A. Ü. Veteriner Fakültesi Patolojik Anatomi Kürsüsü Başkanı
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A CLINICO-PATHOLOGIC STUDY ON CALVES EXPERIMENTALLY INFECTED WITH THEILERIA ANNULATA (Dschunkowsky and Luhs, 1904), Wenyon 1926

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(Theileria annulata Dschunkowsky ve Luhs 1904, Wenyon 1926-ile deneysel olarak enfekte edilen danalar üzerinde kliniko-patolojik araştırma)

Özet: Theileriose'un yıllarca görülmediği bir bölgede yetiştirilmiş, Holstein-Friesian ırkından, 7-8 aylık, dört erkek danaya, hastalık, daha önce Theileria annulata ile enfekte edilmiş Hyalomma detritum, Schulze 1919 türü kenelerle deneysel olarak aktarılmıştır. İnkübasyon devresi 9 - 27 gün sürmüş ve ateşin yükselip 42.1 °C ye ulaştığı görülmüştür. Ölüme kadar saptanabilen semptomlar şöyle özetlenebilir: Hastalığın klinik süresi 4-5 gün, parazitemi (12-59 %), nabız dakikada 92-124, teneffüs sayısı dakikada 48-76, lenf düğümlerinde genel yangılı şişme ve biyopsilerinde Koch cisimciklerinin görülmesi, kan serumunda çok fazla miktarda üre toplanması (124-197 mg üre/100 mg serum), hematokrit değerinin normal sınırlarda (18-28 %) kalmasına karşılık bütün mukoza ve konjunktivalarda derecesi değişen şiddette sarılık, takatsızlık, yem ve sudan kesilmeden sonra zamanla koma ve ölüm.

Ölen veya deneme sonucu nekropsi için kesilenlerde bütün mukoza ve konjunktivalarda değişen derecelerde ikter; hemen hemen bütün baş, boyun, göğüs, karın ve ekstremitelerdeki yüzlek veya derin bütün lenf düğümlerinde yangılı şişkinlik ve etraflarındaki dokular içerisine sarı-yeşilimtrak renkli jelatinöz sıvı infiltrasyonları; seröz zarlarda sarılık yanında subseröz peteşiyal ve ekimotik kanamalar; abomasum mukozasında peteşi ve ekimozlar ile yüzlek erozyon veya çapı 2 cm yi aşabilen değişik şekillerde ve derinliği kas tabakalarına kadar varabilen boz-sarımtrak, ya da kanlı görünüşte nekroz odakları veya bunların yerlerinden dökülüp mukozanın daha da açılması sonucu ortaya çıkan geniş ülserler; gene abomasum'u saran

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periton yaprağı ve altına rastlıyan kısımlarda yangılı ödem ve kanamalar; barsaklar etrafında ve mesenteryumdaki yağlı dokular içerisinde bazen kanlı olabilen sarı-jelatinöz infiltrasyonlar; dalakta yumuşama ve şişme yanısıra subkapsüler peteşi ve ekimozlar. Karaciğerde büyüme, glisson kapsülü altında ve kesit yüzünün derin kısımlarında değişik genişlikte kanama odakları ve solgun renkte, boz nekrozlar ile safra kesesinde durgunluk sonu koyu kıvamlı ve esmer-yeşilimtrak renkli, bulamaç kıvamında safra ve mukozasında peteşiler. Böbreklerde gerek kortikal, gerekse pelvis renalis'te ve özellikle üreterlerin başlangıç kısımlarında çeşitli genişlikte kanamalar, ayrıca korteks'te ortaları boz, etrafı kanlı ve ödemli bir demarkasyon ile çevrili lekeler. Sidik kesesinde bazen parlak bazen bulanık kahve-kırmızısı renkte (hemoglobinüri-hematüri) ve fazlaca miktarlarda idrar birikmesi sonu, kesenin genişleyip çapının 10-15 cm ye kadar ulaşabildiği görülmüştür. Beyin zarlarında ödem ve damarlarında hiperemi ile subdural kısımlarda peteşiyal ve ekimotik kanamalar dikkati çekmiştir.

Histopatolojik yoklamada, bütün lenf düğümlerinde şiddetli akut yangısel reaksiyon ve hiperplazi ile hemen ardından geniş kanamalar, kortikal germinatif merkezlerin tamamen silinmesine kadar giden geniş koagülasyon nekrozları; karaciğerde şiddetli hiperemi ve etraflarında yangısel infiltrasyonlar bulunan değişik genişlikte koagülatif nekroz sahalarıyla portal dokuda değişen şiddetlerde mononüklear hücre infiltrasyonu ve sinüzoitler içerisinde mononüklear hücre proliferasyonu; dalakta şiddetli hiperemi ve kanama sahaları yanısıra nekroz ve hiperplazi saptanır. Böbreklerde hiperemi, ödem ve kanamalarla koagülatif nekroz ve nefroz yanısıra interstitiel dokuda çoğu mononüklear bazen de tek tük nötrofil lökositlerin karıştığı hücre infiltrasyonları; sidik kesesinde ise mukozada yangılı ödem ve kanamalar saptanmıştır. Safra kesesinde yangılı ödem ve peteşiler meydana gelmiştir. Abomasum mukozasının lamina epiteliyalis'inde koagülasyon nekrozu ve kanamalar sonu erozyon ve ülserler ile bu kısımlara lökositlerin infiltre olması dikkati çekmiştir.

