Chinese Society of Comparative Pathology

中華民國比較病理學會

第 82 次比較病理學研討會

消化道病理討論專題

主辦單位

Chinese Society of Comparative Pathology

中華民國比較病理學會

國立臺灣大學獸醫專業學院

中華民國 110 年 12 月 11 日(December 11, 2021)

Schedule

82th MEETING OF COMPARATIVE PATHOLOGY

中華民國比較病理學會 第 82 次比較病理學研討會

消化道病理討論專題

時間：110 年 12 月 11 日（星期六）

形式：臺灣大學獸醫專業學院獸醫三館 B1

電話：02-33663760

Time (時間)	Schedule (議程)		Moderator (主持)
8:30~9:20	Registration (報到)		
9:20~9:30	Opening Ceremony (致詞) 鄭謙仁 理事長		
9:30~10:30	專題演講	主講：陳雅媚 獸醫師 題目：犬貓口腔病理學	鄭謙仁 理事長
10:30-10:45	Coffee Break		
10:45~11:45	專題演講	主講：彭奕仁 副教授 題目：Hepatocellular carcinoma	鄭謙仁 理事長
11:45~13:45	午餐		
13:45~14:10	Case 564	Shih, Chia-Wen (施洽雯), M.D., M.S. [1]; Yeh, Hsuen-Tang (葉顯堂), M.D.[2] 1. Department of Pathology, Lotung Poh-Ai Hospital (羅東博愛醫院病理科) 2. Department of General Surgery, Lotung Poh-Ai Hospital (羅東博愛醫院一般外科)	黃威翔 秘書長
14:10~14:35	Case 565	Jiang, Jia-Wei (江家瑋), DVM, MS[1]; Tsao, Wen-Tien (曹文恬), DVM, MS[1]; Luo, I-Chi (羅怡琪), DVM, MS[1] [1]HOPE Veterinary Pathology Diagnostic Center (霍普獸醫病理診斷中心)	黃威翔 秘書長
14:35~15:00	Coffee Break		
15:00~15:25	Case 566	Lai, Ming-Tsung (賴銘淙),MD. PhD.[1]	黃威翔 秘書長

		[1]Department of Pathology, Taichung Hospital, Ministry of Health and Welfare Taiwan(衛生福利部台中醫院 病理科)	
15:25~15:50	Case 567	Yang, Ya-Wen (楊雅雯), DVM[1]; Liu, Chen-Hsuan (劉振軒), DVM, PhD[1]; Chang, Hui-Wen (張惠雯), DVM, PhD[1]; Pang, Victor Fei (龐飛), DVM, PhD[1]; Wang, Fun-In (王汎熒), DVM, PhD[1]; Jeng, Chian-Ren (鄭謙仁), DVM, PhD[1]; Haung, Wei-Hsiang (黃威翔), DVM, PhD[1]; Chang, Yen-Chen (張晏禎), DVM, PhD[1]* [1] Graduate Institute of Molecular and Comparative Pathobiology, School of Veterinary Medicine, National Taiwan University (國立台灣大學獸醫專業學院分子暨比較病理生物學研究所)	黃威翔 秘書長
15:50~16:15	Case 568	Chang, Junn-Liang (張俊梁), MD, PhD[1]; Liu, Kuang-Ting (劉光庭), MT, MS[1]; Chang, Yueh-Ching (張月清) MT, MS[1] [1]Department of Pathology and Laboratory Medicine, Taoyuan Armed Forces General Hospital, Taoyuan City, Taiwan. (國軍桃園總醫院 病理檢驗部)	黃威翔 秘書長
16:15~	General Discussion (綜合討論) 鄭謙仁 理事長		

台大周邊飲食商圈地圖

目　　錄

Special Lecture (專題演講)

犬貓口腔病理學（Oral pathology of dogs and cats）

陳雅媚 DVM, PhD, DCSVP, DACVP

犬貓口腔腫塊是常見的外科送檢檢體來源，病理獸醫師應對於口腔疾病與腫瘤有基本的了解。口腔內疾病可分為: 炎症、牙齒疾病(disease of teeth)、齒源性腫瘤(odontogenic tumors)、軟組織腫瘤(tumors arising from the soft tissues)、骨腫瘤(tumors of the jaw)、增生(tumor-like proliferation lesions)、齒源性囊腫(odontogenic cysts)、唾液腺病灶(lesions of the salivary gland)等。在犬貓口腔內常見到牙菌斑(plaque)與牙結石(calculus)之形成，增生的細菌可刺激形成牙周病(periodontal disease)。根據影響的範圍，Periodontal disease 可分為三階段，包含 gingivitis, periodontitis, periodontal osteomyelitis。在犬隻，口炎(stomatitis)主要是因為 plaque 持續性刺激所引起。但是在貓隻，stomatitis 是一個複雜疾病，推測是受到多因子所影響，導致動物免疫失調。組成齒源性腫瘤(odontogenic tumors)的成分包含 odontogenic epithelium, mineralized dental matrices, dental papilla, dental follicle。分類 odontogenic tumors 之前，需要了解牙齒的形成(odontogenesis)。在犬隻，最常見的 odontogenic tumor 是 canine acanthomatous ameloblastoma。關於軟組織腫瘤，犬最常見的腫瘤依序為: melanoma, fibrosarcoma, squamous cell carcinoma。貓最常見的軟組織腫瘤依序則為: squamous cell carcinoma, fibrosarcoma, melanoma。Maxillofacial osteosarcoma 主要見於成年大型犬。常見的增生病變包含創傷後所引起的 granulation tissue, gingival hyperplasia, peripheral giant cell granuloma, fibromatous epulis of periodontal ligament origin, fibrous dysplasia 等。這些增生病變需與腫瘤進行仔細區別。

Special Lecture (專題演講)

題目: Hepatocellular carcinoma

講者： 彭奕仁 (Yi-Jen Peng) 副教授

三軍總醫院病理部/國防醫學院醫學系病理學科

Hepatocellular carcinoma (HCC) accounts for 75-85% of primary liver cancer, 6th most common cancer and 4th leading cause of cancer-related death in the world. More than 90% HCC are related to a defined cause including chronic liver diseases and exogenous substances. Molecular changes in multistep carcinogenesis accumulate from premalignant lesions (dysplastic foci/nodule), early HCC to progressed HCC. Typical HCCs are characterized by loss of the normal reticulin framework, increased arterialization, with aberrant arterioles in the parenchyma and sinusoidal capillarization. However, it is a challenge to distinguish between high-grade dysplastic nodule and early HCC, especially in biopsy specimen. Overexpression of more than 2 amoung HSP70, glypican-3 and glutamine synthetase indicates HCC. Several subtypes of HCC have been added in the 5th version of WHO classification including steatohepatitic, clear cell (formerly a “cytological variant”), macrotrabecular-massive, chromophobe and neutrophil-rich. The lymphoepithelioma-like subtype is renamed to lymphocyte-rich. The prognosis of patients with HCC is generally poor.

