

Comparative Pathology Case 28

Contributor : JP Juch (祝志平), MD, MS

Chairman, Department of Pathology, Provincial Hsinchu Hospital.

Clinical History: A 37-year-old male, suffering from severe productive cough with chest pain, fever, and cold sweating for 15 days, was admitted. Chest x-ray revealed cavitory lesion (abscess) over left upper lobe. Tuberculosis was impressed and anti-TB drugs were prescribed but in vain. Sputum for acid fast stain, Gram's stain, and cultures were performed, but no positive result was noted. Under echo-guided lung aspiration, nocardiosis was diagnosed. Sensitive antibiotics were given. The fever subsided and a follow-up chest x-ray showed resolution of pneumonia.

Diagnosis: Nocardiosis of lung.

Histopathological Findings: The tissue from echo-guided aspiration revealed a granulomatous lesion of lung with polynucleated cell infiltration. Neither Langhans' giant cell nor caseation was found.

Histochemistry Results:

- a. Ziehl-Neelsen acid fast stain showed few filamentous branching *Nocardia* (Fite acid fast stain showed more *Nocardia filaments*).
- b. PAS stain showed pinkish *Nocardia* filaments.

Microbiological Examination:

Culture from sputum and lung aspiration showed *Nocardia asteroides*.

Discussion: The nocardiae belong to aerobic actinomycetes, containing 9 species. In man, *Nocardia asteroides* accounts for 86% of infection caused by this organism. While *N. brasiliensis* causes 2% (3 to 9%) and *N. farcinica* is being recognized with increasing frequency (AIDS). They are important parts of normal soil microflora worldwide and cause a variety of diseases in both normal and immunocompromised human and animals.

Nocardiae are facultative intracellular pathogens that can persist within the host.

They show a fungal nature as mycelial development with branching and a bacterial nature as lack of chitin within the cell wall.

Slow develop on Sabouraud dextrose agar and Gram positive, partial acid-fastness may confirm the diagnosis of *Nocardiae*.

Identified *Nocardia* in sputum culture in the absence of disease was noted with an incidence of about 0.02 to 0.05%. Inhalation of airborne fragments or spores is the usual way of lung infection. Man to man transmission has not been reported.

Nocardiosis is both a primary and opportunistic infection process with compromised hosts, and the organ involvement is extensive including: lung (75%), skin and subcutaneous tissue (15%), CNS (5%) generalized dissemination, kidney, liver, heart, spleen, intestine, etc.

The mortality is high (over-all: 50%, brain abscess: 78%, lung: <10%) and the causes of death include sepsis, brain abscess, and overwhelming pneumonia.

Diagnostic Criteria: Diagnosis depends on a high degree of suspicion so as to alert the microbiology and pathology laboratories to employ special methods to identify the organisms.

- a. Smear of sputum or purulent materials (Gram-positive, partially acid-fast, branching rod).
- b. Culture in Sabouraud dextrose agar in room air and at 37°C (observe culture for a few weeks to allow for the slow growth of *Nocardia* species).
- c. Biopsy from bronchoscopy, lung, aspiration or open lung biopsy.
- d. Immunoblot: monoclonal antibody reacted with 54 kDa band.

References :

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Comparative Pathology Case 29

Contributors: MT Tsai (蔡睦宗), JP Hsu (徐榮彬), HT Huang (黃旭田), HH Hung (洪信雄)

Livestock Diseases Diagnostic Laboratories of Pingtung Prefecture

Clinical History: A 0.4 ha freshwater pond reared 30000-40000 largemouth bass, *Micropterus salmonides* for eight months. The accumulative mortality within this period was 90%. Clinically, infected fish, 20-27 cm body length, showed signs of erratic swimming, circling or upside-down, before they died. Affected bass also exhibited marked skin ulcers, sloughed scales, fin and tail rot, exophthalmia, anorexia, emaciation, surface hemorrhages, and distension of the abdomen.

Diagnosis: Nocardiosis of largemouth bass, *Micropterus salmonides* (Lacepede)

Gross Findings: Skin ulcer and distension of the abdomen with numerous creamy-white nodules, ranging from 0.2-2 cm, were present in the gill, serosal surface, mesentery, and in several internal organs, especially the kidney, spleen, muscle, heart, and skin.

