

Comparative Pathology Case 1

Contributor:

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Clinical History: This is a 7-year-old male castrated, mixed breeding dog which had malignant melanoma removed from oral mucosa 3 years ago. Now thoracic radiographs revealed pulmonary densities and mineralization in the heart, and the dog had clinical signs of chronic congestive heart failure. Echocardiographs revealed tumor mass attached to the septal leaflet of tricuspid valve extending into the right atrium and ventricle and possibly invading ventricular septum.

Diagnosis: Myxoma of the right atrium

Gross Findings:

The right ventricle was extremely dilated due mainly to a big lobular tumor mass 4.8x4.2x3.1cm firmly attached to septal leaflet of the tricuspid valve and prolapsed into the right atrium and ventricle.

Histopathological Findings:

Lobules of round cells with oval nuclei were embedded in vacuolized and hyalinized ground substance. There were microvacuoles in the cytoplasm. The cellular lobules were separated by a thin fibrous stroma. In some areas, networks of stellate cells with spindle nuclei were loosely arranged in extracellular myxoid. Irregular foci of mineralization were occasionally observed in the hyalinized areas. Some thin-walled blood channels were identified in the cellular mass. The surface of the tumor was covered by thromboemboli or degenerative endothelium.

Immunohistochemical Results:

Vimentin was weakly positive. Histochemical stain PAS was positive in the matrix. Trichrome stain was positive in the hyalinized areas.

Electron Microscopic Findings:

This tumor consisted of primitive cells with thin membrane, a few simple organellae, and primitive cellular junction. There myxoid material and collagen fibrillae in the matrix.

Discussion:

Myxoma of the left atrium is more common, three times than that of the right

atrium in human beings. Myxoma occurs mostly in the right atrium of dogs. This tumor occurs rarely in the ventricles. Most myxomas are not invasive and are confined to the endocardium in human heart. Cure following complete surgical removal. Thromboembolism is common but metastasis is very rare in human beings and dogs.

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Comparative Pathology Case 2

Contributor:

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Clinical History:

A 5-year-old, healthy female ferret (*Mustela putorius furo*). Which had a mass on the tip of the tail. Radiologically the last coccyx was partially destroyed with radiodense lesion in the periphery.

Diagnosis: Chordoma

Gross Findings:

Grossly the tip of the tail 2.1 Cm in length was submitted. There was a pinkish firm mass 9x14 mm covered by skin. The last coccyx was partially destroyed by the tumor tissue.

Histopathological Findings:

Microscopically, in longitudinally sectioned tail, the tumor consisted of three components, arranged in concentric zones within the mass of the tip of the tail. There were the zones within the mass of the tip of the tail. There were the remains of destroyed trabecular bone in the center, surrounded by cartilage, and lobules of vacuolated polygonal (physaliferous) cells at the periphery. The lobules of physaliferous cells were separated from adjacent normal tissue by a thin fibrous stroma and were composed with distinct borders and single or multiple large, clear cytoplasmic vacuoles. At the margins of the lobules, the tumor cells were smaller with a granular to microvacuolated, eosinophilic cytoplasm. Nuclei were round to oval with stippled to clumped chromatin and an occasionally discernible nucleolus and were often eccentric and hyperchromatic and occasionally distorted by cytoplasmic vacuoles.

Immunocytochemical Results:

Immunohistochemical staining patterns were consistent with previous results of studies of chordoma in various species. The tumors (100%) demonstrated dual expression of keratin and vimentin intermediate filaments. 85% were positive for neuron specific enolase and 75% were positive for s-100 protein. Within all neoplasms three were scattered physaliferous cells with periodic acid-Schiff- positive cytoplasmic granules.

Electron Microscopic Findings:

By electron microscopy, the physaliferous cells contained remnants of endoplasmic reticulum, mitochondria, and cytoplasmic vacuoles.

Discussion:

Chordoma is an uncommon neoplasm which has been reported in human beings, rats mink, dogs, a cat, and ferrets. In a large study of chordoma in Fischer 344 rats, the tumor occurred with a 3:1 male: female ratio, and metastasis to the lung was diagnosed in 75%. In human beings, the tumors arise primarily in the sarcococcygeal and sphenooccipital regions with the remainder arising in the vertebral axis. Chordoma is a slow-growing. Locally aggressive neoplasm with a high rate of recurrence. Up to 30% are reported to metastasize, particularly those of sarcococcygellar or vertebral origin. Chordoma occurs with a 2:1 male: female ratio in human beings.