Case Diagnosis

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（閱片網址：**http://www.ivp.nchu.edu.tw/slidecenter.php?id=507** ）

Case No.	Presenter	Slide No.	Diagnosis
Case 564	施洽雯	21-6128	Epithelioid gastrointestinal stromal tumor (GIST) http://www.ivp.nchu.edu.tw/ivp_slide_view.php?id=1965
Case 565	江家瑋	21-1936	Intestinal intramural hemorrhage/hematoma, small intestine, dog http://www.ivp.nchu.edu.tw/ivp_slide_view.php?id=1972
Case 566	賴銘淙	SE21801181C SE21801483	1. Intestine, small bowel, segmental resection,--- Primitive neuroectodermal tumor(PNET) / Extraskeletal Ewing sarcoma 2. Lung, needle biopsy, ---Small blue cell tumor, compatible with primitive neuroectodermal tumor (PNET) metastasis http://www.ivp.nchu.edu.tw/ivp_slide_view.php?id=1970 http://www.ivp.nchu.edu.tw/ivp_slide_view.php?id=1971
Case 567	楊雅雯	NTU2021-2345A	1. Gastric carcinoma, whit lymphatic infiltration, stomach, dog 2. Lymph node metastasis from gastric carcinoma, dog http://www.ivp.nchu.edu.tw/ivp_slide_view.php?id=1973
Case 568	張俊梁	152933H	1. Descending colon, adenocarcinoma, grade 2; C/W FAP syndrome associated advanced CRC http://www.ivp.nchu.edu.tw/ivp_slide_view.php?id=1975

Case Number: 564

Slide Number: 21-6128

Slide View: http://www.ivp.nchu.edu.tw/ivp_slide_view.php?id=1965

Shih, Chia-Wen (施洽雯), M.D., M.S. [1]; Yeh, Hsuen-Tang (葉顯堂), M.D.[2]

1. Department of Pathology, Lotung Poh-Ai Hospital (羅東博愛醫院病理科)
2. Department of General Surgery, Lotung Poh-Ai Hospital (羅東博愛醫院一般外科)

CASE HISTORY:

Signalment: 64-year-old woman.

Clinical History:

A 64-year-old woman presented with epigastric pain for one day and tarry stool for 3 days. She visited YMUH due to nearly syncope. Esophagogastroduodenoscopy was performed in YMUH and showed a submucosal tumor at antrum of stomach. For surgery was suggested, she presented to the Out Patient Department of General Surgery of Lotung Pohai Hospital. She has past history of hypertensive cardiovascular disease (HCVD) and diabetes mellitus (DM).

The CT scan showed an irregular submucosal enhancing mass measuring about 3.6 x 2.6 cm, in posterior-inferior aspect of gastric antrum. No necrosis or calcification was noted. There is normal size of liver and spleen with smooth contour and normal density. There is no evidence of lymphadenopathy. The chest X-ray was normal. Under the impression of suspicious GIST, distal gastrectomy was performed. The specimen was sent to the department of pathology for pathologic diagnosis. Grossly, the specimen submitted consisted of a partial stomach measuring 14.2 cm of the greater curvature and 13.0 cm of the lesser curvature. Cut section showed a well-defined submucosal tumor measuring up to 3.7 x 3.0 x 2.8 cm. Cut sections of the tumor showed grayish-brown in color and soft-elastic in consistency.

Clinical Pathology:

BUN: 6 mg/dL (6-20 mg/dL), Creatinine: 0.5 mg/dL (0.7-1.3 mg/dL), Glucose: 127 mg/dL (70-100 mg/dL), Na: 142 mmol/L (135-145 mmol/L), K: 3.4 mmol/L (3.5-5.1 mmol/L), AST (GOT): 21 U/L (5-40 U/L), ALT (GPT): 12 U/L (5-40 U/L), RBC: 3.50x10^6/uL (4.6-6.2 x10^6/uL), Hb: 7.3 gm/dL (14.0-18.0 gm/dL), Hct: 31.5 % (40-54%), Plt: 24.2 x10^4/dL (15-40 x10^4/dL), WBC: 5.4 x10^3/uL (4.5 - 11.0 x10^3/uL).

CASE RESULT:

Histopathologic Findings:

Histopathological examination revealed a well defined submucosal tumor. The tumor is composed of proliferated epithelioid cells, irregular in size and shape with round to ovoid hyperchromatic nuclei, moderate amount of clear or eosinophilic cytoplasm and distinct or inconspicuous nucleoli. Cytoplasmic vacuoles were also noted in some of the tumor cells. No tumor necrosis was noted. No significant mitotic figure was noted. No lymphatic duct or blood vessel invasion was noted.

Immunohistochemistry:

Sections of tissue specimen were subjected for immunohistochemical evaluation. On immunohistochemical analysis, the tumor cells were positive for CD117, Dog1, Actin, CD34 and negative for CK, CD56, chromogranin A and synaptophysin. The Ki67 index was less than 1%.

Differential diagnosis:

1. Neuroendocrine tumor.
2. Epithelioid leiomyoma.
3. Epithelioid sarcoma.
4. Epithelioid angiosarcoma.
5. Epithelioid gastrointestinal stromal tumor (GIST).

Diagnosis: Epithelioid gastrointestinal stromal tumor (GIST)

Comments:

In 1983, Mazur and Clark first introduced the vague term “gastrointestinal stromal tumor” (GIST). Originally viewed as smooth muscle tumors (leiomyoblastomas), it is now known as GIST. GIST arises from the interstitial cells of Cajal (ICC). ICCs are pacemaker cells within the myenteric plexus of the smooth muscle layers. ICCs function to set up a peristaltic wave that coordinates the movement of food through the digestive system. Immunoperoxidase staining can show CD34-positive cells surrounding the Auerbach ganglia plexus in the gastrointestinal tract.