Histopathological Findings: The nodular structures described above were typical granulomatous lesions. Lesions found in various organs, including muscle, gill, mesentery, kidney, heart, spleen, liver, and digestive tracts, were similar, although some were multifocal and others more diffuse in distribution. The typical granulomatous foci varied in size and consisted of necrotic tissue debris with some bacterial clumps in the centre, surrounded by epithelioid cells and fibrous connective tissue forming marked fibrous capsules, especially in the parenchymatous organs.

Histochemistry Results: Some long-beaded, filamentous, branching *Nocardia* were usually identified in the central necrotic zone of the granuloma when stained by Ziehl-Neelsen's acid fast stain.

Microbiological Examinations: *Nocardia asteroides* is an obligate aerobe which can be isolated on general bacteriological media, including Ogawa medium, blood agar, BHI agar, and MH agar. Ridged and folded irregular yellow-orange colonies develop within 21 days of incubation at 18⁰C. Growth and biochemical properties of

Nocardia asteroides showed weakly acid fast staining reaction, gram-positive rods, cocci and filaments, inability to hydrolyze casein, xanthine, or tyrosine, and a positive urease test.

Discussion: *Nocardia* spp. are aerobic, filamentous, gram-positive bacteria that are found in nature as soil saprophytes. *Nocardia asteroides* is one of the species most frequently associated with disease and has been recorded from human, dog, cat, cattle, goat, marine mammals, and fish. Nocardiosis (*N. asteroides*, *N. kansasii*) of fish is a systemic disease with lesions localized in the skin and several internal organs, and with the nodular structure typical of granulomata. Several species of fish such as rainbow trout, yellowtail, Formosa snakehead, grouper, and largemouth bass have also been reported to be affected. A differential diagnosis for the granulomatous lesion in fish should include other bacterial diseases caused by *Corynebacterium*, *Mycobacterium*, and *Staphylococcus*; protozoans; fungi; and chemical as well as biological substances. *Nocardia asteroides* is generally considered to be an opportunistic pathogen that infects animals and humans as a result of inhalation or traumatic implantation of infectious soil. In human, the diseases it causes are seen frequently in association with immunosuppression or underlying chronic diseases such as Hodgkin's disease, leukemia, carcinoma, and chronic granulomatous disease of child. There are two common modes of infection by *Nocardia*. Pulmonary nocardiosis (most commonly *N. asteroides*, also *N. brasiliensis*, *N. caviae*) arises from inhalation of the organism, whereas chronic subcutaneous abscesses (mycetomas) arise from contamination of skin wounds, usually on the feet and hands of laborers. Pulmonary nocardiosis induces multiple abscesses and often spreads from pulmonary lesions by way of the blood and establishes metastatic abscesses, usually in subcutaneous tissues and in the central nervous system. Lesions in the brain and the meninges are usually fatal.

Diagnostic Criteria:

1. Systemic, milliary, nodular lesions in skin, gill, muscle, mesentery, and internal organs
2. Typical necrotizing granulomatous inflammation
3. Gram-positive, acid-fast, filamentous, beaded, branching organisms were identified in the central necrotic zone of the granuloma stained by Ziehl-Neelsen's and Giemsa methods
4. Ridged and folded irregular yellow-orange colonies developed in culture media

Treatments: In largemouth bass, medication with TMP-SMX (1:5) at 40 ppm in feed for 1-3 weeks has been successful, and simultaneous application of benzalkonium chloride (2 ppm in water) has improved the outcome of treatment.

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Comparative Pathology Case 30

Contributors: Chen-Hsuan Liu (劉振軒)¹, DVM, MS, PhD; Peri-Jeng Cheng (陳培中)², DVM; Chih-Hsien Lin (林志嫻)³, DVM; Shih-Ping Chen (陳世平)¹, DVM, MS; Chih-Cheng Chang (張志成)¹, DVM, MS

1. Department of Pathobiology, Pig Research Institute, Taiwan. (台灣養豬科學研究所病理生物系)
2. Loving Kindness Animal Hospital, Tainan. (台南慈愛動物醫院)
3. Livestock Disease Control Center, Tainan City. (台南市家畜疾病防治所)

Clinical History: This 3-year-old mixed female dog was presented for sudden onset of difficulty in standing on 3/19/1995, After which, she never stood up, showed poor spirit and all other conditions worsened. On 4/4/1995, the owner gave up medical treatment and requested euthanasia. Similar clinical signs also occurred in another dog from the same house. Neither dog was immunized with canine distemper vaccine.