Theileriose'da genel ikter, hemoglobinüri, hematüri, anemi, çeşitli organlarda seröz ve subseröz kanamalar ile geniş koagülatif nekroz alanlarının şekillendiğinin saptanması, bu hastalığın da Babesiose ve Piroplasmose gibi hemopoietik sistemi etkileyen diğer protozoon hastalıklarıyla büyük benzerlik gösterdiğini kanıtlamaktadır. Ayrıca, klasik bilgiler aksine, ateşin çıkmasından 4-5 gün sonra öldürücü olabileceğinin anlaşılması da önemli bir bulgu olarak değerlendirilmelidir.

Abstract: As a part of a series of studies on the therapy and on the prophylaxis of Bovine theilariasis, a clinico-pathologic investigation was undertaken separately on four of 7-8-month-old Holstein-Friesian bull calves grown in a reportedly theileriasis free area in Turkey.

The clinical signs, post mortem and following histopathological findings obtained form the biopsy or necropsy specimens were discussed in detail and some were illustrated in histopathological microphotographes.

Introduction

Theileriasis is so far known as a congenitally transmissible (13) bovine protozoan infection that seen in even 20-day-old new-borns (4), although it attacks to all ages of adulthood (3, 10, 16). The disease, for several reasons, was not studied in detail for its pathogenesis or pathologic features. Most papers that dealt with this problem took

up some unusual lesions including eye or intestinal changes (8), while some other investigators were concerned with its immunomorphological characters (1), cutaneous lesions (12), and only a few papers were directly involved with the pathology (15) in accord with varying-course of theileria infections (1, 4, 10, 14, 15).

It is proved that the vector of T. annulata is a tick in most of the cases, and 14 different ticks were reportedly kept responsible as to serve as its vector by far (2, 3, 5, 6, 7, 9, 10, 11). Among these, Hyalomma detritum (Schulze, 1919) seems to be the most important one while H. excavatum, H. marginatum, and H. dromedarii may still serve as its transmitter more often than other ticks (2, 6, 9, 11).

Bovine theileraiasis occurs in hyperacute (4), acute and subacute (15) or even chronic forms (12) with different course and clinical features (10).

Edema and hemorrhages being present in almost all, if not all, internal organs and lymph nodes; small necroses and ulcers in the mucosa of abomasum, but only in the most severe cases in the intestines; kidneys and urinary bladders (15). In such cases, glial proliferation and mobilisation together with neuronophagia in some parts of the cerebellum, large hematomas in bone marrow were also noted (15). Edematous eye-lid swelling, conjunctival ulceration and numerous hyperplastic red circular lesions in the wall of intestines (8) were rarely seen lesions as the dry cutan necroses or ulcers (12).

In the histologic examinations of the lymph nodes, obtained from T. annulata infected 63 cattle (1), hyperaemia together with the proliferation and desquamation of epithelial cells, activation of reticular tissues with the increased number of existing macrophages and neutrophylic migrations were the main changes noted at the initial stages. The proliferative process that accompanied with the increased number of basophyles, macrophages and plasmocytes was paralelled by increased rate of RNA synthesis in the later stages. In the declining infections, these increases were developing more rapidly and were coinciding with the marked rise in the amount of gamma-globulins. Koch's bodies were encountered in the lymphatic tissues around the arterioles of the spleen, dermis and lymph nodes (12), also found in the capillary endothelium (15), in the eye lesions (8) were evaluated as a significant finding for the differential diagnosis. The appearance of these bodies indicated unfavorable prognosis, since they multiply very rapidly to invade the peripheral blood stream (12), or obliterate some capillaries resulting in the formation of embolic necroses in some vitally important organs (15).

With this incomplete knowledge, one can easily say that the clinico-pathological symptomes, epidemiological characters, therapy and prophylaxis of Theileria annulata infection in bovine, needed more investigations to be carried out taking up the different aspects of this disease. Therefore, the main purpose of the present study was to deal with the clinical as well as post mortem and histopathological changes taking place in cattle due to the experimental infection with T. annulata.

Materials and Methods

As a part of a series of studies on the therapy and prophylaxis of Bovine theileriasis, experimentally produced by the infection of young bull calves by using preinfected ticks (Hyalomma detritum, Schulze, 1919), four of those sick animals were separately investigated for the clinical and pathological changes taking place due to the infection with this protozoon parasite.