GIST is now known to be the most common mesenchymal tumor in the digestive tract because of increased diagnostic reliability. Population-based studies estimate the annual incidence at 11-18 cases per million. MicroGISTs (< 1 cm) and mini-GISTs (1-2 cm), are quite common. Autopsy studies have identified microGISTs, known variably as GIST tumorlets or GISTlets, in up to 22.5% of patients, and up to 35% of patients > 50 years. Stomach is the most common site of GIST (60%) and follow by jejunum and ileum (30%), duodenum (4 - 5%), rectum (4%) , colon and appendix (1 - 2%) and esophagus (< 1%). GISTs also rarely involve the gallbladder. A small number of GISTs have no apparent connection to the gastrointestinal (GI) tract. These GISTs, known as extragastrointestinal GISTs (EGISTs), involve the omentum, mesentery, retroperitoneum, and perineum. GISTs occur with a peak median age of 64 years at diagnosis. GISTs occur with an

approximately equal sex predilection (47.3% female; 52.7% male). Presenting symptoms include GI bleeding, anemia, nausea, vomiting, abdominal fullness, or a mass. GISTs can also present asymptomatically.

No etiologic factors related to GIST have been identified. CD34 is expressed in 70% of GISTs and was the first immunohistochemical marker that helped to distinguish these tumors from leiomyomas and leiomyosarcomas of the GI tract. In 1998, reports by two groups that GISTs commonly express KIT(CD117) indicating the activating mutations in the protoncogene KIT (CD117)(~75%) and laid the basis that GIST could be defined as a particular tumor entity. The staining of CD117 may be membranous, diffusely cytoplasmic, or concentrated in a dot-like perinuclear pattern. To make a diagnosis of GISTs, immunohistochemical staining of the CD117 and CD34 is required, because they can characteristically express CD34 and CD117 with the positive rate as 98% and 92% respectively. As a sensitive and specific marker of GIST, c-KIT seems to be a useful antibody in diagnosis and differential diagnosis of GIST. The addition of DOG1 (ANO1) as another GIST marker has made the diagnosis quite routine. As DOG1 and CD117 each stain more than 95% of GISTs and, between them, serve to mark essentially all cases. But the biological behaviors of GIST are difficult to predict, some metastasize whereas others remain asymptomatic for years.

Grossly, the tumors are generally well circumscribed, have a fleshy pink or tan cut surface, and may show areas of hemorrhagic necrosis and cystic degeneration.
They range from 1 cm to more than 40 cm, with an average of 5 cm. GISTs have different morphologic, immunohistochemical, and molecular features. There are three histologic types: 1. Spindle 2. Epithelioid 3. Mixed. The pure epithelioid GIST (PE-GIST) was less common than mixed subtype (M-GIST). PE-GIST was more common in females. The mean age of patients is similar in both PE-GIST and M-GIST. PE-GIST most commonly involves stomach, while small intestine is the most commonly involved by M-GIST. Mixed tumors were larger in size (6.0 cm, mean) compared to PE-GIST (4.2cm, mean). Tumors showing PE-GIST subtype were more in the high-risk category, compared to the M-GIST (33% vs 23%). Most cases of M-GIST were in higher pathologic stage (pT3) than the PE-GIST at presentation. M-GIST expressed both c-KIT and DOG-1 more frequently than the PE-GIST (70% vs 55%). Under light microscope, the morphology of GIST looks sometimes like a leiomyoma, sometimes like a Schwannoma. Most gastrointestinal mesenchymal tumors, previously classified as leiomyomas, schwannomas or leiomyosarcomas, are today classified as GISTs on the basis of molecular and immunohistological features. Cases of GIST with focal immunoreactivity for SMA are diagnosed as GISTs with smooth muscle differentiation. Cases of GIST with focal immunoreactivity for S-100 and NSE could be used as the diagnostic criteria of GISTs with nerve differentiation.

The prognosis of GIST depends on tumor size, mitotic rate and site of origin. Coagulative necrosis, mitotic activity over 10/50HPF, high cellularity with obvious pleomorphism are also helpful parameters for diagnosis of malignancy aside from metastasis and invasion. Adhesion over 5 cm in diameter and mitotic activity over 5/50HPF but less than 10/50HPF might be the potentially

malignant parameters. But the effective and reproducible diagnostic parameters for differentiating benign from malignant GISTs are still not clear.

The treatment of GIST including surgical excision and/or chemotherapy. Most GIST are treated with surgical resection. It should be emphasized that these are clinically significant GISTs greater than 2 cm in size that require surgical evaluation and potentially systemic therapy. The identification of KIT gene mutations in most GISTs has made them a paradigm for targeted therapy. The growth of most GISTs is driven by oncogenic mutations in either of two receptor tyrosine kinases: KIT (75% of cases) or PDGFRA (10% of cases). Treatment with tyrosine kinase inhibitors (TKIs) such as imatinib, sunitinib, and regorafenib is effective in controlling unresectable disease; however, drug resistance caused by secondary KIT or PDGFRA mutations eventually develops in 90% of cases. Adjuvant therapy with imatinib is commonly used to reduce the likelihood of disease recurrence after primary surgery, and for this reason assessing the prognosis of newly resected tumors is one of the most important roles for pathologists. Approximately 15% of GISTs are negative for mutations in KIT and PDGFRA. Recent studies of these so-called wild-type GISTs have uncovered a number of other oncogenic drivers, including mutations in neurofibromatosis type I, RAS genes, BRAF, and subunits of the succinate dehydrogenase complex. Routine genotyping is strongly recommended for optimal management of GISTs, as the type and dose of TKI used for treatment is dependent on the mutation identified. Imatinib mesylate (Gleevec): TKI of *KIT* and PD*GFRα* treat *m*etastatic / recurrent GIST. Sunitinib malate (Sutent): TKI of *KIT*, *PDGFRα,* VEGFR treat Imatinib resistant GIST. SDH deficient tumors are less responsive to TKI

The prognosis of GIST depends on tumor size, mitotic rate and site of origin. Lymphovascular invasion is very uncommon in GISTs except in SDH-deficient GISTs, approximately 50% of which metastasize to lymph nodes.

