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Citation	Japanese Journal of Veterinary Research, 6(2), 93-106
Issue Date	1958-06-30
DOI	10.14943/jjvr.6.2.93
Doc URL	<a href="http://hdl.handle.net/2115/1731">http://hdl.handle.net/2115/1731</a>
Type	bulletin (article)
File Information	KJ00002373160.pdf



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# AN OBSERVATION ON BOVINE MALIGNANT CATARRH IN JAPAN

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(Received for publication, April 25, 1958)

## INTRODUCTION

Bovine malignant catarrh (B.M.C.) has been found in Europe from about a century ago and now has a world-wide distribution, occurring in Africa, the U.S.A., Indonesia and Asia. The occurrence of the disease was also recently reported in Australia<sup>5)</sup>.

B.M.C. is acute infectious disease in cattle, characterized by croupous inflammation of the upper respiratory tract and digestive canal, ophthalmia and *meningoencephalitis non-purulenta*.

The disease has been called "Malignant catarrh", "Malignant catarrhal fever", "Malignant head catarrh", "Bovine epitheliosis", "Snotsiekte", "Coryza gangraenosa bovim", "Ingusan" and "Bösartiges Katarrhalfieber des Rindes" etc.

Except for SASAKI and ISHII's clinical observations on a similar disease, the occurrence of the disease has not yet been reported in Japan, although it is a well-known disease as noted above.

Fortunately the authors, however, had an opportunity to conduct examination on the disease in July 1956. Herein they describe the results of histopathological observation of that case together with another case obtained later. The purpose is to bring these to the attention of veterinarians as confirmed cases of B.M.C. in Japan.

## MATERIALS AND METHODS

The materials investigated were supplied by 2 cases. Explanations of the materials are contained in table 1. The first case was diagnosed as an unknown cause disease at the East Veterinary Hospital, Agricultural Mutual Relief Cooperative Association of Hiroshima Village. The second was clinically diagnosed as B.M.C. at the Department of

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Veterinary Internal Medicine, Hokkaido University.<sup>12)</sup> These cases manifested symptoms of "head and eye" form.

TABLE 1. *Summary of Materials Investigated*

CASE NO.	PROTOCOL NO.	BREED	SEX	AGE (Years)	LOCALITY	ONSET OF ILLNESS	TERMINATION NATION	COURSE (Days)	DATE OF AUTOPSY
1	3688	Holstein	♀	3	Ōmagari, Hiroshima	11/VII '56	16/VII '56, †	5	16/VII '56
2	E2201	Holstein Bastard	"	7	Setagaya, Ebetsu	27/IX '56	8/X '56, †	12	8/X '56

After conducting macroscopical observations, the authors collected materials from all parts of the body. The materials were fixed with 10% formol solution; some pieces of the brain were fixed with 95% alcohol. Paraffin or celloidin sections were also prepared.

The sections were stained with hematoxylin-eosin, methylgreen-pyronin, thionine (metachromasia) and NISSL stain (Brain).

## RESULTS

### Case 1, 3688, 3-year-old cow

**Clinical history:** On July 11, 1956, this cow manifested a serous nasal discharge. On July 14, both eyes were affected with complete corneal opacity and the animal showed blindness. Stupor was manifested as a central nervous symptom. On July 15, the nasal and oral mucosa were deep red in color revealing ulcers some of which were covered with pseudo-membranes. The animal lost appetite completely. The skin especially around the teats, manifested scattered necrotic pseudo-membraneous dermatitis. Pulse rate was 90. Urine was gradually decreased in quantity and feces was dry. On July 6, the animal revealed *continentia urinae* before death.

**Anatomical diagnosis:** 1) *Gastritis necroticans et hemorrhagica acuta*, 2) *Pharyngo-laryngitis catarrhalis et necroticans acuta*, 3) Ulcer in oral mucosae, 4) Necrotic dermatitis in *planum nasolabiale* and *papilla mammae*, 5) Iridocyclitis, 6) Multiple yellowish white spots in the kidneys, 7) Slight interstitial nephritis, 8) Slight catarrhal enteritis, 9) Dilatation of right ventricle and atrium of the heart 10) Congestive edema in the lungs, 11) Meningeal congestion and petechial hemorrhages in the brain parenchyma.

