. The death of these animals occurred between 12 to 36 months after their purchase.

Pathomorphological changes

Gross pathology. In general the carcasses were emaciated and hide-bound. The subcutaneous fat and the fat around the heart and kidneys was gelatinised. The main site of lesions was urinary bladder (UB), though ureters, kidneys, liver and spleen also exhibited lesions in some cases. Invariably the UB was distended with varying amount of blood-tinged urine and blood clots. The wall of UB was moderately to severely thickened, hyperaemic, oedematous and corrugated. The mucosal surface of UB exhibited a number of haemorrhagic spots/ulcers but the amount of blood clots was not always directly proportional to the number of haemorrhagic spots/ulcers. Besides these, a number of sessile and pedunculated nodules of different sizes (pin head to marble) and papillary growths were seen scattered over the mucosal surface, without any site of predilection (Fig. 1). The smaller nodules coalesced to form bigger ones. Some of these nodules were congested while others had the appearance and texture of surrounding unaffected mucosa.

The kidneys were congested in some cases while others showed yellowish pallor, with occasional cicatrizations in the cortex. The medulla was soft and congested in general with papillary necrosis in one case. No gross changes could be seen in ureters. The liver was congested in some animals and pale in others. Petechiae on the inferior border of the parietal surface were almost a constant feature in the spleen.



Fig. 1. Multiple papillary growth on the mucosal surface of urinary bladder.

Histopathology

The histopathological changes in UB ranged from inflammation to hyperplasia and metaplasia to anaplasia. Presence of these changes in the same specimen in different combinations was not uncommon. The inflammatory changes were those of chronic cystitis, characterised by large/small mononuclear cell infiltration in submucosa. Occasionally these mononuclear cells formed small aggregates resembling lymphoid follicles. Other changes included proliferation and engorgement of submucosal blood vessels. Among non-inflammatory changes, focal to diffuse and mild to pronounced hyperplasia of lining transitional epithelium was almost a constant feature (Fig. 2). Some of the hyperplastic cells exhibited distinct intracellular vacuolation (Fig. 3). Downward proliferation of hyperplastic epithelium occurred quite frequently but remained confined to submucosal layer only. These hyperplastic cells transformed themselves either in papillomatous pattern (Fig. 4) or in small clusters of solid mass or showed glandular transformation with eosinophilic secretory mass. In central zone of some the "clusters" varying degree of degenerative or necrotic changes occurred resulting in acini-like spaces, giving an adenomatous pattern. The neoplastic changes included characteristic lesions of squamous metaplasia, adenocarcinoma and/or transitional cell carcinoma. Aggregates of neoplastic cells were either localised to the epithelial surface



Fig. 2. Normal (a) and pronounced (b) hyperplasia of transitional epithelium. H. E. x 500.

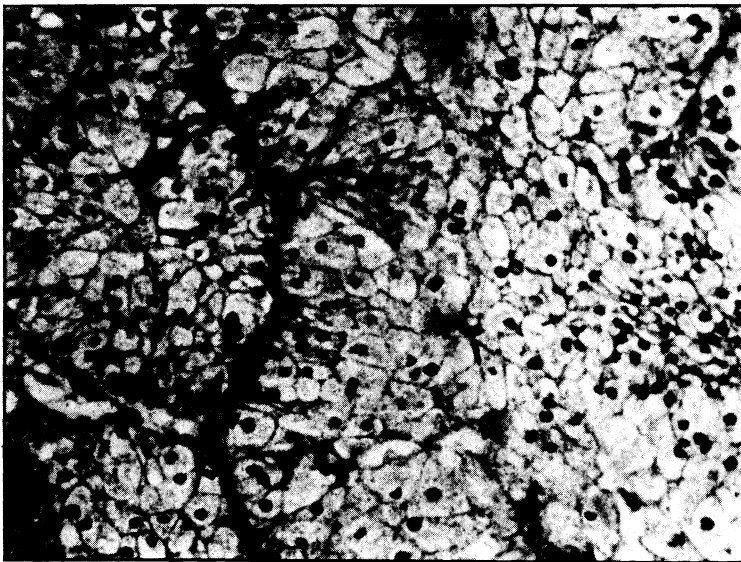


Fig. 3. Neoplastic transitional cells showing intracellular vacuolation. H. E. x 750.

or infiltrated into the oedematous submucosa or even into the muscular coat (Fig. 5). Fibrosis around the neoplastic cell aggregates in muscular coat was occasionally observed. No evidence of metastases in regional lymph nodes was seen.