All four bull calves were 7–8 month-old Holstein-Friesian, and were grown in a State farm reportedly free from theileriasis at least more than 25 years. Each calf was ear-infected with 10 ticks (5 males and 5 females) which were precontaminated with the protozoan parasite in their lymph stage by letting them to suck the blood of a sick cow sufferring from acute theileriasis.

Infected calves were kept under close control for the immediate observation of changing clinical features including body temperature, pulse rate and respiration intervals, in addition to the measurements of the rate of parasitaemia, determination of hematokrit value and the serum urea level daily for each animal, although the pulse and the respiration rates were determined and recorded twice daily. The parasiatemia was graded by taking the percentage of protozoan infected red blood cells in the blood smears obtained daily and stained by routine Giemsa technic. The biopsy specimens were surgically taken from those swollen markedly and readily palpable superficial lymph nodes wich usually was the prescapular node. Hematokrit values were figured out by using Microhematokrit Method at 10,000 rpm for more than 5 minutes. The serum urea levels were measured as in mg of urea per 100 ml by Merckognost Urea Determination Test Papers (Fa. Merck, Darmstadt West Germany).

Post mortem and following histopathological examinations were carried out throughly for every calf; and the tissue sections were embedded in paraffin cut and stained by routine hematoxylin and eosin.

Some organs demonstrating typical lesions were microphotographed for the illustrations.

Results

a. Clinical findings: The first symptom of acute theileriasis in all of cases was the sudden onset of high fever after an incubation period of 9 to 27 days following the ear-infection. The fever went up to 42.1 °C by the last day prior to death, as the terminal pulse (92–214 pulse/ minute) and the rate of respiration (48–76 resp./ minute). The microhematokrit values ranging between 18–28 % by volume did not indicate a severe anemic condition, although the animals were accepted as anemic by blood counts. The serum urea levels rised up to 124–197 mg urea per 100 ml, and this was striking finding to be explained in detail. Icteric appearance of conjunctivae and oral mucous membranes, together with the hairless parts of the skin were more readily detected by the later stages of infection. All of head and neck, cervical and prescapular, inguinal and other palpable lymph nodes were markedly swollen and warmed gradually as the course of the disease was progressed. The inflamed nodes were edematous and notably hardenned by palpation. A yellowish colored gelationus or watery infiltration filled into their surrounding connective tissue was noted during the extirpation of the biopsy specimens or by the necropsy.

Parasitaemia was graded and evaluated by the percent of red blood cells infected with theileria, and was found to be ranging between 12–59 % (*Picture.* 1), during the last days of calves. Parasitaemia was paralelled by the striking rise of the serum urea levels, but not with anemia. All biopsy specimens exhibited a high content of Koch's bodies (*Picture.* 2) wich were encountered more aboundantly during the later stages, or prior to the death of sick animals.

b. Necropsy findings: All mucous membranes and conjunctivae, subcutan connective tissues, peritoneum and abdominal fatty tissues were icteric with their intensity varying from case to case. All head and neck, cervical and prescapular, mediastinal, bifurcational, mesenteric, intestinal, abdominal, sacral, inguinal and other examined lymph nodes were swollen in different degrees and were surrounded by a zone of yellowish-green colored, gelationus to vatery infiltration. Their cut surface showed hyperaemia and varying sized hemorhages in addition to cortically located necroses.These necrotic foci were pale pinkish or grey colored, soft, homogenous but somewhat dry areas that were surrounded by a hyperemic zone or hemorhhages. The cortical ger-

minal portions were watery and exceeding the cut surface out. In such cases, necroses were not detected in early stages.

Lungs and pericardial membranes were edematous and were infiltrated with, in some cases, the similar gelatinous liquid and exhibited aboundant hemorhages of varying size under the pleural and pericardial surfaces or in the deeper portions of the lungs and the heart muscle or even under the endocardium.

The abomasum was the most severly affected organ in the alimentary canal, and contained uncountable hemorhages of different size and depth in the mucous membrane, besides the necrotic foci and the ulcerations. These ulcers were also varying in size and color, as they started as small coagulative necroses, most probably due to the formation of petechiae that causes ischemia or anemia (anoxemia) locally resulting in the death of tissues in this foci, or due to the digestion of local epithelial cells affected by excreted enzymes from the present glands. The necrotic epithelium then was exfoliated by the friction of the content into the stomach lumen to leave an ulcer behind. These ulcers were surrounded by a hyperemic, intensly edematous and inflammed zone due to the secondary infections by the present flora or by other agents might come. In such case, the outermost part of the abomasum was also edematous and infiltrated. Some ulcers were so deep down to submucosa and very irregularly shaped, and they were as large as 2 cm in diameter that look like craters spread over the glandular mucosa.

Yellow colored gelatinous inflitrations were also present in the mesenteric, and periintestinal fat, especially around the veins. No striking inflammatory reaction was noted in the intestinal mucosa, although some slight to moderate enteritis were observed in two of four calves.