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Case Number: 565

Slide Number: 21-1936

Slide View: http://www.ivp.nchu.edu.tw/ivp_slide_view.php?id=1972

Jiang, Jia-Wei (江家瑋), DVM, MS[1]; Tsao, Wen-Tien (曹文恬), DVM, MS[1]; Luo, I-Chi (羅怡琪), DVM, MS[1]

[1]HOPE Veterinary Pathology Diagnostic Center (霍普獸醫病理診斷中心)

CASE HISTORY:

Signalment: A 9-year-old, female spayed, Mixed dog

The animal was referred to valence Animal Hospital in Yilan because of anorexia and vomiting on 2021/6/18. Palpation of the abdominal cavity has no obvious pain reaction. The blood test shows mild high globulin without other abnormal. After one week, the condition has not improved, the appetite is worse. By ultrasound, there is a swelling of the small intestine near the jejunum and the has poor peristalsis. It is suspected that there may be chronic enteritis. Laparotomy was done on 2021/7/5. Laparotomy found that there was abnormal swelling in the intestine, and the peripheral mesenteric lymph nodes showed swollen. Enterectomy and entero-anastomosis was performed and submitted for pathological examination.

Gross Findings:

The received specimen included one segmental of intestine with a ring of dark red area and a larger segmental of intestine with adhesive dark red adipose tissue. On the cut section, the intestine wall of muscular layer was in dark red color comparing to normal section of intestine. The adipose tissue also shows homogeneously dark red color.

CASE RESULT:

Histopathological Findings:

Microscopically, the mucosa epithelium of intestine show no remarkable change. There shows separation of the muscularis layer by lakes of hemorrhage, a disorganized network of fibrin and neutrophilic exudate. There has no lymph node architecture in the peripheral adipose tissue. The adipose tissue also composed of hemorrhage, fibrin and scattered neutrophils infiltration.

Pathological Diagnosis:

Intestinal intramural hemorrhage/hematoma, small intestine

Differential diagnosis:

1. Hematoma

2. Hemangioma / Hemangiosarcoma
3. Congestion (by intussusception or volvulus)

Discussion:

Small intestinal intramural hemorrhage/hematomas are rare in veterinary medicine, with only 5 case report of dogs and scattered in horses before 2017[1, 2, 3]. One report in 1984 reveal three dogs that intramural hematoma of the intestine caused intestinal obstruction. Abdominal pain and vomiting can be seen with intramural hematomas secondary to mechanical obstruction in dogs[1]. In dogs, intestinal hematomas have involved the duodenum, jejunum, and ileum, but often involve the jejunum and small colon in horse[2].

In humans, intramural hematomas may occur anywhere within the gastrointestinal tract but the duodenum is the most common site due to its relatively fixed position at the ligament of Treitz. Other factors include there are rich blood supply from the submucosal vascular plexus, shorter duodenal mesentery adding to limitation of mobility, and the lack of a well-developed serosal layer resulting in decreased ability to tamponade active hemorrhage[4]. Blunt abdominal trauma is the most common cause for intramural duodenal hematomas. Pancreatic disease, anticoagulant therapy, blood dyscrasias, platelet dysfunction, and per oral endoscopic small bowel biopsy have also been implicated as predisposing factors[3].

Among non-traumatic causes, the use of oral anticoagulants is the main etiological factor. Warfarin use was associated with most cases of spontaneous intramural small bowel hematoma and heparin, low molecular weight heparin, and aspirin can also induce. Unlike to other causes of intramural hematomas, the jejunum was the most affected (71.6%) in intramural hematoma induced by anticoagulant therapy, followed by the duodenum (29.8%) and the ileum (15.8%). Compared to jejunal and ileal involvement, thrombocytopenia may result in spontaneous duodenal intramural hematoma among patients who are treated with systemic chemotherapy for malignancies[5,6].

Pancreatic disease includes acute or chronic pancreatitis, pancreatic neoplasm and ectopic pancreas. Compared with traumatic intramural hematoma, which usually occurs at the subserosal layer of the duodenum, the anatomical location of pancreatic-induced intramural hematomas is mostly underneath the duodenal mucosa or, in some situations, the hematoma dissects the muscular wall of the duodenum[7]. The exact mechanism of pancreatic-induced intramural hematoma is still uncertain, but two hypotheses have been postulated. First, the presence of ectopic pancreatic tissue within the wall of the duodenum may develop acute inflammation and subsequent necrosis, and hematoma formation. Second, leakage of pancreatic enzymes in pancreatitis can injure duodenal blood vessels[8].

In dogs, similar to humans, the duodenum is the least mobile portion of the small intestine, and has a richer blood supply than the ileum, producing 5 to 10 times more fluid. This may make the duodenum more susceptible to a large volume of hemorrhage[3]. In the 5 canine cases reported, underlying causes were associated with chronic pancreatitis in two dogs, unknown in two dogs, and one was secondary to a migrating wire foreign body. The lesion can be resolved by resection of the

involved segment of intestine, followed by anastomosis. 4 dogs recovered without complications after surgery[1,2,3].

At present, the accurate diagnosis of intramural hematomas relies on radiological studies, of which contrast-enhanced CT and magnetic resonance imaging (MRI) are the mainstay investigations of choice. Moreover, some indirect radiological signs can be evaluated, which include abnormal dilatation of the stomach and duodenum[7].

The recommended treatment for intramural hematoma in early stage is medicated treatment, including includes continuous nasogastric decompression, adequate intravenous fluid resuscitation and total parenteral nutrition to rest the bowel. Spontaneous local absorption of hematoma can occur in most circumstances. If complications have present or failed medical treatment, surgical excision should be considered[6,7,9].

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Case Number: 566

Slide Number: SE21801181 and SE21801483

Slide View:

http://www.ivp.nchu.edu.tw/ivp_slide_view.php?id=1970

http://www.ivp.nchu.edu.tw/ivp_slide_view.php?id=1971

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CASE HISTORY

Signalment: 54 year old female

Clinical history:

This 54 years old female suffered from acid regurgitation for 2 weeks, epigastric pain,fullness, tenderness, and tarry stool. She had came to ER at CMUH. UGI scope shows gastritis, no bleeding. Due to persistent refractory vomiting, even after drinking water,and poor intake, general weakness. she came to our GI oPD and then admitted for further treatment.