### Histopathology:

#### Visceral organs

**Liver** The liver was slightly congested and edematous in the GLISSON'S capsule. Sinusoids were dilated and reticulo-endothelial cells (R. E. S. cells) were swollen, proliferated and desquamated. These cells were all rounded and showed a tendency toward macrophages. On the other hand, lymphocytic and leucocytic cell infiltration was found in the sinusoids.

Slight fatty infiltration of liver cord cells was shown. Most conspicuous change observed in the liver was the infiltration of lymphocytes, large mononuclears, and histiocytes in the GLISSON'S capsule. Especially cellular infiltration was conspicuous in the periarterial area and some of the arteries showed intima-granulomatous cellular proliferation. Connective tissue proliferation was relatively marked in the periportal area.

*Spleen* The spleen was congested and sinuses were dilated. Petechial hemorrhages were noted in the Malpighian bodies and trabeculae. Perivascular infiltration with large mononuclears, lymphocytes and rounded reticulum cells was conspicuously observed. These changes were also detected in the trabeculae. Large mononuclears were rich in the pulp and R. E. S. cells sometimes showed karyorrhectic changes.

*Kidneys* The kidneys were markedly congested. Accumulation of infiltrating cells (large mononuclears, lymphocytes and histiocytes) were observed in the perivascular and periglomerular areas. In the periarterial area, proliferated adventitia cells and sometimes *Periarthritis nodosa* were noted. *Endarteritis obliterans* was often confirmable. A mere cloudy swelling of tubular epithelium was slightly noted.

*Myocardium* Perivascular infiltration was noted, especially in the epithelial area and some parts of the adventitia of blood vessels were proliferated as nodules. Subepicardial area was edematous and had slight cell infiltration. Adventitia cells were proliferated in the interstitium and scar tissues were scattered in the myocardium.

*Lungs* The lungs showed congestive edema; interlobular connective tissues were markedly edematous. The alveolar walls were thickened and R. E. S. cells were activated. Polymorphonuclears were infiltrated in the alveolar wall. Bronchial epithelia were desquamated and frequently filled the bronchial lumen. Peribronchial and perivascular infiltration was also noted. In these areas, the blood capillaries were newly formed and histiocytes were proliferated.

*Adrenal glands* The adrenal glands were congested. The capsule was markedly thickened. Cellular infiltration was noted in the subcapsular area, especially in the perivascular area. Lymphocytic and large mononuclear infiltration was also observed in medulla.

*Lymphonodi* Marked edema and cellular infiltration were observed in the capsule, trabeculae and hilus. The infiltrating cells were composed principally of lymphocytes, large mononuclears, histiocytes and macrophages. Both cortex and medulla were rich in cells and R. E. S. cells were activated. Perivascular infiltration, fibrinoid swelling of the walls of blood vessels and connective tissues, and necrotic foci were noticeable.

*Mammary glands* Mammary glands were congested. Lymphocytic and histiocytic cell infiltration was manifested in the interstitium.

*Thyroid glands* These showed congestion and petechial hemorrhages in the interstitium.

*Planum nasolabiale* The corneal layer of the epidermis showed hyperkeratosis and the epidermis was covered with fibrinous exudation. Epithelia in the *stratum spinosum* showed a ballooning which resulted in so-called "reticular degeneration." Formation of small vesicles was occasionally seen. Disseminated solitary necroses of the epithelial cells were often found. These lesions were stained with marked acidophilic materials and

presented homogeneous appearance. In the epithelial cytoplasm, RUSSEL's bodies with the appearance of hyaline droplets were frequently observed. Polymorphonuclear, large mononuclear and histiocytic cell infiltration with pycnosis and karyorrhexis was found in the epidermis. In the ballooning area, there were a large number of cells, rich in protoplasm and round or bead-like nucleus. These cells had large acidophilic droplets in the protoplasm. These droplets were negative to thionine and pyronin stain. Another marked lesion noted in the tissue was the formation of ulcers. In the dermis, perivascular infiltration was characteristic and the infiltrating cells were apparently lymphocytes, large mononuclears, histiocytes and occasional plasma cells. Cellular infiltration was detected in the intermuscular tissues and the mucous glands. Interstitial tissues were edematous.