Chordoma arises from notochord or notochordal elements is based primarily on the observation that the neoplasm occurs almost exclusively centrally in the axial skeleton and histologically resembles notochord by both light an electron microscopic examination. The notochord is a rodlike aggregate of cells extending the entire length of the embryo on the midline ventral to the developing neural tube. It is believed to be of mesodermal origin, and, while not retained in higher vertebrates, it is of great significance developmentally.

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Comparative Pathology Case 3

Contributor:

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Clinical History:

A 4-year-old girl was well before. However, there was a minor head injury 2 months ago without definite sequela. Intermittent headaches and change of sleep pattern were noted in recent 2 weeks. She complained of persistent headaches and suddenly fell and got up with just limping of right hemiparesis. One day before this admission, she recovered without definite weakness after treatment with Dexon. No neurological deficits were found. However CT revealed a huge mural cyst with nodular mass, 3x3 cm size, a heavily calcified freckle over the left occipital parietal lob, and slight enhancement of the mass and cystic walls. Mid-line shift was marked. She received craniotomy with a subtotal resection of the tumor, followed by 4600 CGY (whole brain) irradiation therapy and chemotherapy (cisplatin, oncovin, CNU, and TIT). The patient is alive and well 6 months after the operation.

Diagnosis:

Primitive neuroepithelial tumor with ependymal differentiation. Synonym: Ependymoblastoma.

Gross findings:

The cyst was yellowish in color with smooth walls and tan-clear fluid in content. The mural nodule was grayish in color, fragile, and easily sucked.

Histopathological Findings:

Histologically, the tumor was composed of sheets of poorly differentiated oval or spindle cells with a hyperchromatic round or oval nucleus. Mitotic figures were frequent and areas of ependymoblastic (true) rosettes were noted.

Immunocytochemical Results:

Vimentin and GFAP. Focal positive. NF: Negative

Histochemistry results:

Bodian stain: No neurofibrils noted
PTAH: No scanty glial fibers noted

Electron Microscopic Findings:

The compacted tumor cells showed polymorphism, hyperchromatic nuclei, and scanty cytoplasmic organellae. The rosettes formed by cell with apical microvilli immature apical junctional complex, or cilia with basal bodies.

Discussion:

Ependymoblastoma is a very rare supratentorial tumor usually affecting children (median age: 2 years). Our case is a 4-year-old. These tumors may not be directly apposed to the ventricular lining and they tend to be massive but well circumscribed; some ependymoblastomas can be partially neuroectodermal tumor with ependymoblastic differentiation denotes a small blue cell embryonal neoplasm with more than 10% ependymoblastic rosette component. Although it is easy to distinguish these lesions in most instances, in some cases it may be difficult. As previously reported, ependymoblastic rosettes may be seen both in medulloepitheliomas with glial differentiation and in primitive neuroectodermal tumors with multilineage differentiation.

Differentiation Diagnosis:

- 1) Medulloepithelioma
- 2) PNET with multilineage differentiation
- 3) Anaplastic ependyoma

Diagnostic Criteria:

Ependymoblastic rosette (LM), microvilli, and immature junctional complex (EM).

References:

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Comparative Pathology Case 4

Contributor:

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Clinical History:

A three-day-old kid was sacrificed from a herd with an outbreak of diarrhea. It was born in a healthy condition but became listless, inappetent, weak, and diarrheal on the second day.

Dignosis: Intestinal Cryptosporidiosis

Gross Findings:

There were loose intestinal contents in the lumen. Mucosal surface was unremarkable.

Histopathological Findings:

1. Small intestine-Most of the lesions were observed in the jejunum and ileum.
There was a moderate but diffuse villous atrophy; the denuded villi were covered by tremendous numbers of spherical organisms which were not found in the crypts. The surface epithelial cells were cuboidal and loosely arranged. Moderate cryptic hypertrophy was noted and numerous neutrophils were found in the mildly dilated crypts.
2. Spleen-Moderate to severe lymphoid depletion was noted.

Electron Microscopic Findings:

Various stages of a protozoan organism were attached firmly, by feeder organelles, between the microvilli of the intestine and surrounded by bilayered vacuoles. The organisms resided intracellularly but extracytoplasmically. SEM revealed many spherical organisms embedded in between the microvilli of epithelial cells in the small intestine.

Discussion:

Cryptosporidium is a small apicomplexan protozoan, parasitizing on the surface of gastrointestinal and respiratory epithelium in animals and human beings:

C. muris and C. parvum in mammals

C. meleagridis and C. baileyi in birds

C. serpentis in reptiles

C. nasorum in fish.

Its life cycle is similar to coccidian including merogony, gametogony, and sporogony, occurring in the brush border. The infection is transmitted by the ingestion of oocysts.