The past history & Operation history showed 1. Cesarean section (twice), 2. Uterine myoma status post hysterectomy, 3. Acute appendicitis status post appendectomy, 4. Malignant peripheral nerve sheath tumor arising from a left neck pigmented neurofibroma, status post operation on 104/09 and radiotherapy at 大里仁愛醫院, stop for one year, 5. Mild depression told befor.

The abdomen CT showed 1. Marked distension of stomach and duodenum with obstruction due to enhancing mass in proximal jejunum. 2. Suspected multiple metastases at right ovary, lung, liver and jejuneum. Consulation GS and arrange the operation of segmental small bowel resection

LAB data: 1070301-0306

檢驗名稱	檢驗值	單位	結果
CA-125腫瘤標記 (E	163.6	U/ml	危險
CA-125			
CA-199腫瘤標記 (E	7.9	U/ml	正常
CA-199			
癌胚胎抗原檢驗	0.58	ng/ml	正常
CEA			
α－胎兒蛋白檢驗	2.26	ng/ml	正常
AFP α-fetoprotein			
鉀 3.3	mmol/L	偏低	
K(Blood)			
血清麩胺酸丙酮酸轉 22	IU/L	正常	
S-GPT/ALT			
解脂酶 39	U/L	正常	
Lipase			
CRTN 肌酐、血			
Creatinine(B) 0.75	mg/dl	正常	
血中尿素氮 21	mg/dl	偏高	
BUN(Blood)			
血清麩胺酸苯醋酸轉 18	IU/L	正常	
S-GOT/AST			
膽紅素總量 1.3	mg/dl	正常	
Bilirubin total			
白蛋白 4.4	g/dl	正常	
Albumin			

Gross Findings:

The specimen submitted consists of a segment of small intestine measuring 33.0 cm in length and 4.0 cm in circumferences, fixed in formalin. The external surface is shaggy and congested with a focal area of obstruction by polypoid mass. On opening, the mucosa is generally dark brown. On serial section, the tumor is dark-brownish and solid with hemorrhage, measuring 7.0x6.0x6.0 cm in size and located at 4.5 cm to one section margin. The tumor is arising from the intestinal wall and to the lumen with congestion and hemorrhage.

CASE RESULT:

Histopathological finding:

The tumor shows diffuse, sheet of packed cells with small, round nuclei, displaying a monomorphous patterns. The chromatin is finely granular. The nucleoli are inconspicuous. Mitoses is frequent (>20mitoses per 10HPF). Bizarre nuclear atypia is few. The cytoplasm is pale eosinophilic and scanty. Focal tumor necrosis(<50%) with hemorrhage is seen. Melanin pigmentation is not present. Focal perforation and serosal involvement is noted. Bilateral cut ends are free. 12 regional lymph nodes are free from malignancy.
The lung biopsy shows small blue round cell tumor.

Immunohistochemical study:

The tumor cells are positive for CD99 and WT-1 (membranous pattern), Fli-1(nuclear pattern), Cyclin-D1
But negative for CK(AE1/AE3),LCA,S-100, HMB-45. Desmin, SMA, CD117, Dog-1, CD56, CD3, CD20, CD79a, CD30, CD138,CD10,CD5,CD23, Bcl-6
The lung biopsy shows : CD99(+),Fli-1(+), NSE(focal weak+), CK(-), LCA(CD45)(-), S-100(-), Desmin(-)

Differentiated diagnosis:

DDX of Malignant small round cell tumor

1. Lymphoma
2. Melanoma
3. Small cell rhabdomyosarcoma
4. Small cell neuroendocrine carcinoma
5. Desmoplastic small round cell tumor
6. GIST
7. Neuroblastoma
8. Nephroblastoma
9. Primitive neuroectodermal tumor(PNET)

Diagnosis:

1. Intestine, small bowel, segmental resection,---Primitive neuroectodermal tumor(PNET) / Extraskeletal Ewing sarcoma
2. Lung, needle biopsy,---Small blue cell tumor, compatible with primitive neuroectodermal tumor (PNET) metastasis

Discussion:

1. Primitive neuroectodermal tumor (PNET) / Extraskeletal Ewing sarcoma (PNET/ES) is a primitive round cell sarcoma that shows varying degree of neuroectodermal differentiation. In the past, the diagnoses were separated based on light microscopic, electron microscopic, and IHC features of neuroectodermal differentiation, but in recent years, it has been recognized that PNET/ES is a single entity with a shared clinical course and prognosis and similar groups of molecular genetic abnormalities.

2. The histologic spectrum of PNET/ES ranges from a neoplasm composed of uniform small round cells with round nuclei, fine chromatin, scant cytoplasm, and indistinct cell borders to a neoplasm with larger, more irregular cells with irregular nuclear contours, pseudorosettes, a nesting pattern, and even spindle cell morphology. Geographic zones of necrosis are frequently observed, with preserved perivascular clusters of tumor cells.

3. The characteristic IHC profile includes reactivity for vimentin, CD99(usually membranous), and FLI1(nuclear) with variable IHC reactivity for neural markers. IHC can be used to distinguish

PNET/ES from RMS and other small blue round cell tumor mimics, with the recognition that neither CD99 nor FLI1 protein are completely specific for PNET/ES in this contex and that a diagnostic panel of IHC stains is necessary.

4. PNET/ES has a variety of cytogenetic abnormalities that involve the EWSR1 gene, and the most common is a translocation that involves chromosomes 11 and 22 with an EWSR1/ FLI1 gene fusion.Nuclear expression of FLI1 protein is a typical for an PNET/ES with a translocation that involves the EWSR1 gene on chromosome 22 and the FLI1 gene on chromosome 11, but it is not entirely specific.

5. Strong CD99 staining in synovial sarcoma and in primitive hematolymphoid neoplasms, specially lymphoblastic lymphoma, is a potentially serious diagnostic trap that can be avoided by using a panel of IHC studies and molecular analyses. In problematic cases, cytogenetic and molecular genetic tests are useful in the differential diagnosis.

6. Ewing family of tumors- phenotypic differentiation:
   1. CNS primitive neuroectodermal tumors (cPNETs)
   2. Peripheral primitive neuroectodermal tumors (pPNETs): From soft tissues (extraosseous subtype) or bone (osseous subtype).
      (1). Osseous subtype: Ewings sarcoma

(2). Extraosseous subtype: The most common origin is thoracopulmonary region, Askin tumor

Other sites: Kidney, retroperitoneal/paraspinal regions, head and neck areas.