*Tongue* The dermis, especially papillary layer showed marked cell infiltration. The epithelium of *stratum spinosum* revealed solitary necrosis sporadically. Ballooning, formation of RUSSEL's bodies and other changes were similar to that of *planum nasolabiale*.

*Pharynx* Hyperkeratosis, necrosis, ulcer and vesicle formation of the epidermis were found. Cell infiltration was conspicuous in the papillary layer and perivascular area of dermis. Ballooning and formation of RUSSEL's bodies in the *stratum spinosum* were also found.

*Tonsils* The lymph apparatus was enlarged. Marked cell infiltration had appeared in the interstitium of the mucous glands and the intermuscular tissue. Muscle fibers showed hyalinous swelling and degeneration of the mucous glands. Infiltrating cells consisted chiefly of lymphocytes and histiocytes.

*Forestomachs* Numerous focal necroses which reach the *tunica propria* of the mucosa were observed. Superficial layer of necrosed area showed homogeneity, deeply stained with eosin and often accompanied by bacterial accumulations. Around the necrotic area, a reactive layer was formed consisting mainly of fragmentations, polymorphonuclears, large phagocytes and fibrinous exudation. *Tunica propria* was edematous. Cell infiltration reached into the muscular layer and often myodegeneration was observed. Remarkable lesions were perivascular cell infiltration; fibrin thrombi were detected in the larger sized vessels.

*Stomach* The mucosa was severely congested and showed cell infiltration. Subserosa and intermuscular tissues were edematous.

*Intestines* The large and small intestines showed submucous congestion, edema and cell infiltration. Subserosa and intermuscular tissues were also edematous. Lymph apparatus was enlarged.

*Urinary bladder* Submucosal hyperemia and cell infiltration were confirmable.

*Bulbus oculi* In the *lamina propria* of the cornea, marked perivascular cell infiltration was revealed while both adventitia cells and histiocytes were proliferated. Newly formed blood capillaries, and lymphocytic, large mononuclear and macrophagic infiltration were present. Especially, the areas adjacent to the conjunctiva showed marked cell infiltration. The ciliary body, the iris and the chorioid showed similar lesions to those of the cornea. In the area surrounding the *papilla optica*, periarteriitis figures, myolysis and marked cell infiltration were detectable.

Central nervous system

Hyperemia was outstanding in cerebral cortex and meninges. Fresh extravasation into VIRCHOW-ROBIN's space was noted in various portions of the brain. But hemorrhages were not confined within the VIRCHOW-ROBIN's space.

*End-brain* In the frontal cortex, vascular cuffing of middle and small sized blood vessels was striking. Especially middle sized blood vessels were conspicuous. Some of them showed 4~5 layered cuffing. Well-marked tissue infiltration often accompanied.

Diffuse and focal proliferation of glia cells was noted. The latter showed loose small accumulation. These foci were indefinitely demarcated. Constituent cell elements usually contained round nuclei and often were accompanied by rod cells. Degenerative changes in nerve cells usually belonged to acute swelling, but some of them showed severe changes. In general, cytoplasmic changes were conspicuous. Cytoplasm of nerve cells was enlarged, and many nucleoli and nuclear walls were clearly seen. These neural changes were characterized by vacuolization of cytoplasm and loss of structure, loss of basal chromatin and occasionally pycnosis, satellitosis and neuronophagia. In the parietal cortex, meningeal cell infiltration was marked and 6~7 layered cuffing was noted. Hyalinous swelling of small sized vessels was often to be seen. Degeneration of nerve cells was also observed as an ischemic change. In hippocampal area, proliferation and infiltration were clearly shown. In general, meningeal reaction was marked. The infiltrating cells were lymphocytes, large mononuclears, plasma cells and a few eosinophils. The changes of occipital cortex were similar to those of the other cerebral cortex. In the basal ganglia, there were vascular cuffing and diffuse proliferation of glia cells both in grey and white matter. Degenerative changes of nerve cells, such as atrophy, vacuolization of plasma and loss of nuclei were noted. Some parts of the blood vessels revealed fibrinoid swelling. Hemorrhages and hyperemia were noted in various regions.

*Inter-brain* Well-marked perivascular infiltration and diffuse proliferation of glia cells were noted. Slight degenerative changes were found in nerve cells. Fibrinoid swelling in the wall of the small blood vessels was also found. In the hypophysis, granulomatous perivascular cuffing in the anterior lobule was noted.