The spleen was usually enlarged to about double of its size. The consistency was softenned, and a marked number of petechiae or echymoses were seen under the capsula. The cut surface showed intensly increased red pulp, together with the white pulp or germinative foci. The spleen was so hyperemic as to let the blood run freely out. The white pulp underwent to coagulative necroses similar to those found in the lymph nodes or elsewhere.

The liver was so enlarged that its capsule was distended, and the marginal edges were blunt and rounded. There also were marked number of different sized hemorhages under the Glisson's capsule or deep inner portions of the liver lobes besides varied sized necroses.

The necrotic foci, were similarly homogenous, pinkish-red to brown colored, pale spots surrounded by a hyperemic, edematous or inflammatory zone like in other organs. Gall bladder was enlarged as it contained a markedly increased amount of bile that was turned into a dark-green colored, viscous and bloody secretion since there were moderate to severe inflammatory reaction, edema and hemorhages on its mucous membrane and on the outer serosal surface of the sac.

The kindeys, due to the increased blood content, were also enlarged, darkenned, and somewhat hardenned. They too exhibited several types of hemorhages on their cortex, under the fibrous capsule observable when the perirenal fat was removed. Among those hemorhages, some small grey spots or lines where the fibrous capsule was glued and removed with special care. The cut surface of kidneys was bloody and extending outwards, and uncovered some small faded foci that were like nodules surrounded with an inflammatory blood rich demarcation. The renal pelvis usually contained some yellowish-green to red or dark brown colored bloody urine. On the cortical and medullary portions, besides the hemorhages and faded foci, there also were some pale-pink or red-brown colored homogenous necrotic foci which also were surrounded by a hyperemic halo. The beginning portion of the ureters and hylus were usually edematous, and infiltrated severely besides the present hemorhages. Accumulation of the excess amount of bright-red to dark-brown colored and icteric or bloody urine in the bladder (hemoglobinuria and hematuria or billuribinuria) resulted in the marked enlargement of the sac up to about 15 cm diameter in size. Its mucosal wall was thickenned due to the formation of excess edema, aboundant petechiae and echymoses in most cases.

Although no inflammatory changes were detected in nervous system, edema and hemorhages were still present in the meninges of the brain, in the cerebellum and medulla.

c. Histopathological findings: Lymph nodes were mostly edematous and hyperemic. Their peripheric sinuses were enlarged and filled with inflammatory infiltrations that were composed of mononuclear cells as well as polynucleated leucocytes besides a few eosinophylic or basophylic luecocytes among the large number of desquamated endothelial cells seen in the clotted fibrin and serum that distended the sinuses. Medullary sinuses were similarly affected and dilated with infiltrations, however. The most severely attacked part was the cortical germinative centers, as they were intensly hyperplastic in the early stages and underwent to necrosis over time (*Picture.* 3). The

coagulative necrosis occurred and progressed so rapidly that the germination centers were completely destroyed and exhausted (*Picture.* 4) that resulted in severe leucopenia (lymphopenia). Lymph nodes, besides the inflammatory or necrotic changes, exhibited also severe hemorhages spread in every portions.

Similar histologic lesions were observed in the spleen (*Picture.* 5). Like the nodes, coagulative necroses (*Picture.* 6) were found in the severe cases, together with the inflammatory infiltrations and accumulation of too much blood in the spleen.

Although the severity was lesser than those taking place in the lymphatic organs, the liver was also attacked (*Picture.* 7) and contained necrotic foci being located very closely or just around the central veins in most cases. Inflammatory mononuclear cells, endothelilal cells or Kupffer cells were migrating in the sinuses in only heavily infected animals. The inflammatory cells were also accumulating in the stromal connective tissues around the lobuli or blood vessels running in the portobiliary spaces (*Picture.* 8). Some cosinophyles were also observed aroung the necrotic foci formed in affected livers.

The kidneys (*Picture.* 9) were lesser damaged when compared with the lymphatic tissues or with liver. Renal damages included glomerular hyperemia and hypercellularity, swelling the endothelial cells together with the severe parenchymatous degeneration in tubulary epithelium, in addition to the formation of edema and infiltrations into stromal connective tissue spaces of the cortex or medullary parts of the organs. The inflammatory inflitrations were mostly made up by mononuclear, and polynucleated leucocytes, a few eosinophyles and fibroblasts. Some coagulative necrotic foci and petechial or echymotic hemorhages were also present.

Another severely attacked organ was the abomasum that exhibited hemorhages, necroses and erosions (*Picture.* 10) on its mucous membrane, or deeper lesions like ulcers that went down to submucosa or muscular wall. Around the erosions or ulcerations, an inflammatory zone was formed as the demarcation. These inflammatory cells were accumulating in submucosa in the later stages.

Gall bladder mucosa, urinary bladder wall and intestinal mucous membranes were too exhibiting similar lesions like edema, degenerative and necrotic areas that were limited by inflammatory reactions. But only hyperemia and edema was noticed in the meninges of the brain, cerebellum and the medulla, where no necrosis and infiltrations were found.