In goats, cryptosporidium usually infects neonates, causing diarrhea at age about 5-14 day. It also attacks young animals of other species such as calves and lambs.

Cryptosporidium may be associated with immunodeficient conditions as not requirements:

--AIDS

--Combined immunodeficiency in Arabian foals

-- Feline leukemia virus

--Canine distemper

It may also be a secondary organism in enterotoxigenic E. coli, rotavirus, and coronavirus infection.

It usually causes villous atrophy, cryptic hypertrophy, and dilatation with accumulation of neutrophils and necrotic debris.

It is a sporadic disease with minor symptoms, but sometimes it causes fetal diarrhea.

Diarrhea is caused by malabsorption, villous atrophy, and epithelial immaturity. Release of enterotoxin-like substance is suspected.

Diagnostic Criteria:

1. Watery diarrhea, sporadic and self-limiting, or persistent and fatal.
2. Organisms on brush border or fecal smear can be stained by modified Ziehl-Neelsen and auramine O, and Giemsa stain.
3. Villous atrophy.
4. Cryptic atrophy.
5. Cryptic dilatation with abscesses.
6. FA stain.

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Comparative Pathology Case 5

Contributor:

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Clinical history:

A 10 month-old female Lemur fulvus from a group of 8 lemur fulvus was raised in a local zoo. She had bloody and foul-smelling feces for unknown period and died on 1/30/94. The other three of them subsequently showed depression and diarrhea with bloody mucus.

Diagnosis:

(1) Colitis, necrotizing and ulcerative, segmental and transmural, subacute, severe, with intralesional amoeba and Brown lemurs (Lemur fulvus), non-human primate.

(2) Pericolonic peritonitis, necrotizing, segmental, subacute, moderate.

Gross findings:

The lesions were confined to the colon, cecum, and liver. The colon and cecum were filled with large amounts of dark bloody fluid. Their mucosa had multiple (measuring approximately 5cm in diameter) to coalescing ulcerations with a thick layer or yellowish pseudomembrane formation. The liver showed multifocal white spots over the surface.

Histopathologic findings:

Microscopic features confirmed gross observation of necrotizing ulcerative colitis in three colon sections. The affected colon frequently had a flask-shaped ulcer extending into submucosa and muscle layers, with many trophozoites in or particularly at the periphery of the lesions. A heavy infiltrations of mixed inflammatory cells including neutrophils, macrophages, plasma cells, lymphocytes, and eosinophils were present in or along the edge of the necrosis. Other findings were edema, hemorrhage, vascular thrombosis, bacterial colonies, and hyperemia as well as pericolonic peritonitis. The trophozoites of amoeba recognized in tissue sections were irregularly spherical in shape, ranging from 10 to 60 um in diameter. They had distinct or indistinct nucleus with abundant vacuolated cytoplasm, sometimes containing phagocytized erythrocytes or tissue debris.

Histochemistry results:

Many PAS-positive trophozoites were scattered throughout the ulcer sites, primarily along the margins of the necrosis.

Immunocytochemistry results: Not done.

Electron microscopy findings:

The trophozoite with one nucleus in the necrotic areas contained many food vacuoles and inclusions in the endoplasm.

Discussion:

Amoebiasis is an acute or chronic disease caused by a single cell protozoan Entamoeba histolytica. These organisms usually inhabit the intestinal tract and cause amoebic dysentery in man, nonhuman primates and less frequently other animals dogs, cats, rats, and pigs. Amoebic lesions are typically confined to the colon and cecum and produce characteristic flask-shaped ulcers in affected animals. Extra-intestinal dissemination of amoebae in advanced cases, with abscessation in other organs, especially liver, lung, and brain, is a relatively common complication in humans and nonhuman primates.

In a study of human amoebiasis, it has been shown that about 500 million people are infected. In about 10% of the cases the parasite becomes invasive resulting in colitis and extra-intestinal abscesses leading to ~50000 deaths annually. In Taiwan, seven of 145 necropsied nonhuman primate cases (1985-1993) were diagnosed as amoebiasis, variably affecting large intestine, liver, stomach, lung, and brain. In addition, an acute outbreak of intestinal amoebiasis was recently reported at a local elementary school. Mature quadrinucleate cysts most commonly in fecally contaminated water, hands, and food. House flies, cockroaches, and other arthropods may mechanically carry infected feces to food on legs or mouth.