*Mid-brain* Perivascular and tissue infiltration was conspicuous as well as diffuse and loose focal proliferation of glia cells. Small focal accumulations of glia cells and degenerative changes in nerve cells existed in various regions. Dilatation of blood capillaries and petechial hemorrhages were noted.

*Pons* There was a marked perivascular cuffing of the middle sized blood vessels and hemorrhages in the brain substance were noted. Endothelia in the blood vessels were enlarged and adventitia cells were proliferated. The lesions in the pons were similar to those in the other parts of the brain, except for comparatively slight glia reaction.

*Medulla oblongata* Hyperemia and hemorrhages were marked. Glia cells were diffusely proliferated and some of them formed loose small cell accumulations. The most marked abnormality noted in this region was cytoplasmic inclusions in nerve cells of the vagoglossopharyngeal nucleus. The inclusions were homogeneous and acidophilic. Degenerative changes were well-marked in nerve cells of the vagoglossopharyngeal nucleus. The other changes were similar to those in the other regions of the brain.

*Medulla spinalis* Fibrinoid swelling of the small blood vessels occurred scatteringly.

Perivascular infiltration in *formatio reticularis* and degeneration of nerve cells in *columna ventralis* were found.

*Cerebellum* Meningeal cell infiltration was marked. Composite cells were chiefly histiocytes and had a thickened wall. Perivascular cuffing and tissue infiltration were also noted. Diffuse and focal proliferation of glia cells was noted. PURKINJE's cells showed slight degenerative changes.

#### Case 2, E 2201, 7-year-old cow

Clinical history: On August 19, 1956, parturition. On September 27, appetite and milk production were rapidly decreased. Temperature was 41.2°C. Pulse rate was 78. Slight salivation, cloudiness of right cornea, slight lachrymation and severe photophobia were noted. Feces showed no abnormality. On September 28, temperature was 41.4°C. Pulse rate was 90. The other symptoms were similar to those on the previous day. On October 1, left cornea showed cloudiness. Lachrymation and diarrhea were observed. On October 3, the symptoms were the same as on the previous day, except nasal discharge. On the next day, appetite was decreased and animal was depressed. Conjunctivae were hyperemic. Both cornea showed complete opacity. Lachrymation, serous nasal discharge, mucous diarrheal feces and yellowish transparent urine were noted. Erythrocyte count was 8.11 million, the number of leucocytes was 7,300. Neutrophils 37% (rod-form 0.5%, segment-form 36.5%), lymphocytes 60.5%, monocytes 2.5%, eosinophils 0%. Rectal examination: Mucus was rich in rectum and the left uterine horn was enlarged to the size of a child's head with muscular feeling. In the vagina, there was a great amount of purulent exudation. Temperature was 40.3°C. Pulse rate was 90. On October 5, temperature was 39.3°C. Pulse was 96. On October 6, T. 39.5°C, P. 60. Appetite existed. Corneal opacity and lachrymation became severe. Salivation was slight. Peristalsis of the first stomach was increased. Purulent exudation flowed out from the vagina. In the rectum, mucus was abundant in quantity. Erythrocyte count was 6.12 million, leucocytes were 10,800 in number. Neutrophils 62% (rod-form 1.5%, segment-form 60.5%), lymphocytes 34.5%, monocytes 3.0%, eosinophils 0.5%. On October 7, temperature was 39.3°C. Pulse rate was 58. On October 8, T. 38.4°C, P. 70. Neutrophils 73.5% (rod-form 2.0%, segment-form 71.5%), lymphocytes 12.5%, monocytes 14.0%, eosinophils 0%. The animal was killed at the Sapporo slaughter house.

Anatomical diagnosis: 1) Increase of cerebro-spinal fluid, meningeal hyperemia and petechial hemorrhages in the brain substance, 2) Ophthalmia, 3) *Stomatitis et pharyngo-laryngitis catarrhalis subacuta*, 4) Pyometra, 5) *Vaginitis purulenta et necroticans chronica*, *Cystitis purulenta et necroticans chronica*, 7) Slight enlargement of the liver and spleen, 8) *Cholecystitis catarrhalis chronica*.

#### Histopathology:

##### Visceral organs

The changes of visceral organs in this case showed systemic purulent changes on account of pyometra. The changes caused by B. M. C. were slighter than those of case 1.