Diagnosis: Demyelinating canine distemper encephalitis

Gross Findings: On postmortem examination, slight pulmonary edema was noted. All other organs were grossly normal.

Histopathological Findings: The characteristic lesion of the cerebral section at the level of temporal lobe and hippocampus consisted of diffuse spongy appearance and focal non-suppurative inflammatory response. The spongiform change restricted to the white matter and periventricular region contained many variable-sized vacuoles suggestive of demyelination accompanied by proliferation of astrocytes. Nonsuppurative inflammatory lesions in the cortex included neuronophagia, microglial nodules, focal gliosis, and proliferation of capillaries associated with intranuclear and cytoplasmic eosinophilic inclusion bodies in astrocytes and neurons. Syncytia containing many nuclei were occasionally encountered in some of the sections.

Histochemistry Results: Variable degrees of staining of Luxol fast blue-Cresyl echt violet was observed in the demyelinated area, in which myelin loss was observed.

Immunocytochemistry Results: Myelin basic protein (MBP) using ABC method demonstrated myelin debris in the demyelinating tracts. Neurofilament-200 antigen was positive in the axons, in which the periaxonal area showed variable-sized vacuoles.

Electron Microscopic Findings: Paramyxoviral nucleocapsids were rarely found in the nucleus of the affected cells.

Discussion: Canine distemper (CD) is a naturally-occurring, Morbilliviral (family Paramyxoviridae)-induced disease of the systemic infections or CNS infection of dogs and their relatives and exotic species. The age, immune status of the host, and viral strain are the principal factors that may determine the distribution and pathological features and different outcomes of the disease. For example, R252 and A75-17 viral strains have a tendency to cause CNS disease in which the lesions in white matter predominate, and neuronal injury is milder. Infection in young unvaccinated dogs usually results in high morbidity and mortality, occurring initially with respiratory and gastrointestinal signs which precede the neurologic signs by one or two weeks, while mature dogs principally develop CNS infection. CD virus is closely related to bovine rinderpest and measles virus in inducing pathologic and immunologic features, thus CD virus infection is an established animal model system for human measles virus infection. Essentially, both have immunosuppression and development of demyelinating or persistent infection. The lesions in white matter with CD viral infection have a predilection to distribution in the cerebellar peduncles, rostral medullary velum, optic tract, hippocampal fornix, and spinal cord. The findings of lesion distribution and viral presence in the ependymal and choroid plexus epithelium may explain viral dissemination in CSF and lead to affect the anatomic location of white matter described previously. A study of CD virus infection indicated that demyelination occurred about 21 to 24 days after infection, whereas the pathological mechanisms of this selective destruction of myelin sheaths was not clearly identified. Based on the previous studies, it is proposed that demyelination may be caused by the following mechanisms; (1) deleterious effects of CD virus on astrocytes associated with a variety of cytokines release, (2) lytic infection of the oligodendrocytes, (3) an immune attack oligodendrocytes and myelin sheath, or (4) by a "bystander effect" of inflammatory mediators. Multinucleated syncytial cells in measles and CD virus infection may be induced by the viral fusion protein mediated by host tissue proteases. Previous studies proposed that syncytia may be sites of defective viral replication, thus providing the mechanism of viral persistence in the CNS. Additionally, Toxoplasmosis (cases 16 & 17 in 2nd Comparative Pathology Conference) often

occurs with CD in dogs. Lesions of both diseases should be carefully sought in pathological examination.

Diagnostic Criteria:

1. Postmortem diagnosis- clinical history, demonstration of characteristic lesions and cytoplasmic and intranuclear viral inclusion bodies.
2. Virus isolation- difficult
3. Fluorescence antibody technique

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Comparative Pathology Case 31

Contributors: CR Jeng¹(鄭謙仁), DVM, PhD; LL Chueh¹ (關玲玲), DVM, PhD; SP

Chen² (陳世平), DVM, MS; CH Chi³ (季昭華)DVM, MS

1. Department of Veterinary Medicine, National Taiwan University
2. Department of Pathobiology, Pig Research Institute Taiwan.
3. Animal Medical Center, Taipei Zoo

Clinical History: Three adult Malayan sun bears (*Helarctos malayanus*) in a private exhibition were found dead in a 2-week period. No significant clinical signs were noticed by keeper. The slide submitted for this discussion was from the third bear, 6 to 7 year old female that was the only animal being necropsied by NTUVH.