Mild degree of hyperplasia of lining epithelium with degenerative changes were the common features observed in ureters. At places, tendency to keratinization of lining epithelium was also discernible. These hyperplastic changes exhibited downward infiltration and resulted in the formation of acini-like structures and some showed cystic dilations. In one case, neoplastic changes occurred in the lining epithelium. The downward growth of these neoplastic cells almost abutted the muscular layer.

Varying degrees of congestion associated with focal areas of lymphocytic infiltration in interstitial tissue and/or fibrosis was seen in kidneys. Some of the glomeruli exhibited congestion but the majority of them depicted atrophic changes with dilation of Bowman's space, containing proteinous material. Other changes included degeneration of tubular epithelium, occasionally leading to necrosis and engorgement of interstitial blood vessels. The normal architecture of hepatic lobules was disrupted and the hepatocytes exhibited degenerative and atrophic changes. Besides these, varying degrees of biliary hyperplasia and focal areas of fibrocellular (mononuclear cells) reaction were also evident. The microsections of spleen revealed congestion and depletion of lymphoid materials.

Discussion

The present study indicated that the clinical picture and the pathological lesions observed in our cattle resembled those described elsewhere in the world (Plummer 1944; Pamukcu 1955; Mugerá and Nerito 1968; Smith and Beatson 1970; Mc Kenzie 1978). Anaemia was considered to be due to blood loss from haemorrhagic spots/ulcers in UB by some of the workers (Mugerá and Nerito 1968; Singh et al. 1973; Rajendran et al. 1979), while others believed that aplastic changes in bone marrow due to bracken fern was the cause of anaemia (Evans et al. 1954; Clarke and Clarke 1967; Rosenberger 1971) because bracken fern was thought to contain certain radiomimetic substances. Another possibility might be the involvement of both the above-mentioned factors (blood loss and aplastic change in bone marrow) in the development of anaemia. As observed by Rajendran et al. (1979), we also noted lymphopenia with compensatory neutrophilia in this study. On the contrary, Mugerá and Nerito (1968) and Singh et al. (1973) reported lymphocytosis.

The pathoanatomical changes observed in UB were in conformity with those described by earlier workers (Mugerá and Nerito 1968; Moulton 1978; Rajendran et al. 1979; Jones and Hunt 1983). The presence of various changes (inflammatory, hyperplastic, metaplastic and neoplastic) in different combinations indicated that the lesion complex appears to be inflammatory in origin. Body defence mechanism might be responsible for hyperplastic/metaplastic changes occurring in UB and in the course of time neoplastic property is acquired in these hyper-

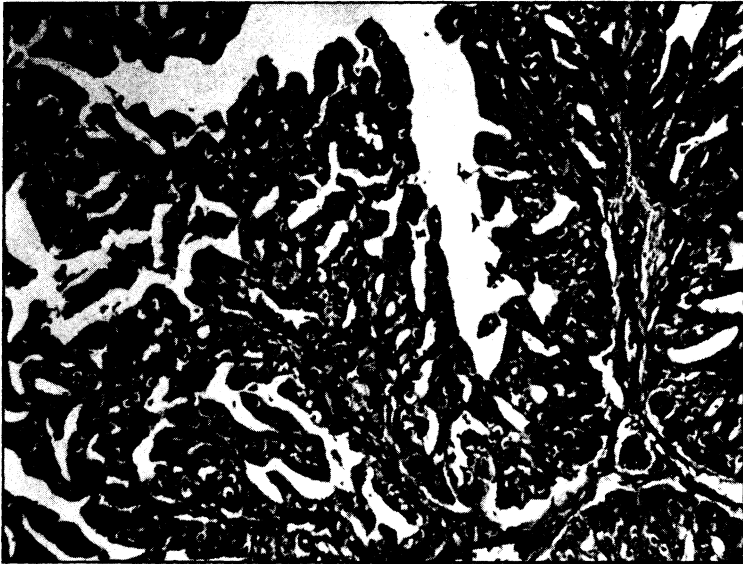


Fig. 4. Neoplastic cells arranged in papillary pattern. H. E. x 500.