Discussion

Contrary to other blood protozoa attacking to erythrocytes, the pathogenesis of anemia and other related lesions produced by T. annulata were not explained in detail, since it propagates in the lymphatic tissues, besides there is not many papers that directly dealt with these aspects (1, 3, 7, 15).

T. annulata reaches the lymph nodes by the blood stream following its transmission to bovine by ticks, especially H. detritum (3, 11) to attack the lymphocytic cells in which it continiously propagates before going into the blood stream (1, 3, 7, 15). Since it spends time during the propagation, the incubation period then changes accordingly, and the occurrence of fever, and the onset of anemia may become late. Theileriasis occurs in acute, subacute and chronic forms and the therapy is usually unsuccesful (2, 9, 10).

High fever, increased pulse and respiration, dyspnoea, dispepsia, immobility, and sudden or slowly arriving, termial coma and death of animal is the course of disease that takes usually more than a week. Very seldom animal can survive after a long reconvelescence period (9, 10). Icterus is seen in only rare cases of chronic form.

Diffuse hemorrhages, and jaundice that is observed in the serosal surfaces are detected during the necropsy, as the first and striking features, but not in all cases (15, 16). Subcutan gelatinous infiltrations were usually noted around the swollen lymph nodes (15). Hepatosplenomegalie, and abomasal ulcers together vith aboundant hemorhages were graded as diagnostic signs of theileriasis (1, 9, 10, 15).

However, the pathogenesis of anemia, abomasal ulcers, the necrotic foci in different organs, the formation of glomerulo-nephritis is not explained in fully detailed form. Some investigators claimed the immunomorphological changes (1), a toxin excreted by the potozoan itself (7); but nobody paid attention to the large amount of tissue destruction that cause to the production of large amounts of toxins that are taken into blood stream and may reach any organ, including bone marrow to block the hemopoietic processes. This point of view is strenghtenned by the facts like the late occurrence of a normocytic-normochromic anemia, together with the formation of lymphopenia, leucopenia, and thrombocytopenia in sick calves, during the later stages of the infection. If a toxin excreeted by the protozoan is accepted, which is not isolated yet, it is hard to explain its action mechanism on bone marrow, while it is produced by parasite being still present in

lymphatic tissues (7). Besides, the occurrence of large amount of necrosis in several organs that must, most probably be, the result of anoxemia or ischemia following the lose of permeability of capillaries, due to the toxins produced in the lymphatic centers by parasitic destruction. This may even help to understand the formation of uremia was present in our calves. Uremia, however, might be related to the kidney or liver damage, that end with large amount of tissue destruction and difficulty in the filtration of the blood.

The excretion of hemoglobin, billuribin or blood in urine, is also related to the destruction of liver and kidneys, rather than the destruction of red blood cells by the protozoan parasite, since the rate of hemolysis is late, and not so high.

The cause of the death of animals is multiple. Such as the abomasal lesions are the important ones for stopping the digestion and dispepsia, and the lose of humoral defense mechanism as the result of the destruction of lymphatic organs, addition to the large lesions like hemorhages and necroses in the vitally important organs may all play some role for the death of sick animals.

More detailed cilinical, biochemical and histological examinations are needed to understand the pathogenesis of theileria infection in bovines.