*Liver* Multiple irregular necrotic foci were found scattered about. R. E. S. cells were activated. In the sinusoid, emigration of polymorphonuclears and lymphocytes was noted. In the GLISSON's capsule, lymphocytes and histiocytes were accumulated.

*Gall-bladder* *Cholecystitis catarrhalis chronica.*

*Spleen* The spleen was congested and hemorrhages in trabeculae were found. The follicles were hyperplastic and R. E. S. cells were activated.

*Kidneys* Serous fluids were contained in the BOWMAN'S capsule. The endothelial cells in the capillary loops showed pycnosis; some of them were swollen. Lymphocytic and histiocytic cell infiltration had occurred in the interstitium.

*Myocardium* Adventitial and histiocytic cell infiltration was manifested in the perivascular and interstitial tissue areas. Partial scar formation and focal myodegeneration were found scatteringly. Lymphocytes and eosinophils were infiltrated into the subendocardium.

*Lungs* Interlobular connective tissues and alveolar wall were thickened. R. E. S. cells were activated and histiocytes were proliferated. Cell accumulation was remarkable in the peribronchial area. *Pleuritis fibrosa chronica* was also noted.

*Lymphonodi* Organized thrombus was detected in the larger blood vessel of the hilus. Hyalinous substance was deposited in the walls of the larger vessels. Periarterial cell distribution might be demonstrated. Aggregations of infiltrating cells (lymphocytes, histiocytes and large mononuclears) frequently showed intima-granulomatous and granulomatous appearance in the adventitia. Lymph follicles were hyperplastic. R. E. S. cells were activated.

*Pancreas* The pancreas showed congestion and perivascular infiltration.

*Adrenal glands* Perivascular infiltration (lymphocytes and histiocytes) was found in the medullary interstitium.

*Forestomachs* Polymorphonuclear infiltration and accumulation were noted in the *tunica propria*. In some parts of the mucosa, focal necroses were distributed and some parts were fibrous.

*Stomach* The stomach was congested. Cell infiltration was conspicuous. Blood capillaries were newly formed. Thrombi were frequently noted in the larger blood vessels. Perivascular cell infiltration was noted in various regions. Infiltrating cells were lymphocytes, histiocytes, and occasionally eosinophils and plasma cells. Multiple hemorrhages were detected. Fibrinous exudation was well-marked and focal necrosis was detected.

*Intestines* *Enteritis catarrhalis chronica.*

*Mammary glands* Cells infiltrated in the interstitium.

*Urinary bladder* Multiple thrombosis, hyalinous swelling in the walls of the blood vessels, multiple necroses, follicle formation and edema were noticeable. A marked cell infiltration was found in the *tunica propria* (*Cystitis purulenta necroticans chronica*).

*Uterus* *Metritis purulenta et necroticans chronica* (Pyometra).

*Cervix uteri* *Cervicitis purulenta chronica.*

*Vagina* *Colpitis purulenta et necroticans chronica.*

#### Central nervous system

Hyperemia was noted in various regions of the brain.

*End-brain* Vascular cuffing was well-marked surrounding numerous vessels, especially middle or small-sized vessels in both the substance of the brain and meninges. The infiltrating cells were lymphocytes, histiocytic cells and occasionally eosinophils. Adventitia

cells were proliferated and endothelial cells were swollen. Glia cell proliferation was diffusely or focally observed. Glia cell foci were scattered about in the cerebral cortex and often accompanied by rod cells. In many nerve cells, degenerative changes were noted such as fragmentation and dissolution of NISSLE bodies, vacuolization of plasma, pycnosis and occasionally neuronophagia. The meningeal reaction was slighter than in case 1. But cell elements were similar to those in case 1. Fibrinoid swelling in the walls of the small vessels was frequently observed in the cerebral cortex. In hippocampal cortex, glia cell proliferation was noticeable. The latter revealed two forms: the one was compact whilst loose undemarcated was the other. Occasionally, nerve cells showed degenerative changes.

*Inter-brain* Petechial hemorrhages were found in the brain substance. Vascular cuffing and tissue infiltration were outstanding. Some such occurrences took a granulomatous shape and formed cell accumulation in a few layers. Small loose nodular glia-proliferation was often seen and frequently accompanied with rod cells. Degeneration of nerve cells was similar to those mentioned above. Perivascular infiltration was noted in the anterior and posterior lobules of the hypophysis. Petechial hemorrhages were found in these areas.