Entamoeba histolytica may range from asymptomatic colonization of the colon and cecum to acute dysentery with bowel perforation or extra-intestinal abscessation. The circumstances under which the commensal parasites become invasive are not fully understood. In an experimental study of germfree mice, results showed that intestinal bacteria such as Aerobacter aerogenes and Escherichia coli probably play an important role in the pathogenesis of amoebiasis. Although the precise host and parasite factors promoting invasion and necrosis are not known, the killing reaction is initiated by the binding of the amoebic galactose-specific adhesion on the amoebae surface. Once cell-cell contact is established, massive surface blebbing of the target cell occurs. This suggests that amoebae secrete factors which alter membrane permeability. The consequent cytotoxic activity is mediated by amoebapore, the

pore-forming peptide, and granule vesicles which resemble the “ cytotoxic granules” of lymphocytes. In addition to the killing effect, amoebae release other virulence factors which inhibit macrophage motility, degrades type I collagen, and destroys extracellular matrix to aggravate lesions.

Diagnostic criteria:

1. Amoebiasis is diagnosed by identification of the trophozoites associated with typical lesions. The trophozoites may contain ingested erythrocytes.
2. The organisms are best seen in smears stained with Lugol’s iodine solution to identify the nuclei of cysts and to stain glycogen.

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Comparative Pathology Case 6

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Clinical History:

A 14-year-old, male, Formosa macaque dies suddenly without obvious illness.

Diagnosis:

Severe, multifocal to coalescing, necrotizing, granulomatous pneumonia, splenitis, and adrenalitis with large numbers of small, thin acid-fast positive, rod bacteria, consistent with simian tuberculosis.

Gross findings:

Numerous pale yellow nodular lesions, ranging from 0.1-0.5cm in diameter, were present on the surface and in the parenchyma all over the lung, liver, kidney, spleen, and adrenal gland. The regional lymph nodes were enlarged and some of them contained similar nodular lesions. Caseous substance was present in the center of many of the nodular lesions.

Histopathological Findings:

The slide submitted contains sections of the lung, spleen, and adrenal gland. In the parenchyma of all three organs, there are multiple, variably-sized, discrete to coalescing necrotic foci. The necrotic foci are composed of a large amount of cellular debris and various numbers of degenerated and dying macrophages and neutrophils with occasional necrotic giant and binucleated cells at the peripheral region. The necrotic foci are surrounded by an indistinct zone of macrophages, neutrophils, lymphocytes, and plasma cells along with mild to moderate fibrin deposition. In the lung, bronchiolar involvement is noted in the distribution of the lesion; in the spleen, bronchiolar involvement is evident in many affected areas. The normal architecture of the spleen has been distorted by the densely distributed necrotic foci, and foci of mild capsulitis are also revealed. Aside from scattered small aggregates of lymphocytes in the sparse remaining normal splenic tissue, there are no recognizable lymphoid follicles. The adrenal gland is severely affected as well but the necrotic foci are mainly located in the cortex; rupturing through the surface and extending to the adjacent connective tissue are seen in a necrotic area close to the capsule.

Histochemical Results:

Ziehl-Nielsen acid-fast stain revealed numerous small thin, positively reacted, intracellular and extracellular, rod bacteria compatible with *Mycobacterium* sp. The microorganisms are mainly present in the peripheral region of the necrotic foci.

Immunocytochemical Results:

Positive reaction is seen in the peripheral region of the necrotic foci with ABC method using antibodies to *M. bovis* and *M. duvalli*.

Discussion:

Tuberculosis has been and remains an important and serious disease of nonhuman primates kept in zoos, labs, or at home as pets. It has long been recognized that TB is rare in wild monkeys not living near humans, but monkeys living near villages are often infected. Primates may be infected by any of the three types of tubercle bacilli: human, bovine, or avian. although the avian has been reported only rarely. Transmission has been achieved by inhalation, ingestion, direct contact, contaminated equipment (thermometers and tattooing needle), and cross infection from other animals. The disease is usually quite insidious and goes unnoticed. Thus, the clinical signs are generally not striking until the disease is far advanced. Lesions associated with TB in apes and monkeys are very similar to those seen in lungs, intestine, and lymphoid tissues of children infected with TB. The major differences between human and TB are the rarity of calcified tubercles and absence of fibrotic reaction in untreated monkeys. Disseminated infection is the usual state in monkeys, but it is relatively rare in human adults though is more frequent in children. Miliary TB with caseous tubercles dotting affected organs seems to be more common in monkeys than in man. A differential diagnosis for gross lesion should include other bacterial diseases caused by *Nocardia*, *Corynebacterium*, and *Flavobacterium*; deep mycoses; lung mite infestation, etc. Identification of the organism is based on staining property (acid-fastness), culture requirement, conventional biochemical tests, HPLC, and nucleic acid probes.