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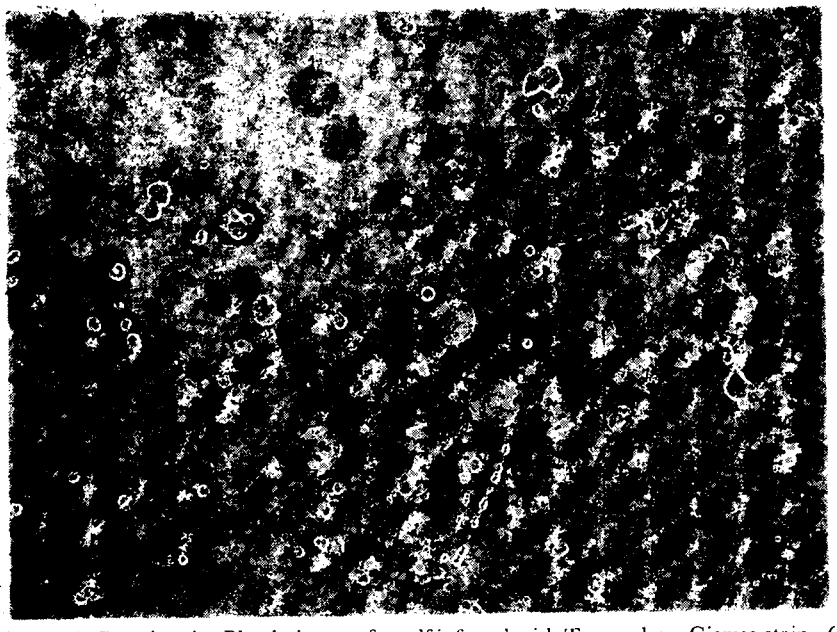
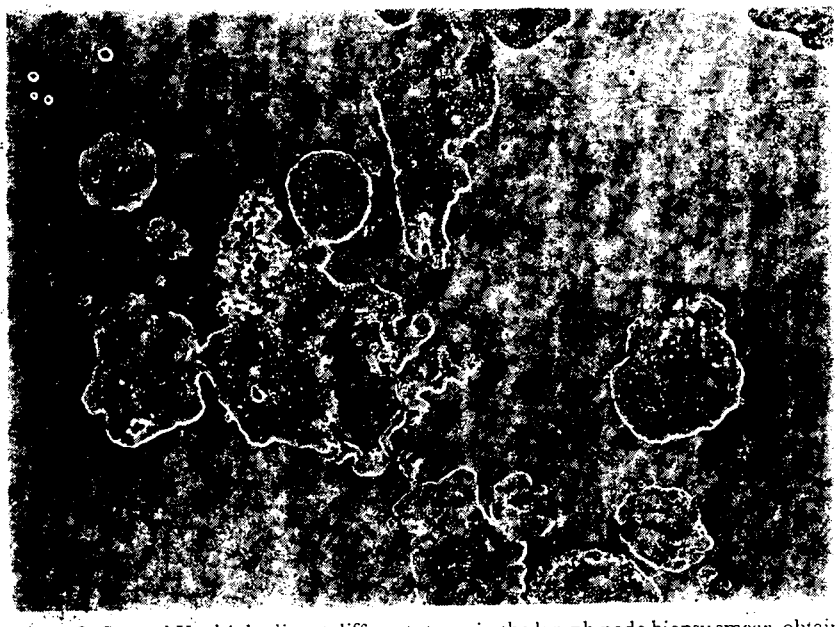
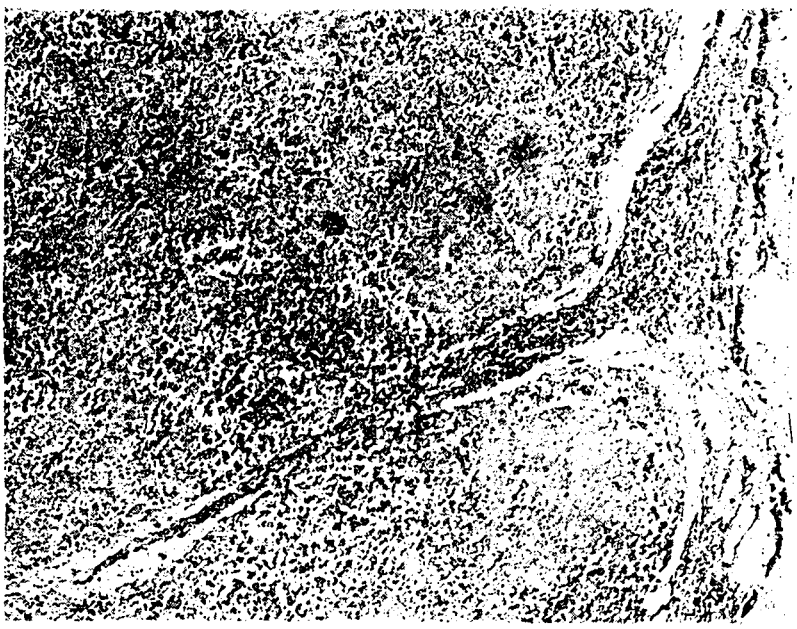


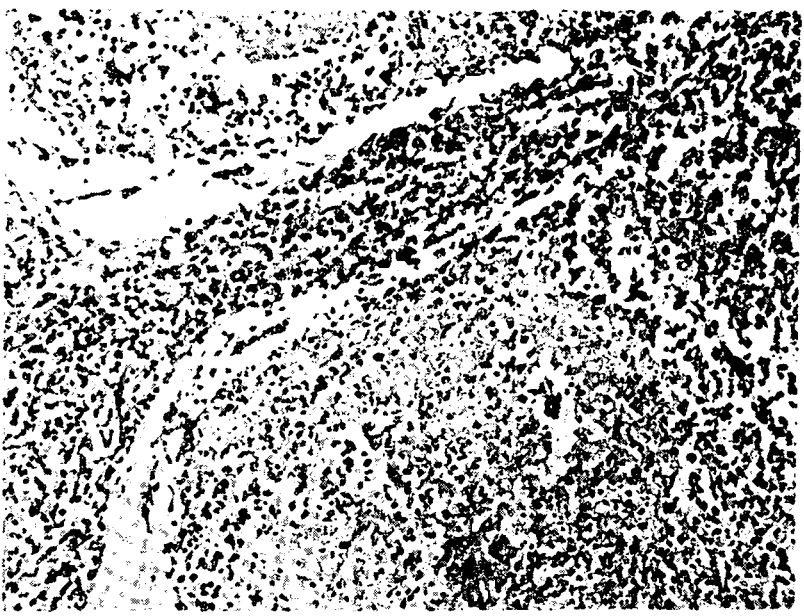
Picture. 1: Parasitemia: Blood picture of a calf infected with T. annulata, Giemsa stain., Oil Immers. XI000. (Parazitemi, T. annulata ile enfekte edilen bir dananın kan tablosu., Gimza boyası, immersiyon, büyütme, XI000)