*Mid-brain* Vascular cuffing was comparatively slight. Minute glia nodules were scattered about in the brain substance. Slight degenerative changes were merely noted in nerve cells. Meningeal hemorrhages were found.

*Pons* Multiple petechial hemorrhages were noted in various regions. Vascular cuffing and tissue infiltration were relatively slight. Minute glia nodules were distributed.

*Medulla oblongata* Same general changes were observed as in the end-brain. No inclusions were detected in nerve cells.

*Cerebellum* Meningeal hyperemia and hemorrhages were remarkable. PURKINJE's cells showed degenerative changes. The other changes were similar to those mentioned above.

#### DISCUSSION

Studies on B.M.C. have been limited only to clinical description, whereas the disease has been found in Europe from many decades ago previously stated. For pathological and etiological studies on the disease veterinarians are indebted to German investigators, mainly to DOBBERSTEIN and to GOETZE and coworker. DOBBERSTEIN investigated the central nervous system histopathologically and pointed out this disease as non-purulent meningoencephalitis. DOBBERSTEIN's findings were confirmed by GLAMSER later in 1926. DOBBERSTEIN and HALSWICK (1928) studied the mucosal lesions of the disease and made etiological investigations by conducting transmission experiments. GOETZE and LIESS (1929) reported a successful transmission of the disease, with blood inoculation, to three cattle out of seven inoculated. However, transmission experiments with brain aqueous humor and lymphatic gland were not successfully made. Meanwhile, in South Africa, a disease called "Snotsiekte" was reported. GOETZE and LIESS, however,

announced that these two diseases are the same one caused by the same infectious agent. From the observations made on more than 40 cases, GOETZE classified the disease into 4 forms clinically: per-acute form, alimentary form, head-and-eye form, and mild form. Especially the head-and-eye form is a well-known one and the present case belong to this form.

At any rate, as it has already been pointed out, attempts at transmitting the disease show not more than about 50 per cent successful. It is understood, however, that a virus is responsible for this disease.

The clinical symptom found in the presently described cases a large quantity of serous or mucous nasal discharge; ulcerative and necrotic inflammation in the mucosa of mouth and *planum nasolabiale*; frequently eye involvement with serous or purulent discharge and corneal opacity, photophobia; and commonly, salivation. Papular, pseudo-membranous and necrotic dermatitis appeared in the mammary gland skin. The central nervous system was often involved giving rise to stupor.

Regardless of the extent of the disease, these cases belong to the head-and-eye form which is identical with the descriptions presented by many workers.

The disease revealed considerable characteristic findings pathologico-anatomically and histologically. The main lesions were seen in the upper respiratory tract and digestive canal, the visceral organs, the eyes and the central nervous system.

The mucosal lesions in the upper respiratory tract and digestive canal are not pathognomonic, but characteristic as pointed out by DOBBERSTEIN and HALSWICK. Cheilitis, stomatitis, glossitis, uvulitis, tracheitis, gastritis and dermatitis were noted. These lesions were manifested, all in the form of the fibrinous necrotic inflammation and occasionally accompanied by ulcer. The cell infiltration in the tunica propria of these regions was conspicuous and endothelial cells were swollen. Perivascular and interstitial cell infiltration was particularly remarkable. The composite infiltrating cells were lymphocytes, large mononuclears, histiocytic cells, plasma cells and occasionally eosinophils. In the epidermis, polymorphonuclear infiltration was remarkable, with vesicles and ulcers often accompanying. The epithelial cells in the epidermis showed ballooning or vacuolization, and accordingly resulted in manifesting of so-called "reticular degeneration". Occasionally solitary necrosis of the epithelial cells was seen. In the cytoplasm of the epithelial cells, acidophilic droplets, that is, RUSSEL's bodies were noted. In the ballooning area, large number of cells which rich in protoplasm and had a round or bead-like nucleus with large acidophilic droplets in the protoplasm were found. It is suggested that these cells were identical with those of DOBBERSTEIN and HALSWICKS' "Schollenleukozyten." These droplets, however, can be considered RUSSEL's bodies

rather than inclusions.