Diagnosis: Severe, multifocal, hemorrhage, cerebellum and cerebrum with basophilic intranuclear inclusions in capillary endothelial cells, compatible with adenovirus infection.

Gross Findings: Disseminated petechial to blotchy hemorrhages were present in the wall of thoracic cavity, trachea, esophagus, epicardium, and serosa of jejunum and urinary bladder. Dark red content was segmentally present in the jejunum. Hemorrhage in the brain was more appreciated in the formalin fixed tissue with a predilection for mid brain, brain stem and cerebellum.

Histopathological Findings: The slide submitted contains sections of cerebrum and cerebellum. Foci of hemorrhage are randomly present in the parenchyma of cerebellum and occasionally in the cerebrum. Basophilic intranuclear inclusion bodies can be found in the endothelium of capillaries and small venules affected.

Electron Microscopic Findings: Transmissible electron microscope examination of the liver revealed viral particles, with an icosahedral symmetry and an average of 80 nm in diameter typical of an adenovirus.

Virus Isolation Findings: Suspensions of liver, kidney, and spleen were inoculated into baby hamster kidney (BHK) cells. Cytopathic effect was noticed from all inocula 36 to 48 hours post infection. Infected monolayers were stained with a rabbit

anti-human adenovirus polyclonal antibody conjugated with fluorescein isothiocyanate, and the result showed intranuclear fluorescence.

Discussion: After reviewing slides from the formalin fixed tissues of the other two bears referred by Taipei LDCC, similar lesions as those seen in this case were revealed. The changes included multifocal hepatic necrosis and formation of intranuclear inclusion as well as hemorrhage and basophilic intranuclear inclusions in the capillary endothelium in the trachea, esophagus, epicardium, serosa of jejunum, and brain. The pathological data combined with the virology and serology findings suggested an epizootic of adenovirus infection in Malayan sun bears. Adenovirus infection with viral isolation was first reported in two captive black bear cubs in 1983. In the same year, an epizootic of adenovirus infection in American black bears at a wildlife park in western South Dakota, USA, was also reported. Of 148 black bears at the park, 28 were known to be affected; 24 died and 4 recovered. Canine adenovirus type I (CAV-1) was isolated from some of those bears. CAV-1 in dogs causes a generalized infection characterized by hepatitis. For this reason, CAV-1 originally was known as infectious canine hepatitis (ICH) virus. The virus also infects foxes, coyotes, wolves, and skunks. The histopathological findings in our case are similar to those described in those reported bears and subsequent experimentally-infected dogs. The widespread endothelial damage is a potent initiator of clotting cascade which may exhaust the clotting factors in a short period of time and cause a tendency of disseminated hemorrhages in tissues and organs.

The future study plan of this case includes:

- (1) to compare the virus isolated from the bear with dog, duck (pigeon), and human adenoviruses by viral restriction endonuclease analysis,
- 2) immunohistochemistry examination with anti-CAV-1 antibody in the infected culture cells and formalin fixed tissue, and
- (3) experimental infection of CAV-1 seronegative dogs with the virus isolated from bear.

Diagnostic Criteria:

- multifocal hepatic necrosis with basophilic intranuclear inclusion bodies
- disseminated hemorrhage in several organs with basophilic intranuclear inclusions in capillary endothelium
- characteristic features of adenovirus in tissue section examined by TEM.

References:

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Comparative Pathology Case 32

Contributor : JF Chia (賈永芳), MD

Department of Pathology, Provincial Fengyuan Hospital.

Clinical History: A 51-year-old female has suffered from lower abdominal pain for several months. Plastic IUD has been worn for over 20 years. The abdominal sonar findings were suspicious of uterine myoma and adnexal mass. Surgical intervention with total hysterectomy and bilateral salpingo-oophorectomy was performed. The present slide is from left tuboovary.

Diagnosis: Actinomycosis of left tuboovary.

Gross Findings: Enlarged and adhered left tuboovary, 6x5x3.5cm, with coarse external surface and, on opening, multiple confluent abscesses.

Histopathologic Findings: The sections of tuboovary showed extensive inflammation, fibrosis, multiple abscesses, and occasionally, granules that were blue-stained with H&E showed peripheral eosinophilic clubbing surrounded by purulent exudate.

Histochemistry Results: Special stains revealed radiating filaments of branching and fragmented gram-positive, nonacid-fast bacilli within granules.