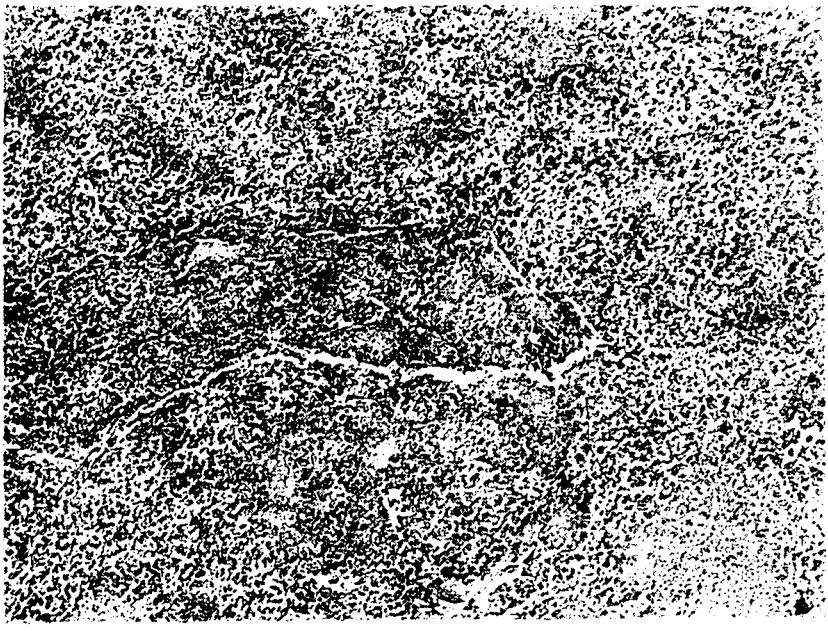
Picture. 2: Several Koch's bodies at different stages in the lymph node biopsy smear, obtained from a calf infected with T. annulata. Giemsa, oil imm., XI000 (Deneysel T. annulatayla enfekte edilen danada lenf düğümünde Koch cisimcikleri değişik gelişim devrelerinde, immersiyon, XI000)



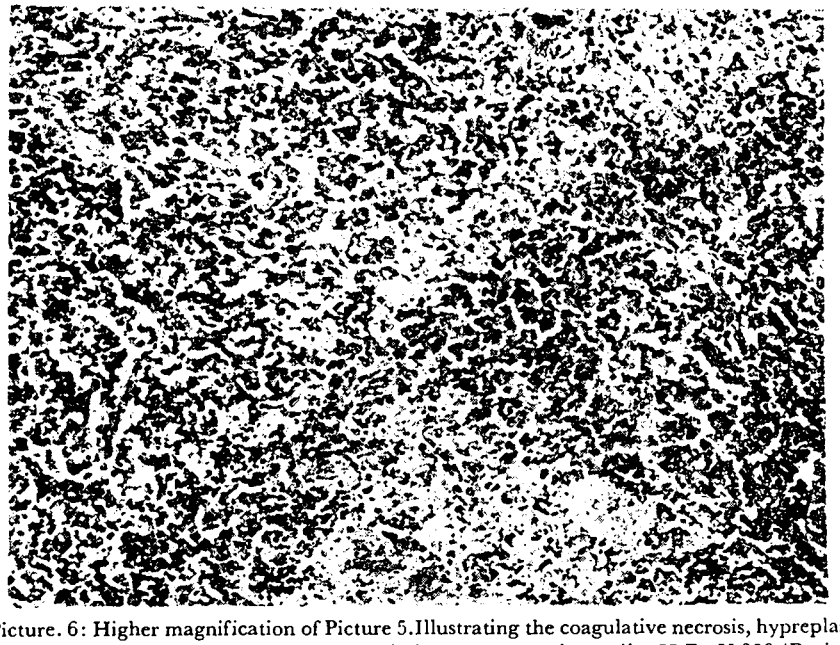
Picture. 3: General view of an exhausted lymph node to show the large coagulative necrosis of germinal centers, and inflammatory reaction into the sinuses., Heatoxylin and eosin Stain, XI00 (Boşalmış bir lenf düğümünde geniş koagülasyon nekrozu ve sinüslerde yangısal infiltrasyon., H.E., XI00)