As for the visceral changes, main lesions were seen in the lymphoid-macrophage system, as pointed out by PLOWRIGHT, PEARSON, PATTISON and others. Specifically, perivascular infiltration predominated in the liver, spleen, kidneys, myocardium, lymph nodes and adrenal glands. That is to say, the activation of lympho-reticular tissues and especially mobilization of adventitia cells was prominent. At the same time, vascular changes were noted in various regions of the body. Case 1 was especially remarkable in vascular changes, such as periarteriitis nodosa or cell infiltration in adventitia area. The infiltrating cells were lymphocytes, large mononuclears and histiocytic cells. In some parts of the brain, there was fibrinoid swelling in the walls of the blood vessels. In the liver, perivascular infiltration in GLISSON'S capsule was remarkable.

Mobilization of R. E. S. cells was observed in all parts of the body. The enlargement of lymph nodes, hyperplasia of splenic follicles and activity of hepatic sinusoidal endothelial cells were demonstrated. There is a tendency for these cells to become macrophages.

BISBOCCI noted a diagnostic value in encephalitis and acute interstitial nephritis. The authors, however made note of the similar lesions in the kidneys as partial phenomena in systemic mobilization of the lymphoid-macrophage system regardless of the intensity. However, very little abnormality of the kidney parenchyma was noted. On the other hand, circulatory disturbances such as hyperemia, hemorrhages and edema were noted in various regions of the body.

The eye revealed conjunctivitis, keratitis and iridocyclitis.

The central nervous system gave evidence of a remarkable non-purulent meningo-encephalitis as DOBBERSTEIN pointed out. The disease has been described as showing similarity to Borna disease. Especially, intense vascular cuffing and tissue infiltration in the brain parenchyma were found. Focal and diffuse proliferation of glia cells was remarkable. Glia nodules were often accompanied by rod cells. Degenerative changes of nerve cells, hyperemia, hemorrhages and edema were certainly observed. Lymphocytes, large mononuclears, histiocytes, adventitia cells, a few eosinophils and occasionally macrophages were infiltrated in meninges and VIRCHOW-ROBIN'S spaces.

In a word, the infiltration of perivascular lymphocytic and large mononuclear cells and proliferation of glia cells were the main changes of the central nervous system.

Degenerative changes in nerve cells were those characteristic to acute swelling and some of them were severe changes. In general, nucleoli and nuclear walls in nerve cells were clearly seen and cytoplasm was swollen. Vacuolization, fragmentation and dissolution of the NISSL bodies in cytoplasm were often found.

Neural changes, characterized by pycnosis, hypochromatosis, karyorrhexis and sometimes karyolysis of nuclei, were rarely seen. Occasionally, neuronophagia was seen scatteringly. These neural changes were observed in various regions of the brain. Such changes belong to the category of outstanding encephalitic changes.

The most problematic changes in the disease were the appearance of cytoplasmic inclusions. GOSS et al. reported that cytoplasmic inclusions were observed in the nasal epithelial cells and PURKINJE'S cell. These inclusions showed various shapes, sizes and varied in number. GOSS et al. classified these inclusions into 3 types: diffuse granular, clustered granular and homogeneous.

On the other hand, STENIUS reported that in 50 per cent of the examined cases acidophilic, cytoplasmic inclusions of 300~500  $\mu\mu$  were found in nerve cells of the vagoglossopharyngeal nucleus. According to STENIUS, inclusions were probably formed as a result of the reproduction of intracellular virus. In the authors' case No. 1, similar inclusions were found in nerve cells of the identical nucleus. As the authors expect to clarify the nature of these inclusions by future study, the present paper does not attempt to present a study along this line.

In the differential diagnosis of B.M.C., the authors mentioned the "mucosal type disease" which has recently been brought to the attention of veterinary men. That is to say, the disease is a newly recognized group of bovine diseases characterized primarily by diarrhea and erosions of the gastrointestinal tract. The first description of such a mucosal disease was given by OLAFSON et al. in 1946. This special syndrom has been known as "virus diarrhea" of cattle and studied by several groups of workers (BAKER et al., PRITCHARD et al.). Another mucosal type disease was recognized by RAMSEY and CHIVERS in 1953. Then it was reported by NIELSEN et al. and others (SCHIPPER et al., SEIBOLD) as a mucosal disease complex. Another variant of the mucosal disease type "muzzle disease" was recently, reported by HOLLISTER et al.

