

# 中華民國比較病理學會九十三年度第三十次比較病理研討會 (血液淋巴專題)

## 議程表

時間:中華民國九十三年三月十三日(星期六) 上午 08:40~下午 17:10

地點:台北市立動物園

地址:台北市新光路二段三十號

主辦單位:中華民國比較病理學會

時 間	議 程
08:40-09:00	報到
09:00-09:10	致詞
09:10-09:30	病例討論 Case208 高雄醫學院附設醫院病理科 黃琬妤醫師
09:30-09:50	病例討論 Case209 屏東防治所 徐榮彬課長
09:50-10:40	專題演講 中興大學獸醫系 謝快樂教授
10:40-11:10	Coffee Break
11:10-11:40	會員大會
11:40-12:00	病例討論 Case210 彰化基督教醫院病理科 余佳娟醫師
12:00-13:30	午餐(中華民國比較病理學會理監事會議)
13:30-13:50	病例討論 Case211 臺灣動物科技研究所 邱慧英研究員
13:50-14:10	病例討論 Case212 耕莘醫院病理科 孫政宏醫師
14:10-14:30	病例討論 Case213 中興大學獸醫系 陳三多教授
14:30-14:50	病例討論 Case214 新光醫院病理檢驗科 朱旆億醫師
14:50-16:10	病例討論 Case215 台大獸醫學系 秦紹儒研究生
16:10-16:30	病例討論 Case216 慈濟醫院病理科 曾柏元醫師
16:30-16:50	病例討論 Case217 台大獸醫學學研究所 涂央昌研究生
16:50-17:10	綜合討論

## Comparative Pathology Case 208

**Contributors:** Wan-Ting Huang (黃琬婷) MD, Kun-Bow Tsai (蔡坤寶) MD, Chee-Yin Chai (蔡志仁) MD.

**Clinical history:** A 45 y/o female has been a case of acute myeloid leukemia diagnosed in 1989 and received chemotherapy. In recent two months, she suffered from vaginal bleeding and visited our OPD. Pervaginal examination revealed a cervical mass with contact bleeding. On Dec 29, 2001, loop electroexcision procedure (LEEP) was performed.

**Diagnosis:** Granulocytic sarcoma (Chloroma) of uterine cervix.

**Gross finding:** The specimen submitted consists of two tissue fragments measuring up to 1.5 x 1.0 x 0.3 cm in size, fixed in formalin. Grossly, they are grayish white and elastic.

**Laboratory result:**

White blood cell count of: 6700/ul (myeloblasts: 0%; promyeloblasts: 0%; myelocytes: 0%; band form of neutrophils, 5.0%; segmental form of neutrophils: 46.5%; eosinophils, 2.0%; basophils, 2.5%; lymphocytes, 39.0%; monocytes, 5.0%); a red cell count of:  $4.51 \times 10^8$  /ul; hemoglobin concentration of 13.9g/dl; a platelet count of  $156 \times 10^3$ /ul.

**Discussion :**

Granulocytic sarcoma (GS) is an unusual variant of myeloid malignancy in which there is an extramedullary tumor mass composed of myeloblasts or myeloblasts and more mature neutrophils. In earlier literature, the granulocytic sarcoma is originally called a chloroma based on the green appearance of the tumor mass. The greenish color is secondary to myeloperoxidase in the tumor cells.

The granulocytic sarcomas are more frequent in children than adults. The most common sites are the bone, periosteum, soft tissue, lymph node and skin, but they have been found in many other organs, including abdominal organs, testis and breast. In the female genital tract, GS occurs more commonly in the ovary. Only few cases have been reported arising from the uterus, vulva or vagina. They usually appear as a solitary, rapidly growing nodular mass with a solid consistency.

Granulocytic sarcomas occur in four clinical situation: (1) in patients with known acute myelogenous leukemia (AML), (2) in patients with chronic myelogenous leukemia or other myeloproliferative disorders (MPD) of blastic transformation, (3) in patients with myelodysplastic syndromes (MDS) and (4) in patients without known hematological disorders (isolated granulocytic sarcomas).

If a myeloid sarcoma occurs in a setting of MDS or MPD, it is equivalent to blast transformation. In a setting of AML, the prognosis of the disease is that of the underlying leukemia. If a granulocytic sarcoma occurs as isolated lesion without any evidence of leukemia, curative radiotherapy to the lesion may result in a very prolonged survival.

Although GS occurring in the female genital tract is quite rare, this diagnosis should be considered in any woman presenting with menometrorrhagia, postcoital and postmenopausal bleeding especially with a previous history of a myeloid malignancy or myelodysplastic syndrome.

### **Diagnostic criteria:**

The tumor is composed of a relatively uniform population of immature cells. Occasionally, immature eosinophils and maturing neutrophils may present. There are three major types (the blastic, myeloblastic and immature types) based on degree of maturation. The blastic type is composed of primal myeloblasts with little evidence of differentiation to the promyelocyte stage. The myeloblastic type reveals myeloblasts which have a slight to moderate rim of basophilic cytoplasm, fine nuclear chromatin and two to four nucleoli. The immature type shows an intermediate degree of differentiation. The differentiated type comprises primarily promyelocytes and later stages of maturation. Immunocytochemistry using anti-myeloperoxidase, anti-lysosome and anti-CD 68 (KP-1) antibodies may be particularly useful.

### **Reference:**

1. Rosai J: 1996 Ackerman's surgical pathology, 8<sup>th</sup> ed.
2. Jaffe ES, Harris NL, Stein H, Vardiman JW: 2001 World Health Organization Classification of Tumours, Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues.
3. Park HJ, Jeong DH, Song HG, et al: 2003 Myeloid sarcoma of both kidneys, the brain, and multiple bones in a nonleukemic child. Yonsei Med J. Vol. 44(4), pp741-743.
4. Shea B, Reddy V, Abbitt P, et al: 2004 Granulocytic sarcoma (chloroma) of the breast: a diagnostic dilemma and review of the literature. The Breast J. Vol.10(1), pp48-53.
5. Mourad W, Kfoury H, Hussein A: 2001 The value of CD34, myeloperoxidase and chloracetate esterase (Leder) stain in the diagnosis of granulocytic sarcoma. Ann Saudi Med. Vol. 21(5-6), pp 287-291.
6. Spethmann S, Heuer R, Hopfer H, et al: 2004 Myeloid sarcoma of the prostate as first clinical manifestation of acute myeloid leukaemia. Lancet Oncol. Vol 5, pp 62-63.