7. Diagnosis of PNET in Human:

Translocation involves the EWSR1 and the FLI1 genes

1. Fluorescent in situ hybridization (FISH)
2. Reverse transcriptase-polymerase chain reaction (RT-PCR)
3. Immunohistochemistry stain: CD99, FLI-1

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https://emedicine.medscape.com/article/855644-overview

Case Number: 567

Slide Number: NTU2021-2345
Slide View: http://www.ivp.nchu.edu.tw/ivp_slide_view.php?id=1973

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CASE HISTORY:

Signalment: A 11-year-old, castrated male, mongrel dog

The patient had presented anorexia and chronic vomiting for two months, which didn't improve after supporting treatments like antiemetic. There were enlarged stomach, greater and lesser curvature, and thicken muscularis revealed under USG. Thus, the excision of partial stomach and gastric lymph nodes was performed for pathological examination.

Gross Findings:

The gastric specimen submitted was firm and thick. On the cross section, the muscularis layer was apparently thickened extending from submucosa into muscular layer. On the cross section of two irregular lymph nodes, the structure of cortex and medulla were blurred.

CASE RESULT:

Histopathological Findings:

Stomach:

The gastric glands are diffuse hyperplasia, dilated and desmoplasia. The neoplastic cells along with gastric glands infiltrated into the submucosa and muscularis with lymphocytic infiltration. The neoplastic cells severely destroyed the arrangement of muscularis with neoplastic cells infiltration. The neoplastic epithelial cells have moderate to severe amount of indistinctly bordered, basophilic and polychromasia cytoplasm, round to ovoid nuclei containing prominent nucleoli and hyperchromatism. There are variable numbers of signet ring cells which contain a large central vacuole containing mucin. There are some the neoplastic emboli in the lymphatic vessels. Marked anisocytosis and anisokaryosis can be observed. Mitotic is active. The surgical margin is dirty.

Gastric lymph nodes:

There are numerous neoplastic cells and signet ring cells in the capsule of lymph nodes and occupying a large portion of cortex and medulla sinus that destroyed the lymphoid follicles, germinal

centers and trabecula. Additionally, neoplastic cells infiltrated into the adipose tissue near the lymph node.

Pathological Diagnosis:

1. Gastric carcinoma, whit lymphatic infiltration, stomach
2. Lymph node metastasis from gastric carcinoma

Differential diagnosis:

4. Gastric carcinoma
5. Gastric adenoma

Discussion:

Tumors of the canine gastrointestinal (GI) tract are uncommon that are less 1% of all reported neoplasms. However, adenocarcinoma is the most common in canine gastric malignant tumor, comprising 47 to 73% of all gastric tumors. Canine gastric carcinoma typically developed in old age, the rang of age is 8-10. In addition, it seems to occur more frequently in male than in female dogs among all subtypes of gastric carcinoma. Although there haven't been researches for the breed predisposition and clear etiology, some articles reveal the higher occurrence for several breeds, indicating the importance of genetic factors in the etiology of gastric cancer. For example, in Sibling Cairn terriers, few cases of hypertrophic gastritis (Ménétriers-like disease) progressing into superficial signet-ring-type gastric carcinoma are reported.

Gastric carcinoma usually occurs in the distal stomach. In a retrospective study, among 30 dogs, over one-half patients had gastric carcinoma in pylorus and body. At clinical signs, it is usually so mild that it's not easy for early diagnosis. The clinical signs occur due to space-occupying gastric mass, which are some non-specific signs such as chronic vomiting or anorexia and so on. At gross lesion, it may be found a leather-bottle stomach, and the surface of mucosa may have discrete, polyploid lesion or ulcerated plaques. In two retrospective study, the sites usually having metastasis are lymph nodes, either local or distal. It is corresponded with our case.

According to histopathologic features, there are two subtypes under Lauren system.

One is intestinal type, which indicates it has distinct glandular structure with lumen and the epithelial cells is well-differentiated and well-polarized. It has the infiltration of the apparent groups of acini with interacinar stroma. It has less extracellular mucin than diffuse type, and low mitotic index with wide pleomorphism. Another type is diffuse type, which the infiltration of neoplastic cells is random, either singly or in small clusters. It has less glandular structures than intestinal types, which the diffuse type of gastric adenocarcinoma is more common in the dog.

There is another histological classification from WHO, which divided into 5 subtypes. First is papillary type, it forms exophytic folds which are supported by fibrous stroma. Next is tubular type, the neoplastic cells present in tubules within connective tissue. The other one is signet ring cells type, which is saying that the majority of cell is signet ring cells displacing the nuclei. Fourth, mucinous

type indicates that over 50% of neoplastic cells produce mucin and there are pools of extracellular mucin. The last one is undifferentiated type, it presents severe desmoplasia with high cellularity and pleomorphism. Accompanied with the signet ring cells and extracellular mucin.

About treatment, complete surgical excision is the only curative option. However, if the patients have metastasis, it makes the complete resection difficult due to wide range of excision. The survival time in untreated dogs is less 3 months. If under surgical excision, the survival time will be prolonged, however some cases may only have 2 days. The poor prognosis may be due to the late diagnosis, which the patient died soon after diagnosis compatible with lymph nodes or other organs metastasis.

Back to this case, the signalment of the patience containing old age, gender and clinical signs, is consistent with the predisposition of the previous research. In this case, the poor prognosis which the animal died two days after the surgery may be associated with late diagnosis that he had lymphatic and distal metastasis to abdomen organ. Thus, although the excision of one-half stomach had performed, it still couldn't prevent the progression of the tumor.

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Case Number: 568

Slide Number: 152933H
Slide View: http://www.ivp.nchu.edu.tw/ivp_slide_view.php?id=1975

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CASE HISTORY:
Signalment: A 31-year-old female

Clinical history:

A 31-year-old female visited at our ER Department due to persistent abdominal pain and vomiting several time since four days ago.

The patient was robust in the past. She has a history of thalassemia diagnosed two months ago, and endometriosis of the left ovary post-oophorectomy. Four days ago, she suffered from abdominal pain and vomiting developed. She called at Taoyuan Hospital and received the EGD (Esophagogastroduodenoscopy) and gastroesophageal reflux disease (GERD) was told with medications. She was no episodes of defecation with bloody stool. He denied any changes in appetite or weight loss. He was admitted under the abdominal pain, cause be determined, thalassemia with microcytic anemia.