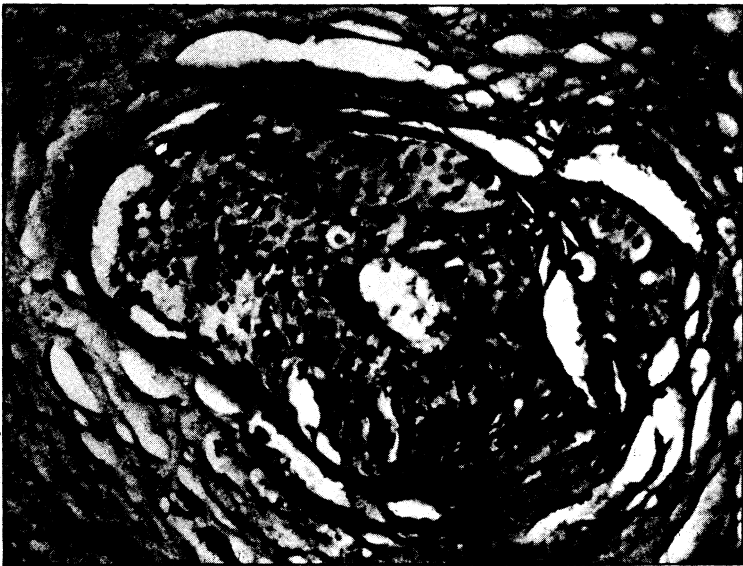


Fig. 5. Infiltrated column of neoplastic cells in the muscular coat of urinary bladder surrounded by fibrosis. H. E. x 750.

plastic/metaplastic cells. This explains the reason for the long latent period needed for the development of neoplastic lesions in UB of animals suffering from EBH.

The adenomatous structures in the submucosa showed either eosinophilic secretion in their lumina or evidence of central degenerating/necrotic mass. However, it could not be ascertained whether these adenomatous structures represented glandular metaplasia or were the areas of central necrosis in "clusters of solid mass" because central necroses are commonly seen in rapidly growing neoplasms like mammary cancers. This aspect needs further study.

Numerous factors have been suggested to be of causal significance in EBH, but still these remain unsettled. Experimental studies have suggested the involvement of bracken fern (*Pteridium aquilinum*) as the causative factor (Rosenberger and Heesch 1960; Pamukcu et al. 1967; Price and Pamukcu 1968; Mc Kenzie 1978) because tannin exhibiting carcinogenic activity has been found in bracken fern (Wang et al. 1973, 1975). However, this does not rule out the possibilities of other factors like dietary deficiencies, poisonous plants, excess of molybdenum, deficiency of lime and various infectious agents including viruses (Moulton 1978).

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Enzootická bovinní hematurie: klinická a patomorfologická studie

U 7 dospělých jedinců skotu byly sledovány klinické a patomorfologické symptomy spontánní enzootické hematurie. Průběh nemoci byl zpočátku asymptomatický, později se objevila krev v moči, anémie a lymfopénie. V terminálním stadiu nemoci byla zvířata krajně vyhublá. Patomorfologické nálezy převažovaly v močovém měchýři, i když byla postižena játra (biliární hyperplazie), močovody a ledviny. Stěna močového měchýře byla hyperemická a edematózní, významnými nálezy byla chronická cystitis, papilomy, metaplasie skvamózních buněk, karcinomy přechodných buněk a adenokarcinomy. Tyto nálezy jsou detailně popsány, etiologie je diskutována.

Энзоотическая гематурия крупного рогатого скота: клинические и патоморфологические исследования

У 7 взрослых особей крупного рогатого скота проводились исследования клинических и патоморфологических симптомов спонтанной энзоотической гематурии. Протекание болезни было сначала асимптоматическим, позже появилась кровь в моче, анемия и лимфопения. На терминальной стадии болезни животные были крайне истощены. Патоморфологические анализы преобладали в мочевом

пузыре, хотя и поражена была печень (билиарная гиперплазия), мочеточники и почки. Стенка мочевого пузыря была гиперемическая и отечная. Важно было установление хронического цистита, папилломы, метаплазии чешуйчатых клеток, карциномы переходных клеток и аденокарциномы. Приведенные анализы детально описаны, этиология обсуждается.

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