Clinico-pathologically, there are some differences between "virus diarrhea", "mucosal disease" and "muzzle disease", but the etiology of these diseases is unknown. When consideration is given to individual conditions, it is possible to consider that these diseases have similarity to a certain extent.

Mucosal type disease has some clinical similarities to B.M.C., but encephalitic changes, ophthalmia and inclusions were never shown in this disease microscopically. As the lesions of mucosal type disease are localized in the gastrointestinal tract, differentiating between the disease of the mucosal type and B.M.C. is not difficult.

Foot and mouth disease, vesicular stomatitis and rinderpest have some similarity to B.M.C.

However, foot and mouth disease has special lesions in buccal cavity and hoof clefts, very rapid spread in herd, no nasal or ocular discharge and usually is not fatal.

Vesicular stomatitis is similar to foot and mouth disease.

As the rinderpest shows rapid diffusion, it can easily be differentiated from B. M. C. without the necessity of conducting pathological investigation.

A similar disease has already been reported by SASAKI and ISHII in Japan, but accurate diagnosis is difficult on the basis of clinical observations alone. B. M. C. can surely be diagnosed by microscopical observations without conducting isolation of the virus.

#### SUMMARY

The authors made histopathological investigations of 2 cases of B. M. C. in Hokkaido in 1956.

Histopathologically speaking, the main lesions were found to be located in the mucosa of the upper respiratory tract and digestive canal. Fibrinous necrotic inflammation was commonly observed, while ulceration and vesicle formation characterized lesions in these areas. Ballooning degeneration was a feature of the stratified epithelial lesions and occasionally RUSSEL's bodies were observed in the cytoplasm of epithelial cells. Marked non-suppurative meningo-encephalitis was noted in the central nervous system. Acidophilic cytoplasmic inclusions were found in the nerve cells of the vagoglossopharyngeal nucleus in the *medulla oblongata* in one of the two cases. But inclusions were not found in any other regions.

The authors wish to express their gratitude to Prof. YAMAGIMA for his kind direction and for his review of this study, and also to Prof. NAKAMURA (Chief of the Department of Veterinary Internal Medicine of this University) for his kind supply of clinical data and materials for the study.

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## EXPLANATION OF PLATES

## PLATE I.

- Fig. 1. Ballooning in the epidermis of *planum nasolabiale*. Hematoxylin-eosin stain (H.-E.).  $\times 120$ .
- Fig. 2. Vesicle formation in the epidermis of pharynx. H.-E.  $\times 120$ .
- Fig. 3. Necrosis in the epidermis of *planum nasolabiale*. H.-E.  $\times 120$ .
- Fig. 4. Erosion in pharynx. H.-E.  $\times 120$ .

## PLATE II.

- Fig. 5. *Gastritis necroticans et hemorrhagica acuta*. H.-E.  $\times 85$ .
- Fig. 6. *Periarteriitis nodosa*. H.-E.  $\times 70$ .
- Fig. 7. Perivascular cellular infiltration in the hilus of the lymph node. H.-E.  $\times 85$ .
- Fig. 8. Perivascular cellular infiltration in the cornea. H.-E.  $\times 85$ .

## PLATE III.

- Fig. 9. Vascular cuffing in the brain. H.-E.  $\times 120$ .
- Fig. 10. Vascular cuffing in the brain. H.-E.  $\times 120$ .
- Fig. 11. Nodular proliferation of glia cells in end-brain. NISSL stain.  $\times 120$ .
- Fig. 12. Acute swelling of nerve cells in inter-brain. NISSL stain.  $\times 480$ .

## PLATE IV.

- Fig. 13. Acute swelling of nerve cells (chromatolysis) in end-brain. NISSL stain.  $\times 480$ .
- Fig. 14. Acute swelling and satellitosis in end-brain. NISSL stain.  $\times 480$ .
- Fig. 15. Cytoplasmic inclusions of nerve cell in the vagoglossopharyngeal nucleus. H.-E.  $\times 2,000$ .
- Fig. 16. Cytoplasmic inclusions of nerve cell (Shadow cell) in the vagoglossopharyngeal nucleus. H.-E.  $\times 2,000$ .