She is a Taiwanese. She has no systemic disease except thalassemia was told two months ago. She had no habit of social alcoholic beverages drink or use illicit drugs. No history of traveling or going to abroad in recent six months. She was denied allergy to food or drugs. She denied any family genetic history or cancer.

In admission, physical examination, body height, 165 cm; body weight, 64 kg; vital sign showed BT, 36°C; PR, 82/min; RR, 19/min; BP, 115/60 mmHg. General appearance showed alertness with ill-looking. HEENT conditions were no conjunctiva, no icteric sclera, or palpable mass over head and neck areas. Heart was regular heart beats, S1→S2, S3→S4, no thrill. Chest showed symmetric chest wall expansion, clear breath sound, no rhonchi, no wheezing or basal rales. Abdomen was soft and ovoid, distend, normal bowel sound, no shifting dullness, mild tenderness, and rebound tenderness, Muscle guarding (+), local tenderness over McBurney site (-), or no palpable liver or spleen. Back and spine showed no spine deformity, no costovertebral angle knocking pain. Genitourinary showed no hernia, no deformity or sexual organs. Extremities showed no clubbing or cyanosis or pitting edema. Neurological examination showed non-remarkable significant or neurological defect. Digital rectal examination showed non-tenderness or nodularity. Others were non-contributions.

Laboratory results (Clinical Pathology) and Imaging study:

The laboratory data included the CBC, Hb was 5.1 gm/dL (14.0-18.0), WBC was leukocytosis with 4.5 x 10^3/ul (4500-11000), N/L was 76/12.7, Hct, 20.2; MCV, 50.1; MCH, 12.7; MCHC, 25.2. The biochemistry results showed within normal limits. The serum tumor biomarkers included CA199, AFP, CEA, PSA, and beta-HCG displayed within normal limits. The CxR image showed no significant finding. Sonography of the abdomen showed mild ascites, no abnormal finding. The CT-scan of the abdomen and pelvis showed lobulated thickened over the mid-descending, sigmo-descending junction, and sigmoid colon with mechanical bowel obstruction. In addition, regional lymph nodes enlargement was noted. There also presented two small nodules measured 2.1 cm and 2.5 cm in the right adrenal gland, and suspected metastatic lesions was considered. Bilateral pleural effusion and small amount of ascites was also found. Colonoscopy revealed many large pedunculated or fungate polypoid masses over the rectum and distal sigmoid levels. In addition, there also presented multiple sessile and pedunculated polyps from sigmoid colon to descending colon, located at 20 cm to 50 cm in levels above anal verge. So, the suspected malignancies and FAP syndrome was first considered. Subsequently, the colonoscopic mucosa biopsy was performed. Esophagogastroscopy showed reflux esophagitis, Los Angeles grade A, and mild chronic gastritis, and duodenal poly s/p polypectomy. Subsequently, she underwent subtotal colectomy under the final pathological diagnosis.

Gross Findings:

The specimen submitted consisted of a segmental terminal ileum measure 6 cm in length and 4 cm in diameter of the lumen, and subtotal colectomic colonic tissue fragment measure 64 cm in length and 4 to 6 cm in the maximal diameter of the lumen. Appendix measured 5.5 cm in length and 1 cm in maximal diameter of the lumen. On sections, an irregular ulcerative fungate mass measured 5 x 4 x 3 cm over the descending colon with lumen narrowing to nearly total obstruction, and multiple polypoid masses were distributed the whole colonic lumen. These polypoid masses measured 6 x 4 x 2 cm in the largest one.

CASE RESULT:

Histopathologic Findings:

Microscopically, the cecum, ascending, transverse, descending colon demonstrated pictures of distributed multiple tubular, villous, and tubulovillous adenomas with low to high-dysplasia, and malignant transformed to adenocarcinomas. The malignant cells directly invaded onto the mascularis propria and subserosa. The pericolonic lymph nodes showed metastatic adenocarcinoma in 2 out of 37 lymph nodes. The appendix showed fecalith and severe congestion with free from tumor involvement

Differential Diagnoses:

1. Multiple adenomatous polyps: Tubular, villous, tublovillous adenomas with high-grade dysplasia.

2. Adenomatous polyps malignant transformation to adenocarcinomas
3. Familial adenomatous polyposis (FAP) syndrome associated with colorectal adenocarcinoma.

Immunohistochemistry:

These lymphoma cells showed positive for histochemical staining for PAS and mucin stains. These carcinomatous cells demonstrated positively diffusely immunoreactivity for pan-CK, CD20, CEA, Muc-1, increase expression for CDX2 and proliferative Ki-56 labeling index, focal positive for CK7, and overexpression for EGFR (Allred score 5/3+2). The dMMR/MSI (MLH1, MSH2, MSH6, PMS2) in IHC analysis showed no-significant result. The patient was assigned to CRS OPD for the continuation of the diagnostic and therapeutic process.

Anatomic Diagnosis:

- **Descending colon, adenocarcinoma, grade 2; C/W FAP syndrome associated advanced CRC.**
  - Pathological TNM stage: pT3N1bM1a (correlate with clinical M), with metastases to right adrenal gland, Stage IV based on the 8th ed. AJCC staging system.

Follow-up and workup:

She received loop colostomy with adhesiolysis with decompression, colonoscopy, subtotal colectomy and colo-anal anastomosis with adhesiolysis, drainage of intra-abdominal abscess with diverting ileostomy, revision of ileostomy and sigmiodoscopy during hospitalized days.

Discussion:

Familial adenomatous polyposis (FAP, or classic FAP,) is a genetic, rare an autosomal dominant inherited condition in which numerous adenomatous polyps form mainly in the epithelium of the large intestine. While these polyps start out benign, malignant transformation into colon cancer occurs when they are left untreated. Three variants are known to exist, FAP and attenuated FAP (originally called hereditary flat adenoma syndrome are caused by APC gene defects on chromosome 5 while autosomal recessive FAP (or MUTYH-associated polyposis) is caused by defects in the MUTYH gene on chromosome 1. Familial adenomatous polyposis (FAP) is an inherited disorder characterized by cancer of the large intestine (colon) and rectum. People with the classic type of FAP may begin to develop multiple noncancerous (benign) growths (polyps) in the colon. When a person has more than 100 adenomatous colonic polyps, he will be diagnosed. Adenomatous polyps are areas where normal cells in the human colon form masses inside the intestine. The average age of polyps in FAP patients is about 15 years old. Most people with FAP will have multiple colonic polyps by the age of 35. Therefore, if FAP is not recognized and treated at an early stage, a person may develop colorectal cancer.