## Comparative Pathology Case 209

**Contributors** : Jung-Pin Hsu (徐榮彬) DVM; Ming-Lian Lee (李明廉) DVM; Yi-Pin Lu (魯懿萍) DVM; Hsin-Hsiung Hung (洪信雄) DVM.

Pingtung Hsien Livestock Disease Control Center, Pingtung, Taiwan (屏東縣家畜疾病防治所)

**Clinical history**: This case was reported from a farm raised about 5000 layers in Pingtung County. The morbidity of this case was 80% (4000/5000) and the mortality was about 55% (2200/4000) when layers were at the age of 9 weeks old. Affected layers showed anorexia, depression and with obviously clinical signs of pale in the crest, face and foot. In addition, the clotting time from affected layers blood samples was increased and blood plasma was more translucent than normal and the packed cell volume (PCV) range significantly dropped to 3-12%.

**Gross findings**: The gross lesions of hemorrhage could be observed in the muscles of chest, legs and heart. Moderate to severe atrophy on thymus and bursa of Fabricius were also noticed. Moreover, the color of bone marrow showed pale to yellowish with fatty infiltration.

**Histopathologic findings**: It showed the number of myeloid and hematopoietic cells depletion and replaced by adipose tissue in bone marrow from anemic layers, and thymus and bursa of Fabricius severe lymphoid depletion. Furthermore, the total DNA of liver, thymus and bone marrow were extracted respectively from infected layers and analyzed by polymerase chain reaction (PCR) method. The sequencing results indicated an identical 400-bp amplicons of CIA virus were found from the infected samples.

**Diagnosis**: Chicken Infectious Anemia (CIA) in Layer

**Discussion**: Chicken infectious anemia (CIA) is caused by avian circovirus and commonly affects the young susceptible chickens with clinical signs of severe anemia and immunosuppression in the commercial producing farm. The causative agent chicken infectious anemia virus (CIAV) was first isolated in 1979 in Japan. Although serologic tests suggest that the virus has no public significance but it constitute a serious economic threat especially to the broiler industry. Because infections are associated with vertical transmission and because of potential for inducing infection alone or in combination with other pathogens sub clinical infections may result in increased mortality and condemnations. There is strong evidence that CIAV infection is immunosuppressive. Immunosuppression in anemic chickens is indicated by an increased susceptibility to bacterial and fungal secondary infections and by enhanced pathogenicity of adenovirus,

reovirus and Newcastle disease virus.

The chicken infectious anemia virus is approximately 25 nm in diameter and contains a circular, singlestranded DNA genome. The genus Circovirus includes porcine circovirus, psittacine beak and feather disease virus and chicken infectious anemia virus. CIAV can spread both horizontally and vertically. Histologically, there is complete atrophy of lymphoid cells in a wide variety of tissues. In the bone marrow, that number of myeloid and hematopoietic cells depletion and replaced by adipose tissue, and thymus and bursa of Fabricius severe lymphoid depletion. In addition, the clotting time from affected layers blood samples was increased and blood plasma was more translucent than normal and the packed cell volume range significantly dropped to 3-12% (normal value: >30%). In this case the total DNA of liver, thymus and bone marrow were extracted respectively from infected layers and analyzed by polymerase chain reaction (PCR) method. The sequencing results indicated an identical 400-bp amplicons of CIA virus were found from the infected samples.

#### **Diagnostic criteria:**

1. Clinical history : severe anemia.
2. Histopathological finding : lymphoid depletion.
3. CIAV DNA analyzed by PCR.

#### **Differential diagnosis:**

1. Aplastic anemia (osteopetrosis virus, erythroblastosis virus, MDV, IBDV).
2. Intoxication with high doses of sulfonamides, mycotoxins (aflatoxin).

#### **References:**

1. Calnek, BW. Diseases of Poultry. 10th ed. Mosby-Wolfe Iowa US. 739-756, 1997.
2. Calnek BW, Lucio-Martinez B, Cardona C, Harris RW, Schat KA, Buscaglia C. Comparative susceptibility of Marek's disease cell lines to chicken infectious anemia virus. Avian Dis 44: 114-124, 2000.
3. Cardona C, Lucio B, O'Connell P, Jagne J, Schar KA. Humoral immune responses to chicken infectious anemia virus in three strains of chickens in a closed flock. Avian Dis 44: 661-667, 2000.
4. Cardona CJ, Oswald WB, Schat KA. Distribution of chicken anemia virus in the reproductive tissues of specific-pathogen-free chickens. J Gen Virol 81: 2067-2075, 2000.
5. Chettle NJ, Eddy RK, Wyeth PJ, Lister SA. An outbreak of disease due to chicken anemia agent in broiler chickens in England. Vet Rec 124: 211-215, 1989.
6. Chiu CS, Hong CYJ, Lee JJ, Hisao M, Chueh LL. A Taiwanese isolate of chicken anemia virus causes apoptosis in the culture cells. J Chin Soc Vet Sci 27: 74-79, 2001.
7. Drén CsN, Kant A, VanRooselaar DJ, Hartog L, Noteborn M H M, Koch G. Studies on the pathogenesis of chicken infectious anemia virus infection in six-week-old SPF chickens. Acta Vet Hung 48: 455-467, 2000.

8. Goryo M, Sugimura H, Matsumoto S, Umenura T, Itakura C. Isolation of an agent inducing chicken anemia. *Avian Pathol* 14: 483-496, 1985.
9. Hagood LT, Kelly TF, Wright JC, Hoerr FJ. Evaluation of chicken infectious anemia virus and associated risk factors with disease and production losses in broilers. *Avian Dis* 44: 803-808, 2000.
10. McNulty MS, Connor TJ, McNeilly F, Spackman D. Chicken anemia agent in the United States: isolation of the virus and detection of antibody in broiler breeder flocks. *Avian Dis* 33: 691-694, 1989.
11. McNulty MS. Chicken anemia agent: A review. *Avian Pathol* 20: 187-207, 1991.
12. Scott ANJ, Connor TJ, Creelan JL, McNulty MS, Todd D. Antigenicity and pathogenicity characteristics of molecularly cloned chicken anemia virus isolates obtained after multiple cell culture passages. *Arch Virol* 144: 1961-1975, 1999.
13. Todd D, Creelan JL, Mackie DP, Rixon F, McNulty MS. Purification and biochemical characterization of chicken anaemia agent. *J Gen Virol* 71: 819-823, 1990.
14. Todd D, Mawhinney KA, McNulty MS. Detection and differentiation of chicken anemia virus isolates by using the polymerase chain reaction. *J Clin Microbiol* 30: 1661-1666, 1992.
15. Yuasa N, Taniguchi T, Yoshida I. Isolation and some characteristics of an agent inducing anemia in chicks. *Avian Dis* 23: 367-385, 1979.

## Comparative Pathology Case 210

**Contributors:** Chia-Chuan Yu (余佳娟), Yueh-Min Lin (林岳民), Julia Huei-Mei Chang (張惠媚). Department of Pathology, Chang-Hua Christian Hospital (彰化基督教醫院)

**Clinical history:** A 77-year-old female patient has the past history of type 2 diabetes mellitus with medical control. She suffered from soreness of right arm for three months. She denied any trauma. She received traditional Chinese medication for the soreness. However, the symptoms did not subside. She then had severe right arm pain and could not raise her right arm. She visited our hospital on 2003/11/17. No swelling was noted. The X-ray was arranged and revealed fracture of right humeral neck. Under the impression of fracture of right humeral bone, ORIF and bone biopsy were performed on 2003/11/20.