Discussion: Actinomycosis is a world-wide, chronic, suppurative, abscess-forming disease of man and lower animals. The most characteristic pathologic finding is basophilic or amphophilic granules comprising organized mass of actinomycete filaments. Splendore-Hoeppli reaction is usually present. The principal agents are *Actinomyces israelii*, *A. naeslundii*, *Arachnia propionica*, and, in cattle, *Actinomyces bovis*. The identification of the organisms is based upon their morphological, physiological, and biochemical studies. They should be differentiated from eumycotic mycetoma, nocardiosis, and botryomycosis. Gram, GMS, and Cross-Coates acid-fast stains are helpful. A fluorescent antibody stain may facilitate detection of the organisms. Human infections most commonly involve the cervicofacial area. Genital actinomycosis has been described mainly in women using intrauterine devices. The adnexal involvement usually is unilateral, with destructive, often multiple, abscesses involving the ovary and fallopian tube. Actinomycosis in lower animals is similar to the disease in humans, and the cervicofacial type in cattle,

"lumpy jaw," is most common. Penicillin is the drug of choice, and prolonged treatment (6 to 18 months) is generally required.

Diagnostic Criteria:

1. Suppurative, granulomatous inflammation, fibrosis, and multiple abscesses.
2. Basophilic granules containing filaments of branching, fragmented, gram-positive, nonacid-fast bacilli, showing peripheral eosinophilic clubs, and surrounded by purulent exudate.

References :

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Comparative Pathology Case 33

Contributor: Hoi Weng Chu (朱海榮), MD

Chief, Department of Pathology Wei Gong Memorial Hospital.

Clinical History: A 38-year-old male patient presented with a painful tumor mass, about 7-8 cm, of the left wrist for 4 months. Physical and laboratory examinations revealed carpal tunnel syndrome. There is no history of trauma or local injection of the wrist. Total excision was performed and patient was discharged shortly.

Physical examination revealed a firm and elastic mass with mild tenderness of the left wrist. The overlying skin is intact and this is , beside the lungs, the only site of joint involvement. Entrapment syndrome of the median nerve and atrophy of opponens pollicis muscle and positive tinea sign.

Chest film revealed fibroproductive lesion in bilateral upper lung fields and right CP angle, suggesting pulmonary tuberculosis. VDRL was non-reactive.

X-ray of the left wrist and hand showed features of arthritis with osteopenia around radio-carpal, MCP, PIP and DIP joints associated with soft tissue but without bony fracture.

Electromyography revealed findings of entrapment neuropathy of left median nerve with polyphasic potential of left opponens pollicis muscle.

At operation, a deep soft tissue tumorous growth with adhesion to tendons and median nerve and ulna nerves are noted. Total excision with neurolysis was performed under general anesthesia.

Gross findings: Fragments of tan soft synovial-like tissue were received in formalin.

Microscopic findings: There is extensive caseating granulomata involved synovial and adjacent soft tissue. Fibrinoid exudate is noted covering the synovial membrane. In addition to the granulomata. there is lymphoid and plasmacytic infiltration and fibrosis.

Discussion: Skeletal tuberculosis is rare in developed countries, but the incidence is increasing among patients with HIV infection, and those on chronic immunosuppressive therapy. Furthermore, drug-resistant strains of tuberculosis are now emerging. The most common site of skeletal involvement is the spine. Peripheral joint involvement can affect the synovium, bone and cartilage. Presentation as a tumor mass is unusual.

Diagnosis depends on recovery of the organisms from the joint. Demonstration of pulmonary lesions or a positive purified protein derivative test is helpful but not pathognomonic. Synovial biopsy is essential in the diagnosis, with demonstration of acid-fast bacilli in tissue.

Therapy includes antibiotics and surgical debridement. Triple-drug therapy is usually started using rifampin, isoniazid, and ethambutol. In resistant infections, a fourth drug such as streptomycin or PAS is added. The duration of treatment is for 6-12 months.

Reference:

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Comparative Pathology Case 34

Contributor: SD Cheng (陳三多), DVM, PhD

National Chung Hsing University Veterinary Teaching Hospital

Clinical History: A 13-year-old, body weight 7.6 Kg, male, mixed dog was brought to the veterinary hospital because of an enlarged right lateral testis.

Diagnosis: According to the histopathological report, a final diagnosis of interstitial cell tumor (Leydig cell tumor) was made.