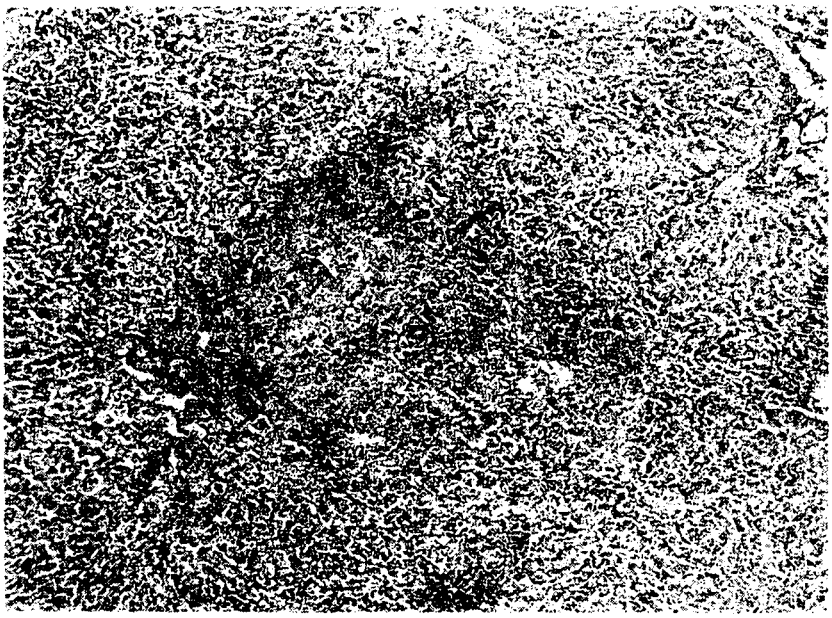
Picture. 4: Higher magnification of Picture. 3 X 250 (Resim 3'ün daha fazla büyütülmüş görünüşü X 250).



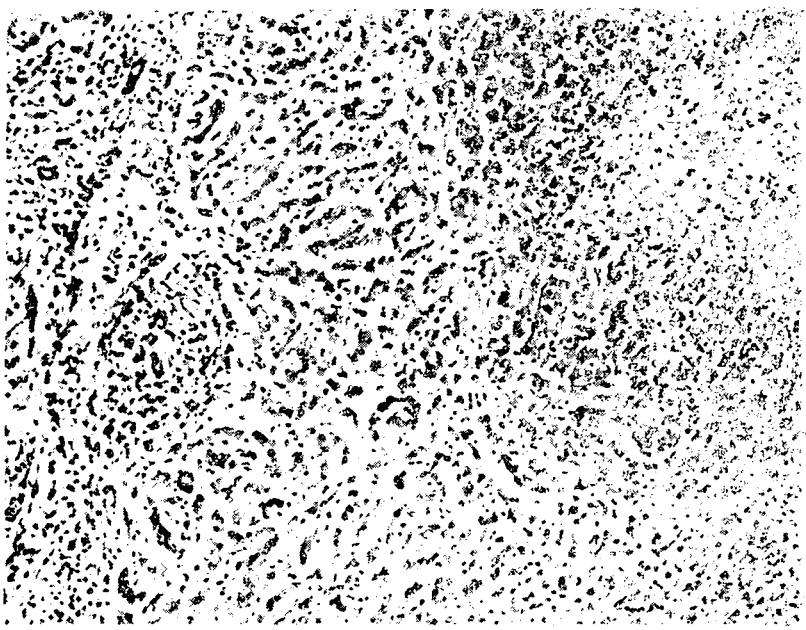
Picture. 5: Spleen with large necroses similar to nodes., H.E., X100 (Dalakta geniş nekrozlar, H.E., X100)



Picture. 6: Higher magnification of Picture 5.Illustrating the coagulative necrosis, hypreplastic response of germinal parts, and accumulation of mononuclear cells., H-E., X 250 (Resim. 5'in daha büyütülmüş şekliyle dalakta nekroz, hiperplazi ve yangısel hücrelerin yığılmaları., H.E., X 250)



Picture. 7: Same necroses in the liver of a calf infected with T. annulata., H-E., X100 (T. annulata ile enfekte dana karaciğerinde ayni tip geniş nekrozlar., H-E., X100



Picture. 8: Higher magnification of liver to note the necrosis, edema, severe inflammatory infiltrations., H-E., X 250 (Karaciğerde nekroz ve yangısel infiltrasyonları gösteren daha büyütülmüş resim., H-E., X250)

Picture. 9: Mononuclear infiltration into stroma, parenchymatous degeneration of tubulary epithelium and cellularity of glomeruli., H-E., X250. (Böbrek stromasında mononüklear infiltrasyon, tubüllerde parenkim dejenerasyonu, glomerüllerin hücreden zengin görülüşü. H-E., X250)

Picture. 10: Coagulative necrosis in the abomasal epithelium that is going into erosion and and ulceration., H-E.,X250 (Abomasum'un epitel katında koagülatif nekroz sonu erozyon ve ülserleşmeğe gidiş., H-E., X250)