**Laboratory data** (2003/11/19)

WBC: 11900 /uL	Monocyte: 5.53%
RBC: 4.19* 10 <sup>6</sup> /uL	Eosinophil: 0.16%
Hb: 13.5 g/dL	Basophil: 0.43%
Platelet: 218000 /uL	LDH: 728 u/L
Segment: 76.1%	Alk-P: 179 u/L
Lymphocyte: 17.8%	β <sub>2</sub> -microglobulin: 2.71 mg/L

**Gross finding:** The specimen submitted consisted of several soft tissue and bony fragments measuring up to 1.5×0.6×0.4 cm in size, fixed in formalin. Grossly, they were brownish and elastic.

**Histopathological finding:** It showed diffuse infiltrate by large lymphoid cells in the marrow space, which contained vesicular nuclei and prominent nucleoli. Immunohistochemical study demonstrates CD3 (-), Leukocyte common antigen (+), CD20 (+) and Bcl-6 (focal +).

**Diagnosis:** primary non-Hodgkin's lymphoma of bone, diffuse large B cell, right humerus

**Work-up and staging:**

1. Chest X-ray (11/24): right humeral shaft fracture s/p ORIF
2. Bone marrow biopsy (11/28): no evidence of lymphoma involvement
3. Abdominal CT (11/26): no hepatosplenomegaly, no lymphadenopathy

4. Bone scan (11/27): moderately increased activity area in noted in proximal right humerus

Staging: stage IE

**Discussion:** Primary non-Hodgkin lymphoma of bone is an uncommon malignancy. It accounts for approximately 2% of all bone tumors and 5% of all extranodal lymphomas and < 1% of all non-Hodgkin lymphomas. It clinically defined as “lymphoma presenting in an osseous site with no evidence of disease elsewhere for at least six months after diagnosis”. It may appear at any age and occurs mostly in patients over 20 years of age. It occurs predominantly in males. In general, non-Hodgkin’s lymphomas have a predilection for the truck bones, including the ribs, sternum, pelvis and clavicle. The major long tubular bones, such as the femur and humerus, are the most frequently involved sites in the appendicular skeleton.

Insidious and intermittent bone pain is the most common symptom. Local tenderness and swelling may be present. Pathological fracture can be the initial symptoms. The radiographic features are variable. Osteolysis is the predominant change with the resulting appearance of a moth-eaten destructive lesion. Cortical disruption with extension into soft tissue is frequently seen. Periosteal new bone formation can be present but is often limited.

Microscopically, the tumor consists of sheets of lymphoid cell with variable nuclear characteristics that depend on the type of lymphoma. In adults, the most common subtype seen as primary lymphoma of bone is diffuse large B-cell lymphoma which accounts for 60~90 % of cases.

Radiation therapy and chemotherapy are the primary treatment of non-Hodgkin’s lymphoma of bone. The usual chemotherapy is CHOP for several cycles. Surgery is recommended in patients with fractures. Due to the relative rarity of this disease, standard treatment protocols have not been developed.

### **References:**

1. David TM, Amdur, Robert J, Mark TS, Nancy PM, Virkus, WV. Stage IE primary non-Hodgkin's lymphoma of bone. *Clin Ortho & Related Res.* 405: 216-22, 2002.
2. Huebner-Chan D, Fernandes B, Yang G, et al. An immunophenotypic and molecular study of primary large B-cell lymphoma of bone. *Mod Pathol.* 14: 1000-7, 2001.
3. Laurence dL, Kristina MB. Marek A. Edward K. Thomas D. Henry JM, Nancy LH. Diffuse large B-cell lymphoma of bone: An analysis of differentiation-associated antigens with clinical correlation. *Am J Surg Pathol.* 27: 1269-77, 2003.
4. Olavo P, Telma M, Alberto TC, et al. Primary bone lymphoma in 24 patients treated between 1955 and 1999. *Clin Ortho & Related Res.* 397: 271-80, 2002.
5. Valerae OL, Gregory P, John A, Dorota D, Anthony GM, Terrance DP, Michael



AS. Oncologic outcome of primary lymphoma of bone in adults. *Clin Ortho & Related Res.* 415: 90-7, 2003.

6. Peter Bullough. Orthopaedic Pathology. 2004
7. Howard D Dorfman, Bogdan Czerniak. Bone Tumors. 1998.

## Comparative Pathology Case 211

**Contributors:** Hue-Ying Chiou (邱慧英), D.V.M., Woon-Fa Chang (張文發), D.V.M., MS, Division of Animal Medicine, Animal Technology Institute Taiwan (台灣動物科技研究所動物醫學組)

**Clinical history:** The penguin was collected from a group of imported animals. During post-entry quarantine, clinical signs of progressive depression, weakness, and lethargy had been noticed by the owner.

**Diagnosis:** Avian malaria, African black-footed penguin

**Gross findings:** At necropsy, the lesions included hepatomegaly, splenomegaly, hydropericardium, with subcutaneous and pulmonary edema.

**Histopathological findings:** Microscopically, the most lesions contain striking exoerythrocytic schizonts in the liver, lungs, spleen, kidney, and other organs. Reticuloendothelial hyperplasia is marked. Multiple degeneration and necrosis are noticeable in the myofiber of the myocardium. Some exoerythrocytic schizonts appear within the endothelial cells, reticuloendothelial or circulating histiocytes. Heavy inflammatory cells of lymphocytes and macrophages infiltrating the portal areas are observed. Kupffer cells and macrophages within the liver contain of malaria pigment.