Diagnostic Criteria:

- Widely disseminated, military, nodular lesions.
- Characteristic necrotizing granulomatous inflammation.
- Presence of small, thin, acid-fast positive, rod bacteria.
- Positive immunocytochemistry reaction with ABC method using antibodies to *M. bovis* and *M. duvalli*.

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Comparative Pathology Case 7

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Clinical History:

A 39-year-old female, G4P4, suffering from abdominal fullness for half a month, was admitted for PE which revealed ascites and sonography showed adnexa mass on Mar. 24.1994. Her past history revealed lower abdominal pain in Mar. 1991. but sonography showed no remarkable change. On Nov. 15.1993. productive cough & chest pain were noted. CXP revealed pneumonic patch with pleural effusion over right lower lung field. After treatment with antibiotics, the condition improved. For adnexa mass (R/O malignancy) was impressed, studies for tumor nature were performed.

Diagnosis:

Pelvic tuberculosis, fallopian tube, right; omentum and peritoneum, disseminated; endometrium.

Gross Findings:

1. The oviduct is diffusely coated with fibrinous exudates and shows marked swelling and congestion. No fibrinated end is found. On serial sectioning, the lumen is narrowed and necrotic areas are noted.
2. The partially resected omentum is markedly thickened (1.1 cm) and coated with fibrinous exudate. On cut, it is unremarkable.
3. The endometrium is grossly unremarkable.

Histopathological Findings:

Extensive typical granulomas are noted in the wall of the oviduct (including the tubal peritoneum). Caseation is noted in the central portion of the lesions. However, there are only scattered epithelioid tubercles to be found in the omentum. The endometrial tissue contains few epithelioid tubercles scattered within the stromal or glandular elements.

Histochemistry Results:

Ziehl-Neelsen acid-fast stain is performed with Tb bacilli to be noted.

Discussion:

Tuberculosis is an increasingly common infection in the 1990's. Even if only one bacillus is inhaled, infection may be established if the immunity is not at normal condition.

Fortunately, most people can be free of this disease without knowing the pathogen inside. After inhalation of Tb bacilli, pulmonary inoculation can lead to involvement of other areas of the body. The pathways include lymphatic, blood stream, contiguous, and intracanalicular spread.

Tb bacilli can survive many years and recrudescence. Post-primary disease can become manifest with pregnancy, stress, other disease, or old age.

Pelvic TB is commonly a reflection of systemic disease and behaves as such. There are cases of tubal TB that show strong evidence of association with previous pulmonary TB (maybe 10 years later). Various studies bear out the thesis that tubal TB is always secondary to a focus elsewhere in the body. However, the oviduct is almost always the primary seat of TB in the female genital organs. If there is involvement of endometrium, cervix, or lower genital tract, we can say with assurance that there is primary tubal disease. The Tb bacilli reach the tube by the blood stream (most frequently) from a distant focus, generally the lung, which may be in an active stage, but frequently is in a quiescent state.

Gross appearance of tubal TB is not distinctive, but if the tubal peritoneum is studded with tubercles and there is associated ascites, then granulomatous origin is identified. In our case, military nodules are noted over liver surface, intestinal wall, and tubal peritoneum. Although cancer peritoneum was also suspected, it turned out to be TB tubercles by frozen section diagnosis.

Microscopical findings of the oviduct showed tuberculous pyosalpinx with tubercles involving from mucosa to serosa. There are caseation, epithelioid tubercles, and Langhans' giant cells. The fimbriated end is not found but expulsion of exudates through the fimbria into the pelvic cavity is noted as the peritoneum is studded with tubercles that seem much younger than the oviduct ones. There is also endometrial lesion which was curetted just before menstruation.

Diagnostic Criteria:

The diagnosis of our case is established by 1. histological criteria (extensive granulomatous reaction with caseation and Langhans' giant cells). 2. bacteriologic stain (acid-fastness) 3. clinical therapeutic trial (CXR improved). Although TB culture and serology (ELISA) was not performed, we believe that in this high prevalence area, it is important to start the anti-TB therapy. If only endometrial curettage is submitted, it is difficult, it is difficult to make diagnosis for there is usually no well-formed

tubercles to be found, and the occult disease may only involve limited parts of the endometrium. If curettage is performed just before menstruation, however, usually there will be more well-formed lesions to be found.

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