Gross Findings: The whole right swelling testicular tumor was covered with a capsule. Soft, tense, and reddish surface was noted. The actual size of the tumor was 11.5x 6.5x 3 cm. Abundant vasculature was present after cutting the tumor.

Histopathological Findings: The slides submitted contain only sections of testes obtained from orchiectomy. In the parenchyma of the right testicular tumor, there were dense and eosinophilic tumor cells. Round nuclei and abundant cytoplasm were noted in the round and polygonal tumor cells. A lot of mitotic figure of the tumor cells and some giant tumor cells with apparent nucleoli were also observed. Some tumor cells also contained many granules. The perivascular cells got more activity, but the cells of other sites showed liquefactive necrosis. The left testis still showed normal spermatogenesis.

Discussion: Testicular tumors are the second most common tumor of the male dog at a prevalence of 5-15%. Sertoli cell tumors (SCT), Seminomas (SEM), and interstitial cell tumors (ICT), the most common histologic types of testicular tumor, occur with approximately equal frequency in the dog. Cryptorchid males have a risk 13.6 time greater of developing SCT or SEM than normal males. Virtually all ICT occur in descended testicles. ICT are often incidental findings in older, intact male dogs, and they occur more often than found by clinical detection or necropsy. The average age of occurrence is 11.5 years. There is no apparent breed predilection for ICT, which arises from the Leydig cells of the testicle. These tumors remain within the testicle and are usually surrounded by a dense, fibrous capsule. ICT are pink or tan in color and tend to bulge out from the cut surface. Metastasis does not occur. They have been associated with increased testosterone levels, thought to lead to an increased incidence of perineal hernias and perineal adenomas. Preoperative tissue biopsy of fine-needle aspiration cytology is rarely performed since the results of

these tests will not alter the treatment, which is castration. Large descended testes with fixation to the scrotal skin are best managed with castration and scrotal ablation. The prognosis for ICT is uniformly excellent. The ICT cells with abundant cytoplasm are round or polygonal. The nuclei of ICT cells are small, round, and ovoid. The differential diagnosis for swelling testis in clinic should include scrotocele, testicular tumor, epididymitis, orchitis, spermatocele, varicocele, and scrotal edema.

References:

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Comparative Pathology Case 35

Contributor: YS Ho (何逸僊), MD, MS

Associate Professor of Pathology, Chang Gung Medical College, Taiwan

Clinical History: A 16-year-old female was admitted to EGMH because of epigastralgia for 20 hours. The abdomen pain was predominant in epigastric region in the beginning, and it then gradually shifted into the lower abdominal area. There was no fever or dysuria. Therefore, she received an appendectomy under the impression of acute appendicitis. The patient is well 6 months after the surgery.

Diagnosis: Carcinoid tumor, classic type

Gross Findings: The appendix is 9 cm in length and 0.5 cm in maximal diameter. A poorly circumscribed tumor with 0.3 x 0.3 x 0.2 cm in size and tan-yellow color was found over the cuffing surface of the appendiceal tip.

Histopathological Findings: Histologically, the tumor was composed of clusters of small monotonous cells with occasional acinar formation. It had invaded through the muscular layers. No mitosis was seen. There was pus in the lumen.

Histochemistry Results:

Argyrophil stain: Positive

Mucin stain: Negative

Immunocytochemical Results:

Cytokeratin AE1/AE3: Negative

CEA: Negative

NSE: Positive

Chromgranin: Positive

S-100: Positive

Electron Microscopic Findings:

Not done

Discussion: The carcinoid tumor accounts for 85% of all appendiceal neoplasms. The appendiceal carcinoid tumors are almost always clinically incidental findings. Most patients are operated on for acute appendicitis. The tumors are classically

yellow and often have ill-defined margins when grossly visible. However, a large percentage of these tumors are not grossly evident and are found only on microscopic examination of the appendix. Typically, a 1 to 3 mm focus of bland-appearing neuroendocrine cells is noted near the tip of the appendix. The cytoplasm may have an obvious granularity; argyrophil stains or electron microscopy reveals the presence of neurosecretory granules. Prognosis of the carcinoid is best correlated with serosal and/or lymphatic involvement. Those tumors exceeding 2 cm in diameter behave in a malignant fashion. One histologic variant of carcinoid tumor of the appendix is mucinous or goblet cell carcinoids.