**Laboratory results:** No significant microbiology organism was isolated.

**Discussion:** There are many diseases of the aves class that have the potential to affect penguins, including Newcastle disease, highly infectious avian influenza, infectious bursal disease, pullorum disease, fowl typhoid, duck virus enteritis, duck virus hepatitis, avian chlamydiosis, avian infectious bronchitis, avian infectious laryngotracheitis, mycoplasmosis, tuberculosis, fowl cholera, avian pox, marek's disease, reticuloendotheliosis, avian encephalomyelitis, penguin herpesvirus-like infection, puffinosis-like virus, aspergillosis, blastomycosis, actinomycosis, bumblefoot, endoparasites, ectoparasites, haemoparasites (*plasmodium relictum* or *plasmodium elongatum*, and *Babesia* spp), and mosquito-borne viral encephalitis (Japanese encephalitis, Eastern, Western and Venezuelan equine encephalitis, West Nile virus, St. Louis encephalitis). Malaria occurs in birds, humans and other primates, and is caused by protozoal parasites in the genus *Plasmodium*. *Plasmodium* spp.

pathogenic for domestic poultry are found mainly in Africa, Asia and South America. Some 65 *Plasmodium* sp. have been isolated from over 1,000 different species of birds. Avian malaria is an important disease of penguins. It is caused by *plasmodium relictum* or *plasmodium elongatum*. *Plasmodium relictum*-associated avian malaria is a high-mortality disease of captive penguins in North America and a recognized disease of wild and stranded Jackass penguins. The infectious organisms are transmitted by vector species such as the *Culex* mosquito, and are more likely to occur when penguins are housed in outdoor exhibits. They are most devastating to first year and superannuated birds. It is characterized by acute onset and rapid death, often with few premonitory signs of illness. Icterus and anemia are often not evident. In penguins, reticuloendothelial hyperplasia is often marked, but hemozoin pigment formation is variable. The parasites pass through two stages of asexual reproduction within the vertebrate host: exoerythrocytic and intraerythrocytic. Exoerythrocytic replication within the liver occurs first; the merozoites that are produced eventually break out of the hepatocytes and invade erythrocytes. Once in the cytoplasm of an erythrocyte, the merozoites progress through several morphologic stages. In the 'ring' stage, the protozoan contains a centrally located vacuole and a peripheralized, red nucleus. With development into the trophozoite stage, food vacuoles are formed from invagination and pinching off of the host cell's cytoplasm. Evaluating thin blood smears for parasitemia and monitoring differential and total white blood cells counts for a lymphocytic leukocytosis ( $\geq 19,000/\text{mm}^3$  with 50% or more lymphocytes) are diagnosis of malaria in penguins. Oral administration of 0.3 mg/kg primaquine phosphate once a day for ten days combined with an initial dose of 10 mg/kg chloroquine phosphate and additional doses of 5 mg/kg at 6, 10, and 24 hours has proven successful in treating penguin malaria. Control programs may include removal of mosquito breeding areas, utilization of mosquito-feeding fish in standing ponds, mosquito trapping, and/or selective use of pesticides. Enclosed exhibits can minimize access of mosquitoes to malaria-susceptible bird species. Quarantine and import controls should be used to reduce the risk of importing infected birds.

#### **Diagnostic criteria:**

1. The diagnosis of malaria is usually established by demonstrating the organisms in erythrocytes in thin or thick smears stained with Giemsa's or Wright-Giemsa stain.
2. Reticuloendothelial hyperplasia and the presence of mature shizonts in the cytoplasm of reticuloendothelial cells, and endothelial cells of the capillaries.
3. Marked leukocytosis due to an extreme lymphocytosis is highly suggestive of malarial infection and should increase the index of suspicion.
4. Intense and severe anemia

#### **References:**

1. Fowler ME. Zoo and Wild Animal Medicine. 2nd. ed. W.B. Saunders Co. p.294-313, 1986.
2. Graczyk TK, Brossy JJ, Plos A, Stoskotf MK. Avian malaria seroprevalence in jackass penguins (*Spheniscus demersus*) in south africa. J Parasitol p. 703-707,1995.
3. Lombard E, Brossy JJ, Blackbeard J. Malaria in an African penguin. British Journal of Haematology p.577, 1999.
4. Meyer MC, Olsen's OW. Essentials of parasitology. Wm.C.Brown publishers p.25-30, 1992.

## Comparative Pathology Case 212

**Contributor:** Jeng-Hung Suen (孫政宏), Fur-Jiang Leu (呂福江), Chia-Ing Jan (詹佳穎)

### **Clinical history:**

A 34-year-old woman, paramedical staff of our hospital, has suffered from flu-like syndrome for one month. The symptoms and signs include rhinorrhea, sorethroat, dry cough (sometimes productive with yellowish sputum), fever, occasional chillness, and myalgia, which are off and on and last for one month. She visited our ENT and took some medicine for symptom relieve. Body weight loss for 1.5 Kg was noted and bilateral neck lymphadenopathy was palpated by herself in recent days, especially on the right side where a group of enlarged lymph nodes are present. Pain is absent and tenderness is minimal. Therefore, excisional biopsy was performed to rule out the possibility of malignant lymphoma and TB, and frozen section examination during the operation was done.

**Diagnosis:** Kikuchi disease (histiocytic necrotizing lymphadenitis)

### **Gross findings:**

The specimen submitted for frozen section exam consists of a piece of lymph node, measuring 1.2 x 1.2 x 0.7 cm in size, unfixed. Grossly it is tan soft in color and consistency with small focal areas of yellowish necrotic-like tissue.

### **Histopathological finding:**

The lymph node architecture is partially preserved. There are some patchy areas of necrosis with irregular-shaped border and occasional confluence. The necroses are randomly distributed, but more prominent in the cortex region with wedge shape. Numerous nuclear debris surrounded by copious histiocytes are noticed in the necrotic areas. Neutrophil is absent.

### **Special stains:**

Negative for acid-fast bacilli. The lymphocytes surrounded the necrotic areas are mainly immunoreactive for CD3, while the histiocytes are immunoreactive for CD68.

### **Laboratory results:**

EB VCA IgM: Negative

EBV-EA+NA1-IgA: Positive (>6.0)

CBC/DC: WNL

RPR/VDRL: Negative

Anti-HIV: Negative

Anti-HCV: Negative

Biochemistry (AST, ALT, LDH, sugar, creatinine) : WNL

### **Discussion:**

A histologically distinct form of subacute necrotizing lymphadenitis was first described in Japan in 1972 by Kikuchi and independently by Fujimoto. The disease has been called Kikuchi disease, Kikuchi-Fujimoto disease, histiocytic necrotizing lymphadenitis, Kikuchi necrotizing lymphadenitis, phagocytic necrotizing lymphadenitis, subacute necrotizing lymphadenitis, and necrotizing lymphadenitis.<sup>1</sup>

Although more common in east Asia, the disease has been reported in many areas of the world, including Europe, U.S., and Australia. Kikuchi disease (KD) occurs most often in young women (mean age, 30 years; male/female ration, 1:4).<sup>3</sup> The most common clinical manifestation is cervical lymphadenopathy with or without fever; additional findings may include fever, sore throat, weight loss, sweats, chillness, myalgia, arthralgia, splenomegaly, and skin rash.<sup>3,4</sup> Laboratory abnormality may include leukopenia, an elevated trasaminase level, and and elevated serum lactate dehydrogenase level.

In almost all cases, the course is benign, self-limited, and followed by complete recovery within one to 3 months without specific treatment.<sup>5</sup> Recurrence of disease may occur but is infrequent, and fatalities are exceptional.<sup>2</sup>

In addition to the mature necrotizing lesion, 3 other lesions (stages) have been described: (1) an early proliferative lyphohistiocytic lesion with numerous atypical mononuclear cells, which is sometimes misdiagnosed as malignant lymphoma, (2) a prenerotizing phagocytic lesion with numerous histiocytes and single cell necrosis, and (3) a late postnecrotic xanthomatous (foamy cell) form.<sup>5</sup> It indicates that KD may progress from an early proliferative phase to a necrotizing phase and, finally, to a xanthomatous (resolving) stage. However, features of all three stages may be present at the same time.