Signs & Symptoms of the classic FAP is characterized by hundreds to thousands of colorectal adenomatous polyps, with polyps appearing on average at age 15 years. Without colectomy, affected

individuals usually develop colorectal cancer by the third or fourth decade of life. FAP is also associated with an increased risk for cancer of the small intestine including the duodenum, and cancer of the thyroid, pancreas, liver (hepatoblatoma), central nervous system (CNS), and bile ducts, although these typically occur in less than 10% of affected individuals.

Synonyms of Familial Adenomatous Polyposis include adenomatous polyposis of the colon (APC), familial multiple polyposis (FAP), hereditary polyposis coli multiple polyposis of the colon. Subdivisions of FAP include attenuated FAP, familial adenomatous polyposis, Gardner syndrome, Turcot syndrome, etc. Not all symptoms of FAP are cancer-related. Some additional features of FAP may include: Osteomas, which are non-cancerous bony growths, usually found on the jaw. Extra, missing, or unerupted teeth. Congenital hypertrophy of the retinal pigment epithelium (CHRPE). This is an eye condition that is present at birth that does not affect vision, but it is a condition that an eye doctor may see during an examination with a special instrument called an ophthalmoscope. Non-cancerous skin changes, such as epidermoid cysts and fibromas, and adrenal masses.

Colorectal cancer (CRC) accounts for over 8% of all deaths annually worldwide. Between 2 and 5% of all CRCs occur due to inherited syndromes, including Lynch syndrome, familial adenomatous polyposis, MUTYH-associated polyposis, Peutz-Jeghers syndrome, juvenile polyposis and Cowden/PTEN hamartoma syndrome. What are the estimated cancer risks associated with classic FAP and its subtypes? Colorectal cancer, up to 100% if polyps not removed, desmoid tumor, 10% to 20%; small bowel (intestines), 4% to 12%; pancreatic/ampullary cancer, 2%; papillary thyroid cancer, 2% to 25%; hepatoblastoma, 1.5%; brain or central nervous system tumor, less than 1%; stomach cancer, 5%; bile duct cancer, slightly increased risk; adrenal gland cancer, slightly increased risk. Making the diagnosis of FAP before the development of colon cancer is important not just for the individual, but also for the sake of other family members who may be affected. Two diagnostic methods exist: FAP diagnosis is made in younger people by the presence of the typical polyps and in immediate relative with FAP or by genetic testing.

Genetic counseling is recommended for individuals with FAP and their at-risk family members. This is very helpful to properly obtain and interpret genetic testing. In this patient has no history of family inherited malignant disease, there is no way to trace whether he is directly related to genetics. The inherited CRC syndromes are a series of diseases that have specific mutations that predispose to CRC, so these are more aggressive and have a worse prognosis since they correlate with other tumors and some do not respond to chemotherapy. Early diagnosis is a challenge for physicians due to the absence of pathognomonic clinical findings. The pathogenesis of this case is very similar to the previous reported cases.

In our case, we went to the emergency room because of abdominal pain and suspected intestinal obstruction. In the laboratory tests, there was thalassemia with severe anemia. Subsequent endoscopy of the upper gastrointestinal tract and lower gastrointestinal tract revealed that there were polyps in

the duodenum, and the colon endoscopy revealed prominent lumps in the sigmoid colon and descending colon, suspected of malignancy Tumor. In addition, multiple polyps were found from the sigmoid colon to the ascending colon. So it may also be related to FAP syndrome. Then the pathological report of the large intestinal mucosal section was confirmed to be adenocarcinoma. Then the patient underwent subtotal colectomy. Unfortunately, the complications occurred in the process of treatment, She received again went through intra-abdominal abscess drainage and diverting ileostomy. Finally, he was discharged from the hospital after multidisciplinary cross-team treatment. He was transferred to the colorectal surgery clinic to continue medication and follow-up. Whether thalassemia is related to FAP is worth exploring. At present, there is still no evidence in the literature to show that thalassemia is directly related to the incidence of colorectal cancer. Subsequently, we tracked her family history and found no other family members had similar illnesses.

Although the majority of CRCs develop via a chromosomal instability pathway, approximately 12-15% have deficient DNA mismatch repair (dMMR) which is characterized in the tumor by microsatellite instability (MSI). Tumors with the dMMR/MSI develop from a germline mutation in an MMR gene (MLH1, MSH2, MSH6, PMS2), i.e., Lynch syndrome, or more commonly from epigenetic inactivation of MLH1 MMR gene. CRCs with dMMR/MSI status have a distinct phenotype that includes predilection for the proximal colon, poor differentiation, and abundant tumor infiltrating lymphocytes. Decades have passed since the underlying molecular etiologies of the most common hereditary forms of colorectal cancer (CRC), Lynch syndrome, and familial adenomatous polyposis (FAP) were first described. With the advent of next-generation sequencing (NGS) panels, the landscape of hereditary CRC testing has changed dramatically. The evolving field of cancer genetics offers great challenges and opportunities for improved CRC management. Genetically, CRC is a very heterogeneous disease with many factors playing key roles in pathogenesis. There are two types of CRC, hereditary with an incidence of between 5% and 10% with APC (FAP, aFAP) or MMR (HNPCC) genes affected, and sporadic colorectal cancer with an incidence of 90-95% with a lot of mutations in variable genes that accumulate during pathogenesis (APC, KRAS, MMR, microRNA, CIMP etc.). Knowledge of the molecular pathogenesis of CRC (hereditary, sporadic) is crucial for treatment, assessment of risk, prognosis, and patient follow-up.

Conclusion:

FAP is not recognized and treated in early stage, there is a very high likelihood that a person will develop colorectal cancer. Individuals with FAP also have an increased chance of developing cancer in other organs, including the stomach, small intestine, and the pancreas and biliary tree. Familial adenomatous polyposis (FAP) is a rare disease where a number of precancerous polyps develop in the large intestine, increasing chances for cancer. Preventive surgery is the standard treatment.

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