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Comparative Pathology Case 36

Contributor: S K Liu (劉錫光), DVM, PhD

Consultant, Pig Research Institute Taiwan

Clinical History: An eleven-year-old castrated male Siamese cat had weight loss, anorexia, alopecia, and focal cutaneous erythema. The erythema resolved posttherapy.

Diagnosis: Hepatic neuroendocrine carcinoma (hepatic carcinoid) in a Siamese cat.

Gross Findings: The cat was emaciated. Multiple, grayish-white, circular lesions with dark centers, 0.5 to 2.5 cm in diameter were seen in the liver. Peritoneal carcinomatosis was indicated by numerous, small, whitish firm nodules, 2 to 5 mm in diameter, on the peritoneal, omental, mesentery and serosal surfaces of the intestines. Several firm, whitish nodules 5 to 18 mm in diameter, were seen in the lung lobes.

Histopathologic Findings: The cells were cuboid, oval, or spindle hyperchromatic, with vesiculated nuclei and abundant, eosinophilic, granular cytoplasm. They were arranged in various-sized groups of acinar and rosettelike structures, some with lumens, separated by thin, fibrovascular stroma. The neoplastic cells close to the stroma were arranged perpendicularly to it. In some areas, the cells were arranged in solid sheets. Mitotic figures and lymphatic invasions were frequently observed. The neoplasm had metastasis to the rest of the hepatic tissue.

Immunocytochemistry Results: The neoplastic cells did not react to neuron-specific enolase, cytokeratin, or S-100 stains.

Electron Microscopic Findings: Neurosecretory granules were seen in the cytoplasm of the neoplastic cells particularly in the cells around the bile canaliculi.

Discussion: Primary hepatic neuroendocrine carcinomas are rare, in human patients, cats, and dogs. These tumors can be distinguished from other hepatic neoplasms, i.e., hepatocellular carcinoma and bile duct adenocarcinoma, by their distinct morphologic features.

Diagnostic Criteria: The cuboid or low columnar neoplastic epithelial cells arranged in cords or rosettelike structures closely associated with fibrovascular stroma.

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Comparative Pathology Case 37

Contributors: Kevin YH Lin (林永和) DDS, MS, SJ Su (蘇順景), MD, PhD, Steve GN Chang (張俊寧), MD, MS Hsieh (謝銘勳), MD
Taipei Medical College Department of Pathology

Clinical History: This is a case of a 9-year-old Chinese boy who was admitted to our hospital on July 20, 1995 with the chief complaints of pain and swelling of the left thigh for about one week and mild fever, rhinorrhea, and cough for about three days prior to the admission.

About two weeks before admission, the patient was involved in a minor vehicular accident while riding a bicycle. Except for the vague pain noted where the patient was hit, there were no other signs and symptoms at the time. There were no sudden changes in body weight, in appetite, nor in bowel habit.

Past History: Two years before admission, the patient was involved in a vehicular accident wherein he sustained a laceration wound on the right cervical area, which was sutured and has healed. Not known to have any systemic diseases. No known allergies to any food or medication.

Family History: No known hereditary diseases.

Physical Examination on Admission :

Consciousness: clear

Vital Signs: BP=120/80 mmHg

PR=86/min

RR=20/min

BT=36.6°C

(am)

=38.5°C (pm)

HEENT: grossly normal

Neck: supple, (-)JVE, (-)LAP, 5 cm long scar noted on the right side of the neck.

Chest & Lungs: clear breath sounds, no rales.

Heart: regular heart rate and rhythm, no murmurs heard

Abdomen: flat, soft, no tenderness

Extremities: freely movable, no pitting edema, (+) swelling, redness, tenderness and local heat noted on the middle/lower 1/3 of the left thigh, (-) lymphadenopathies in the inguinal region

Clinical Impression: Cellulitis, middle to lower third, anterior left thigh.

Clinical Course: Upon admission, blood was drawn for baseline laboratory examinations and an x-ray of the left thigh was done which revealed a soft tissue mass over the middle to lower third of the left femur. Suspecting a malignancy, an MRI was done which revealed an irregular tumor mass about 4.33 x 6.53 cm in size that is located in the med-ant-lat aspect of the middle to lower third of the femoral region. Subsequently, an angiogram done revealed a hypervascular soft tissue tumor with periosteal reaction and a bone scan with Tc99 revealed marked absorption by the soft tissue mass. Since malignancy could not be ruled out, an incisional biopsy was done on July 29, 1995 for which the pathologic report was a (?) sarcoma. A maximum debulking operation was arranged for the patient on August 3, 1995. His subsequent hospital stay was uneventful and he was finally discharged on August 29, 1995, condition stable.