Several features of KD suggest that the cause is likely to be infectious or autoimmune. 21 cases of KD occurring in association with SLE have been reported. Many studies focus on the presence of viral protein, mRNA, or DNA in the cells of KD to establish the relationship between KD and viruses (EBV, HTLV-1, Parvovirus B19, HSV-1, HSV-2, CMV, HHV-8, HIV).<sup>1,3,8</sup> However, as so far, no infectious agent has been proven to be etiologically related.

### **Diagnostic criteria:**

1. The lymph node architecture is partially preserved.
2. Patchy areas of randomly distributed necrosis with irregular-shaped border and occasional confluence. The necroses are more prominent in the cortex region with wedge shape.
3. Numerous nuclear debris surrounded by copious histiocytes are noticed in the necrotic areas.
4. Neutrophil is absent.
5. ruled out fungus, TB, cat-scratch, infectious mononucleosis (EBV), or other pathogen infections by histopathological features on H&E, clinical information, or special stains if indicated.
6. The most important differential diagnosis is from malignant lymphoma. But this is usually not difficult if clinical information is correlated and histomorphological features has been properly evaluated. Immunostain or other procedure are usually unnecessary. However, in difficult case assays for T-cell receptor monoclonity (by PCR test followed by high-resolution gel electrophoresis) may be helpful.<sup>7</sup>

#### **Reference:**

1. Hudnall SD, M.D. Kikuchi-Fujimoto disease. Is Epstein-Barr virus the culprit?. *Am J Clin Pathol.* 2000 Jun;113(6):761-64
2. Dorfman RF, Berry GJ. Kikuchi's histiocytic necrotizing lymphadenitis: an analysis of 108 cases with emphasis on differential diagnosis. *Semin Diagn Pathol.* 1988;5:329-345
3. Chiu CF, M.D., PhD(中國醫藥大學). Virus infection in patients with histiocytic necrotizing lymphadenitis in Taiwan. *Am J Clin Pathol* 2000 Jun;113(6):774-81
4. Chamulak GA. Kikuchi-Fujimoto disease mimicking malignant lymphoma. *Am J Surg Pathol.* 1990;14:514-523
5. Kikuchi M. Histiocytic necrotizing lymphadenitis (Kikuchi-Fujimoto disease) in Japan. *Am J Surg Pathol.* 1991;15:197-198
6. Chen YH (台中榮總). Kikuchi disease in systemic lupus erythematosus: clinal features and literature review. *Journal of Microbiology, Immunology&infection.* 31(3):187-92, 1998 Sep.
7. Lin CW (台大). Spontaneous regression of Kikuchi lymphadenopathy with oligoclonal T-cell populations favors a benign immune reaction over a T-cell lymphoma. *Am J Clin Pathol* 2002 Apr; 117(4):627-35
8. Huh J (漢城). *Journal of Korean Medical Science.* 13(1):27-30, 1998 Feb. (only abstract is available).

## Comparative Pathology Case 213

**Contributors:** Yi-Jin Chern (鄭玉津), DVM., San Duo Chen (陳三多), DVM, PhD.  
Institute of Veterinary Pathology, National Chung Hsing University

**Clinical history:** A male, mongrel dog, showed severe emaciation and weakness when submitted to local animal hospital. Radiographs and Sonographs found that some tumor-like masses distributed in many visceral organs, and then euthanasia was performed.

**Diagnosis:** Lymphoma, multi-centric type.

**Gross findings:** Many whitish nodules were found in heart, liver, lung and kidney. The spleen was severely enlarged and most lymph nodes were swollen. The cut surfaces of nodules were pale to grayish, soft to moderate hardness, demarcated in round to ovoid or irregular with various sizes. The small intestinal wall was thickened by a layer of pale substance.

**Histopathological findings:** All involved organs were infiltrated by a great number of lymphocytes, in which, the organs were enlarged and the tissues were distended by the neoplastic cells. These immature lymphocytes infiltrated in the intercellular spaces between cardiac muscles, the submucosa and muscularis layer of small intestine, and around the portal triads and central veins of liver. They extensively distributed in the cortex and medulla of kidney, but not extended into the tubular lumens and glomeruli. The tumor cells were large, with vesicular nuclei, and showed a high number of mitotic figures. They were more solitary and anisocytotic depending on the differentiating degree. The more mature lymphocytes contained a compact and dark stained nucleus with little cytoplasm. The undifferentiated lymphocytes contained a large nucleus with a prominent nucleolus and pale stained cytoplasm. They fulfilled the matrix of spleen or lymph nodes to show a starry –sky appearance.

**Electron Microscopy:** The tumor cells were various in size and shape. The nuclei were round or ovoid and the euchromatin was abundant in large immature lymphocytes, but heterochromatin was evident in small mature lymphocytes. The nucleoli were large and prominent. It always existed 2 to 4 in a nucleus. Most cells contained little cytoplasm and few organelles, such as, mitochondria and rough endoplasmic reticulum.

**Diagnostic criteria:**



1. The tumor cells were round or ovoid, contained large nuclei, few cytoplasm and invaded almost all internal organs.
2. The lymphocyte, compared with other cell types, was relatively devoid of cytoplasmic organelles as confirmed by ultrastructural observation.

**Discussion:** Lymphoma is a very common tumor in dog, which is usually described into the terms of alimentary, cutaneous or subcutaneous; multicentric or generalized, thymic or mediastinal; solitary, regional, or extranodal. Multicentric type is most common in dogs. Untreated dogs with multicentric lymphoma have a life expectancy averaging 10 weeks. In this case, massive tumor cells invade heart, liver, spleen, lung and kidney. It should be useless to treat the weakness dog. Because its histological feature is very similar to histiocytoma and transmissible venereal (TVT) cells, therefore, it is difficult to differentiate these cells in histological sections and all these cells are called round cells. Generally speaking, TVT cells always arranged compactly or grew in cords and were divided into some nests by a little fibrous connective tissue. Those cells also contained a round or ovoid nucleus and abundant cytoplasm. Similar figure was found in the histiocytoma except the nuclei were pleomorphic. Contrarily, the lymphoma cells were round with various amounts of cytoplasm. In immunohistochemical staining, both TVT and histiocytoma cells were positive to vimentin, but negative to keratin, desmin, S-100, and neuron-specific enolase (NSE). No response could be found in the lymphoma. In ultrastructural observation, the nucleus of TVT cells contained abundant euchromatin with one or two prominent nucleoli. The cytoplasm contained many organelles, e.g. mitochondria, rough endoplasmic reticulum (RER), ribosomes, Golgi complex, lysosomes ect.. Many microvilli protruded from the cytoplasmic membrane and interdigitated between two adjacent cells. In degenerated TVT cells, the most obvious lesions were the dilatation of RER and mitochondrial swelling. On the other hand, the histiocytoma cells contained abundant cytoplasm with a moderate number of organelles, and the lymphoma cells contained little cytoplasm and few organelles only. Conclusively, the ultrastructural features are the most useful to differentiate the TVT, histiocytoma, and lymphoma.

### **References:**

1. Andreasen, C.B., E.A. Mahaffey and J.R. Duncan. 1988. Intermediate filament staining in the cytologic and histologic diagnosis of canine skin and soft tissue tumors. *Vet. Pathol.* 25:343-349.
2. Batamuzi, E.K. and B.M. Kessy. 1993. Role of exfoliative cytology in the diagnosis of canine transmissible venereal tumor. *J. Small Anim. Pract.* 34:399-401.
3. Cockrill, J.M. and J.N. Beasley. 1975. Ultrastructural characteristic of canine transmissible venereal tumor at various stages of growth and regression. *Am. J. Vet. Res.* 36:677-681.

4. Desnoyers, M.M., D.M. Haines and G.P. Searcy. 1990. Immunohistochemical detection of intermediate filament proteins in formalin fixed normal and neoplastic canine tissues. *Can. J. Vet. Res.* 54:360-365.
5. Gatter, K.C., C. Alcock, A. Heryet and D.Y. Mason. 1985. Clinical importance of analysing malignant tumors of uncertain origin with immunohistological techniques. *Lancet* 8:1302-1305.
6. Huhn, D. and P. Meister. 1978. Malignant histiocytosis: Morphologic and cytochemical findings. *Cancer* 42:1341-1349.
7. Moore, P.F. 1986. Utilization of cytoplasmic lysozyme immunoreactivity as a histiocytic marker in canine histiocytic disorders. *Vet. Pathol.* 23:757-762.
8. Moore, A.S., B.R. Madewell and J.K. Lund. 1989. Immunohistochemical evaluation of intermediate filament expression in canine and feline neoplasms. *Am. J. Vet. Res.* 50:88-92.
9. Nielsen, S.W. and P.G. Kennedy. 1990. Tumors of the genital system. In J.E. Moulton, 3rd ed. *Tumors in domestic animals*. Berkeley, University of California Press, USA. pp. 498-502.
10. Rabanal, R.H., D.M. Fondevila, V. Montane, M. Domingo and L. Ferrer. 1989. Immunocytochemical diagnosis of skin tumors of the dog with special reference to undifferentiated types. *Res. Vet. Sci.* 47:129-133.
11. Sandusky, G.E., W.W. Carlton and K.A. Wightman. 1987. Diagnostic immunohistochemistry of canine round cell tumors. *Vet. Pathol.* 24:495-499.
12. Susaneck, S.J. and S.J. Withrow. 1989. Tumors of the skin and subcutaneous tissues. In S.J. Withrow, E.G. MacEwen, eds. *Clinical Veterinary Oncology*. JB Lippincott Company, Philadelphia, USA. pp. 152-153.
13. Wellman, M.L. 1990. The cytologic diagnosis of neoplasia. *Small Anim. Pract.* 20:919-938.

## Comparative Pathology Case 214

**Contributors:** Pei-Yi Chu (朱旆億), MD; Yuh-Yu Chou, MD (周玉瑜); Yen-Chung Chen (陳彥仲), MD; Tong-Jong Chen, MD (陳東榮)( 新光吳火獅紀念醫院病理檢驗科 )

**Clinical history:** A middle-aged women suffered from intermittent fever, body weight loss and a progressively enlarged left-sided neck mass in recent 2 months. She visited a medical center in Taipei where neck CT and gastric endoscopic examination were done. Due to back pain and epigastralgia, she visited the other hospital one month after. Abdominal CT examination revealed diffuse thickening of the gastric wall with retroperitoneal, para-aortic and mesenteric lymphadenopathy. Lymphoma was highly suggested. She received repeat endoscopic biopsy and further oncological surveys and management in Shin-Kong Wu Ho Su Memorial Hospital.

**Diagnosis:** CD30 (Ki-1)-positive anaplastic large cell lymphoma (ALCL)

**Gross findings:** The specimen submitted consists of 7 tissue fragments measuring up to 0.4 x 0.3 x 0.1 cm. in size, fixed in formalin. Grossly, they are white and elastic.

**Histopathological findings:** Section shows gastric mucosa with ulcer debris as well as numerous large hyperchromatic cells in haphazard pattern. The tumor cells have pleomorphic nuclei with coarse chromatin, small nucleoli and moderate amount of cytoplasm. No obvious glandular structure is seen. Immunohistochemical studies of cytokeratin (CK), epithelial membranous antigen (EMA), HMB-45, vimentin, desmin, leukocyte common antigen (LCA), CD20 (L26), CD45RO UCHL-1), and CD30 are done. Almost large tumor cells reveal positive reactivity for LCA, CD30, and vimentin, and negative staining for the other antibodies.

**Discussion:** Since the first description by Stein et al in 1985, CD30 (Ki-1)-positive ALCL has been considered a distinctive clinicopathologic entity in the hematopoietic malignancy. It accounts for approximately 3 % of adult non-Hodgkin's lymphoma and 10-30% of childhood lymphoma. Although CD30 (Ki-1)-positive ALCL is first considered as a T-cell lymphoma, both B-cell and null phenotypes have also been reported. ALK (anaplastic lymphoma kinase)-positive ALCL occurs most frequent in the first three decades of life with a prominent male predominance. In contrast, the patients of ALK-negative ALCL are generally older with a mild female predominance and a poorer prognosis. The most commonly involved sites are lymph nodes. Extranodal

involvements including bone marrow, skin, bone, soft tissue, lung, liver and stomach are less common. Gastric involvement is rare, either primary or systemic. Our patient is a systemic ALCL involving lymph nodes, stomach and lung. After one course of CHOP chemotherapy, she got dramatic improvement of symptoms.

**Diagnostic criteria:**

- (1) ALCL is usually characteristic of large lymphoid cells with abundant cytoplasm and irregular nuclei. The so-call “hallmark cell” is presented in variable portion in all variants of ALCL. Hallmark cells show eccentric, horse-shoe or kidney-shaped nuclei with eosinophilic cytoplasm.
- (2) Special stain profiles: tumor cells are usually CD30-positive. Most of them are also positive for EMA. ALK is expressed in 60-85% of the cases and is the most specific marker for ALCL. The majority of ALCL expressed T-cell antigens and expression of B-cell antigens or null-cell type is also reported.