Laboratory Examinations:

1.CBC

| | 7/20 | 7/28 | 7/29 | 8/4 | 8/24 |
|-------|------------------------|------------------------|------------------------|------------------------|------------------------|
| WBC | 7,800 | 10,600 | 11,000 | 9,700 | 5,600 |
| RBC | 3.71 x 10 ⁶ | 3.41 x 10 ⁶ | 3.24 x 10 ⁶ | 3.09 x 10 ⁶ | 3.44 x 10 ⁶ |
| Hgb | 11.6 | 10.0 | 9.7 | 9.3 | 10.5 |
| Hct | 33.5 | 30.7 | 28.6 | 27.7 | 31.9 |
| Plt | 359,000 | 669,000 | 229,000 | 452,000 | 296,000 |
| MCV | 90.2 | 90.0 | 88.6 | 89.5 | 92.6 |
| MCH | 31.3 | 29.3 | 29.9 | 30.1 | 30.5 |
| MCHC | 34.7 | 32.6 | 33.9 | 33.6 | 33.0 |
| RDW | 12.3 | 12.2 | 12.5 | 12.5 | 15.0 |
| Seg | 76 | | 86 | 84 | 61 |
| Lymph | 18 | | 9 | 15 | 33 |
| Mono | 6 | | 5 | | 6 |

2.Biochemical Examinations:

7/20

| | | | |
|-----|-------|-----|----------|
| FBS | : 120 | CRP | : 3.07 ↑ |
| Na | : 136 | ALP | : 159 ↑ |
| K | : 4.8 | GPT | : 6v |
| Cl | : 98 | GOT | : 22 |
| Ca | : 8.6 | BUN | : 7.4 |

| | | | |
|------|------------|-------|---------|
| Chol | : 123 ↓ | Crea | : 0.5 ↓ |
| Trig | : 75 | u.a. | : 2.8 |
| TP | : 6.2 | AFP | : 0.85 |
| Alb | : 3.0 ↓ | CEA | : 1.03 |
| TBil | : 0.7 | -HCG | : 0.3 |
| Dbil | : 0.1 | CA125 | : 15.43 |
| ASLO | : Negative | | |

Diagnostic Criteria:

1. Well-defined tumor
2. Zoning phenomenon (as described above)

Differential Diagnoses: Because myositis ossificans is a benign, nonproliferative and self-limited disease, it is important to clearly distinguish this lesion from extraskeletal osteosarcoma. This is best accomplished on the basis of the characteristic zoning phenomenon of myositis ossificans.

Osteosarcoma often displays more disorderly growth of hyperchromatic and pleomorphic cells with lace-like rather than trabecular osteoid formation and sometimes, a "reverse zoning effect". It also shows a greater degree of cellular atypia and infiltration of neighboring tissue in a destructive manner.

Some benign lesions may also be confused with myositis ossificans; they include posttraumatic periostitis, exuberant fracture callus, and proliferative myositis. The former often shows an ossified mass attached to the bone with a broad base. The second is usually associated with a discernible fracture line on standard x-rays. The latter rarely contains minute foci of osteoid or bone but is characteristically associated with a diffuse proliferation of plump fibroblasts.

Discussion: Myositis ossificans is a benign pathologic change and, for the welfare of the patient, it is very important and necessary to make a correct diagnosis, most especially to differentiate it from extraskeletal osteosarcoma. There is a variable degree of difficulty in the diagnosis of this disease because occasionally, condensed atypical fibroblasts, myofibroblasts, or prominent mitotic activity can be found in the central area or intermediate zone of the lesion or even in the early stages of the lesion. Therefore, a small piece of biopsy specimen can easily be the cause of a mistake in pathological diagnosis. In such a situation, the patient's age, clinical history, radiological, CT, MRI, and angiogram findings should all be taken into consideration. The patient's age and clinical history is of special importance in the diagnosis of myositis ossificans because there is usually a history of trauma and is

usually found in the young as in our case. Although myositis ossificans could also be found in those older and with apparently no known history of trauma, it is more likely that they had some minor or forgotten trauma in the past. It is found that infectious diseases could also cause myositis ossificans and hence, myositis ossificans in the elderly usually present as smaller, multiple focal lesion rather than the larger, singular lesion in the young.

Treatment: Total excision is necessary and enough.

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