**Reference:**

1. World Health Organization Classification of Tumours, Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues edited by Elaine S. Jaffe, Nancy Lee Harris, Harald Stein, James W Vardiman. p230-p235
2. Falini, Brunangelo. Anaplastic large cell lymphoma: pathological, molecular and clinical features. British Journal of Haematology. 114(4):741-760, 2001.
3. Morris, et al. Alk+ CD30+ lymphomas: a distinct molecular genetic subtype of non-hodgkin's lymphoma. British Journal of Haematology. 113(2):275-295, 2001.
4. Nakamura, Shotaro et al. Rapidly Growing Primary Gastric CD30 (Ki-1)-Positive Anaplastic Large Cell Lymphoma. Digestive Diseases & Sciences. 43(2):300-305, 1998.
5. Narita, Michihiko et al. Primary gastric lymphomas: Morphologic, immunohistochemical and immunogenetic analyses. Pathology International. 46(9):623-629, 1996.

## Comparative Pathology Case 215

**Contributors:** Shao-Ju Chin (秦紹儒), Jane-Fang Yu (余珍芳), Victor Fei Pang(龐飛), Shih-Chien Chin(金仕謙), Chen-Hsuan Liu (劉振軒), Chian-Ren Jeng(鄭謙仁)\*

**Clinical history:** A 3-years-old male koala, imported from Australia to Taipei Zoo on 9/18/2001, revealed good health and body condition until 11/26/2002. The animal was depression, and showed variable appetite. Enlarged abdomen and increased body weight (from 6.86 to 8.2 kg during a week) were noted. After necessary examinations and available treatments, the symptoms did not subside and it died one week later. Further pathological examinations were performed.

**Diagnosis:**

Lymphoma, mixed type, koala

**Gross findings:**

Significant hydrothorax and ascites were noted. Multiple lymph nodes, including bronchial and mesentery, were enlarged and present with white, yellow color in the cut surface. White firm tissue covered lower abdominal vessels, mesentery and organs of the abdominal cavity.

**Histopathological findings:**

Sheets of round, lymphoid neoplastic cells are found in multi-organs including lymph nodes, liver, spleen, adrenal gland, pancreas and diaphragm. The nuclear size of tumor cells is small to medium (one to two RBC), and is often present with prominent one or few nucleoli. The cytoplasm is scant to moderate and cell boundary is distinct. Mitosis is rare.

**Laboratory results:**

Immunohistochemistry results revealed positive in vimentin and negative in desmin, CK and S-100. The panel of cell marker staining by anti-human antibody were all negative.

**Discussion:**

The first detailed survey of lymphoid neoplasia of the koala was presented in 1961. From the literature review, lymphoid neoplasia in the koala is not uncommon, and probably the most common form of neoplasms occur in the koala. The lymphoid neoplasia may be responsible for the major mortality in captive koalas, which can be classified by its solid organ involvement into several types as follow: nodal, cervicomedial, abdominal, atypical and mixed. The highest prevalent mixed type appear in 70% of all lymphoid

neoplasia cases. Many cases of the lymphoid neoplasia occur in middle aged koalas without sex predilection, and the predominance of T cell lymphoid neoplasms is demonstrated, in contrast to the case of the dogs, cattle and humans from western countries, in all of which the B cell type is dominant. Although lymphoma or lymphoid leukemia is common seen in many cases and often associated with mixed tumors, there is no information available on the immunophenotype of lymphoid neoplasia or lymphoid leukemia in koala and other Australian marsupials. Morphologically, tumors are most commonly composed of cells with round, medium sized nucleoli, and scant cytoplasm. In contrast to the dog, which large lymphoblastic cells is mostly; and in feline, immunoblastic type cells are predominant. Large cell types also predominate in bovine and porcine cases. Leukemia in lymphoid neoplasia of the koala is common, and often associated with hepatic and splenic infiltration, but it is often difficult to determine whether the leukemia is primary or secondary. Follicular tumors, which are common in humans but rare in the dog and cat, are not seen in koalas. Although endogenous retrovirus has been identified in this species, presence of the virus in both health and diseased (tumor) individuals makes an inconclusive role of the virus in this lymphoid neoplasia.

**Diagnostic criteria:**

1. Sheets of lymphoid tumor cells in the multiple abdominal and thoracic organs.
2. Anti-human CD3 and CD5 for T cells and CD79b for B cells are reliable.

**Reference:**

1. Connolly JH, Canfield PJ, Hemsley S, Spencer AJ. 1998. Lymphoid neoplasia in the koala. Aust Vet J. Vol. 76(12), pp819-825
2. Wilkinson R, Barton M, Kotlarski I. 1995. Identification of koala T lymphocytes using an anti-human CD3 antibody. Dev Comp Immunol. Vol. 19(6), pp537-545
3. Canfield PJ, Hemsley S. 1996. Thymic lymphosarcoma of T cell lineage in a koala. Aust Vet J. Vol. 74(2), pp151-154.
4. Canfield PJ, Brown AS, Kelly WR, Sutton RH. 1987. Spontaneous lymphoid neoplasia in the koala (*Phascolarctos cinereus*). J Comp Pathol. Vol. 97(2), pp171-178.

**Contributor:** Bo-Yuan Tseng (曾柏元) MD; Yung-Hsiang Hsu (許永祥) MD

**Clinical History:** A 15-year-old girl had bothered from recurrent skin lesions since Jan. 1997. The condition of skin lesions got in progression gradually. Several times of skin biopsy had been done. MRI of bilateral legs showed soft tissue edematous change, No osteomyelitis nor abscess was noted. She had received 4 courses of retinoic acid therapy and oral steroids for controlling her condition since Sep. 2003. However, fever, elevation of liver function, hepatomegaly and pancytopenia developed. Finally, she expired due to hepatic failure on Dec. 16, 2003. Autopsy was performed.

**Diagnosis:** Cytophagic histiocytic panniculitis with terminal hemophagocytic syndrome

**Gross Finding:** The skin lesions showed erythematous induration with central eschar or purpurish patches on bilateral lower limbs, cheeks, forearms and back. About 1000 C.C bloody ascites were obtained. The liver showed hepatomegaly and weighed 1750 gm with marked fatty change.

**Histopathological Findings:** Previous skin biopsy showed mixed lobular and segmental dense infiltration with tissue necrosis and karyorrhexis. Autopsy specimens showed mild infiltration of inflammatory lymphohistiocytes in the subcutaneous tissue of left thigh, left forearm and right face. Besides, cytophagocytosis and erythrophagocytosis by a few large benign-looking histiocytes were occasionally seen. Immunohistochemical studies showed UCHL-1 (CD45RO)+ and L26 (CD20)-. T-cell receptor gene rearrangement was evaluated by a polymerase chain reaction assay and failed to detect positive finding. It also showed histiocytic hyperplasia and florid hemophagocytic syndrome with numerous histiocytes containing multiple phagocytosed erythrocytes and leukocytes in the bone marrow, bilateral hilar and mesenteric lymph nodes, spleen, liver and bilateral lungs.

**Discussion:**

Cytophagic histiocytic panniculitis was first described in 1980 by Winkelmann and Bowie as a rare subtype of panniculitis that usually follows a fatal course, with a terminal hemophagocytic syndrome. The hemophagocytic syndrome is characterized by the proliferation of histiocytes and phagocytosis of blood elements, hepatosplenomegaly, and coagulopathy. Subcutaneous panniculitic T-cell lymphoma can be associated with hemophagocytosis. A relationship between cytophagic histiocytic panniculitis and subcutaneous panniculitic T-cell lymphoma has been raised. Whereas Craig et al believe that cytophagic histiocytic panniculitis and subcutaneous T-cell lymphoma are separate benign and malignant entities, Marzano et al suggest they represent a clinical spectrum with a natural disease progression from a benign panniculitis to malignant lymphoma.

Comparison of the clinical course of cytophagic histiocytic panniculitis and subcutaneous panniculitic T-cell lymphoma reveals initial similarities with subcutaneous panniculitic lesions, either alone or with accompanying hemophagocytosis. However, closer investigation revealed the presence of a malignant lymphocyte infiltration in subcutaneous panniculitic T-cell lymphoma and the absence in cytophagic histiocytic panniculitis. Emphasis has been placed on gene rearrangement studies to establish malignancy and to differentiate between cytophagic histiocytic panniculitis and subcutaneous panniculitic T-cell lymphoma.

**Diagnosis criteria:**

1. Subcutaneous panniculitis with mature T lymphocytes and cytologically benign histiocytes
2. Associated hemophagocytosis in reticuloendothelial system
3. T-cell receptor gene rearrangement studies negative finding

**References:**

1. Marzano AV, et al. Cytophagic histiocytic panniculitis and subcutaneous panniculitis-like T-cell lymphoma. Arch Dermatol 136: 889, 2000.
2. Craig AJ, et al. Cytophagic histiocytic panniculitis: A syndrome associated with benign and malignant panniculitis: Case comparison and review of the literature. J Am Acad Dermatol 39: 721, 1998.



Contributors: Yang-Chang Tu (涂央昌) DVM, Yi-Xing Zhuo (卓宜興), DVM, Chen-Hsuan Liu (劉振軒), DVM, MS, PhD Graduate Institute of Veterinary Medicine, National Taiwan University

Clinical History:

A 12-year-old female Persian cat showed rough hair, loss of appetite, and moderate emaciation, and died one month after the onset of the clinical signs.

Diagnosis:

Mucosal associated lymphoid tissue (MALT) lymphoma, small intestine

Gross findings:

Necropsy examinations revealed multiple ulcerative lesions of varying sizes on the mucosa of the posterior small intestine.

Histopathological findings:

Marked neoplastic lymphoid cells infiltrating the lamina propria with a few residual crypts and extending into the submucosa were observed. The small to medium-sized lymphocytic cells had a scant rim of eosinophilic cytoplasm and oval to irregularly shaped nuclei containing coarse clumped hyperchromatic chromatin. Pyknotic and karyorrhectic cellular debris was scattered among the neoplastic cells.

Discussion:

MALT lymphoma in cats is more common than adenocarcinoma or leiomyomatous tumors. The lymphomas are usually seen in cats over 5 years of age, whereas multicentric cases have a wider age range, being seen in cats from 1 to 18 years old. There is no consistently reported breed or sex predisposition. The sites of MALT lymphoma, in decreasing order of frequency, are the jejunum, ileoceocolic junction, duodenum, colon, and stomach.

The mucosal associated lymphoid tissue (MALT) of the gastrointestinal tract in humans can be the primary site of lymphoma, and such tumors rarely coexist with carcinomas or leiomyomas. Most cases occur in adults with a median age of 61 and slight female preponderance (male: female ratio 1:12). Their growth seems to be dependent upon continuous stimulation of the immune system by an infectious agent, such as *H. pylori*, or some other entity, termed an antigen, that the body recognizes as foreign. This antigen-driven growth permits these tumors to be treated by eliminating the stimulus that generated the original, normal immune response. In the stomach they are associated, in greater than 90% of all cases, with the bacteria called *Helicobacter pylori*. The histological classification may vary from low to high grade. Grading has been classified into low, intermediate and high grade. Other terminology of primary and secondary

high-grade lymphomas has been adopted. In the histology of secondary high-grade lymphomas, there is evidence of low-grade component.

MALT lymphoma is an extranodal lymphoma comprising morphologically heterogeneous small B-cells including marginal zone cells, small lymphocytes, and scattered immunoblast and centroblast-like cells. The infiltrate is in the marginal zone of reactive B-cells follicles and extends into the interfollicular region. In epithelial tissue, the neoplastic cells typically infiltrate the epithelium, forming lymphoepithelial lesions. MALT lymphoma may be diffuse or localized; when localized, the lesion can bulge intraluminally or be intramural. The tumors may be restricted to one site in intestinal tract, or multiple tumors may occur at various levels. The tumors can be plaque-like, nodular, or fusiform in shape. Fusiform intramural or transmural lesions frequently balloon outward because the invaded muscle atrophies; leaving rows of lymphocytes supported only by parallel bands of delicate reticulum fibers. Diffuse lesions present as thickened rigid mucosal folds in the stomach, and in intestinal cases the mucosal surface has a granular, or cobblestone appearance. T cells tumors exhibit epitheliotropism, exemplified by early lesions in which tumor infiltration is intraepithelial and in the periglandular lamina propria, whereas B cell tumors start in germinal centers in the submucosa.

#### Reference:

1. Elaine SJ, Nancy LH, Harald S, James WV. Pathology and genetics of tumors of haematopoietic and lymphoid tissues. *In: WHO*.
2. Hendrick MJ, Mahaffey EA, Moore FM, Vos JH, Walder EJ: Histological classification of mesenchymal tumors of skin and soft tissues of domestic animals. *In: WHO International Classification of Tumors of Domestic Animals*, ed. Schulman FYS, 2nd Series, volume 2, pp. 1–62. Armed Forces Institute of Pathology, Washington, DC, 1998.
3. Malek SN, Hatfield AJ, Flinn IW. MALT Lymphomas. *Curr Treat Options Oncol* 4:269-279, 2003.
4. Meuten DJ. Tumors of endocrine glands. *In: Tumors in domestic animals*. 4<sup>th</sup> ed. Iowa State Press, Berkeley, pp 607-696, 2002.
5. Toishi M, Miyazawa M, Takahashi K, Hyogotani A, Haba Y, Kato K, Muramatsu A, Nishiyama M, Ozawa K, Nanbu A, Miyata K. Mucosa-associated lymphoid tissue lymphoma; report of two cases. *Kyobu Geka* 57: 75-79, 2004.