A Feline Intestinal Adenocarcinoma in Domestic Shorthair Cat: A Case Report

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Abstract

A 15-year-old, spayed female domestic shorthair cat was presented with clinical signs of weight loss, decreased appetite, and chronic vomiting persisting for more than 3 months. The cat had been given fenbendazole, probiotics, and a hydrolyzed diet; however, the symptoms, including vomiting and diarrhea, waxed and waned. The biochemical results revealed that feline pancreatic lipase, serum folate, and serum cobalamin were still within normal limits. Diagnostic imaging, including abdominal radiograph and ultrasonography, revealed a mass-like lesion cranially located in the urinary bladder and a significant thickening of the small intestinal wall. Due to the marked thickening and apparent obstruction of the jejunal wall, a jejunal resection and anastomosis were performed. The resected jejunal tissue was submitted for fungal culture and histopathologic examination. The microscopic diagnosis of the resected tissue was intestinal adenocarcinoma. Fungal culture on Sabouraud dextrose agar (SDA$^+$) was identified as *Aspergillus* sp. with a suspect of *A. fumigatus*. However, no fungal elements were detected by histopathology, and there was no positivity on Periodic Acid Schiff staining. Thus, a fungal infection is indefinite. Abdominal ultrasound conducted three days post-operation revealed a normal wall's thickness, normal peristalsis, and no dilation of the small intestine. There was no evidence of ascites or peritonitis. No signs of recurrence were detected during the 78 days post-operation. Nevertheless, the disease relapsed with neoplastic abdominal effusion, and a cat died four months after the operation.

รายงานสัตว์ป่วย: มะเร็งลำไส้ชนิดอะดิโนคาร์ซิโนมาในแมวไทยขนสั้น

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บทคัดย่อ

แมวพันธุ์ผสมขนสั้น เพศเมีย ทำหมัน อายุ 15 ปี มาเข้ารับการตรวจและรักษาที่โรงพยาบาลสัตว์ประศุอาทร ด้วยอาการ น้ำหนักลด ความอยากอาหารลดลง และอาเจียนเรื้อรังมากกว่า 3 เดือนแมวเคยได้รับการรักษาด้วยยาเฟนเบนดาโซล โปรไบโอติก และอาหารประเภทโปรตีนไฮโดรไลซ์ แต่ยังคงมีอาการอาเจียนและท้องเสียอยู่เป็นระยะ ผลการตรวจค่าชีวเคมีในเลือด แสดงระดับเอนไซม์ไลเพส ระดับโฟเลต และโคบาลามินในเลือดยังอยู่ในระดับปกติ ภาพถ่ายรังสีช่องท้องและการตรวจช่องท้อง ด้วยคลื่นเสียงความถี่สูงแสดงถึงลักษณะคล้ายก้อนเนื้ออยู่บริเวณหน้ากระเพาะปัสสาวะ และพบการหนาตัวของผนังลำไส้เล็ก อย่างมีนัยสำคัญ แมวได้รับการผ่าตัดตัดต่อลำไส้เพื่อตัดลำไส้ส่วนที่หนาตัวออกแล้วส่งชิ้นเนื้อเพื่อส่งตรวจวินิจฉัยด้วยวิธีการ เพาะเลี้ยงเชื้อราและการวินิจฉัยทางพยาธิวิทยา ผลวินิจฉัยชิ้นเนื้อทางจุลพยาธิวิทยา บ่งบอกว่าเป็นมะเร็งลำไส้ชนิดอะดิโนคาร์ซิโนมา ผลการตรวจด้วยวิธีการเพาะเชื้อราพบเชื้อราชนิดแอสเปอร์จิลลัส ฟูมิกาตัส แต่เนื่องจากไม่พบสายใยของเชื้อราจากการตรวจทาง จุลพยาธิวิทยาจากตัวอย่างที่ย้อมด้วยสีฮีมาท็อกไซลินและอีโอซินและสีย้อมชนิด Periodic Acid Schiff จึงคาดว่าอาจมาจากการ ปนเปื้อน ผลการตรวจช่องท้องด้วยภาพสะท้อนคลื่นเสียงความถี่สูงสามวันหลังจากการผ่าตัดพบว่า ลำไส้เล็กมีความหนา และ มีอัตราการบีบตัวเป็นปกติ ไม่พบการขยายตัวของลำไส้และ ไม่พบภาวะท้องมานหรือภาวะเยื่อบุช่องท้องอักเสบตลอด 78 วัน หลังการผ่าตัด อย่างไรก็ตาม แมวกลับมาด้วยภาวะน้ำในช่องท้องที่มีเซลล์มะเร็งเป็นองค์ประกอบและเสียชีวิตที่ 4 เดือนหลังผ่าตัด

คำสำคัญ : มะเร็งชนิดอะดิโนคาร์ซิโนมาในแมว มะเร็งลำไส้ เนื้องอกในช่องท้อง

Introduction

Feline intestinal adenocarcinoma (FIA), a highly malignant form of non-hematopoietic gastrointestinal tumors, constitutes nearly one-third of all feline intestinal tumors (Rissetto et al., 2011). It ranks as the second most common alimentary neoplasm in cat, representing 7-27% of all alimentary tumors, following lymphoma, which range from 44-63% in the literature (Rissetto et al., 2011; Willard 2012; John et al., 2017; Czajkowski et al., 2022). The aggressive nature of this disease often leads to intestinal obstruction due to its annular stenosing growth pattern (Patnaik et al., 1976; Cribb 1988).

Most feline intestinal neoplasms are found in the small intestine, with 61-97% of all intestinal tumors. However, one report noted that 69% of intestinal adenocarcinoma (ACA) was diagnosed in the colon. Specifically, ACA is predominantly found in the small intestine, accounting for 82% of cases (Rissetto et al., 2011). Although some earlier studies reported approximately equal representation, intestinal ACA is typically more common in males (Patnaik et al., 1975, 1976; Turk 1981; Cribb 1988). In several studies on intestinal neoplasms, particularly those investigating intestinal ACA, the Siamese cat breed is often the most represented (Patnaik et al., 1976; Turk 1981; Cribb 1988; Kosovsky et al., 1988).
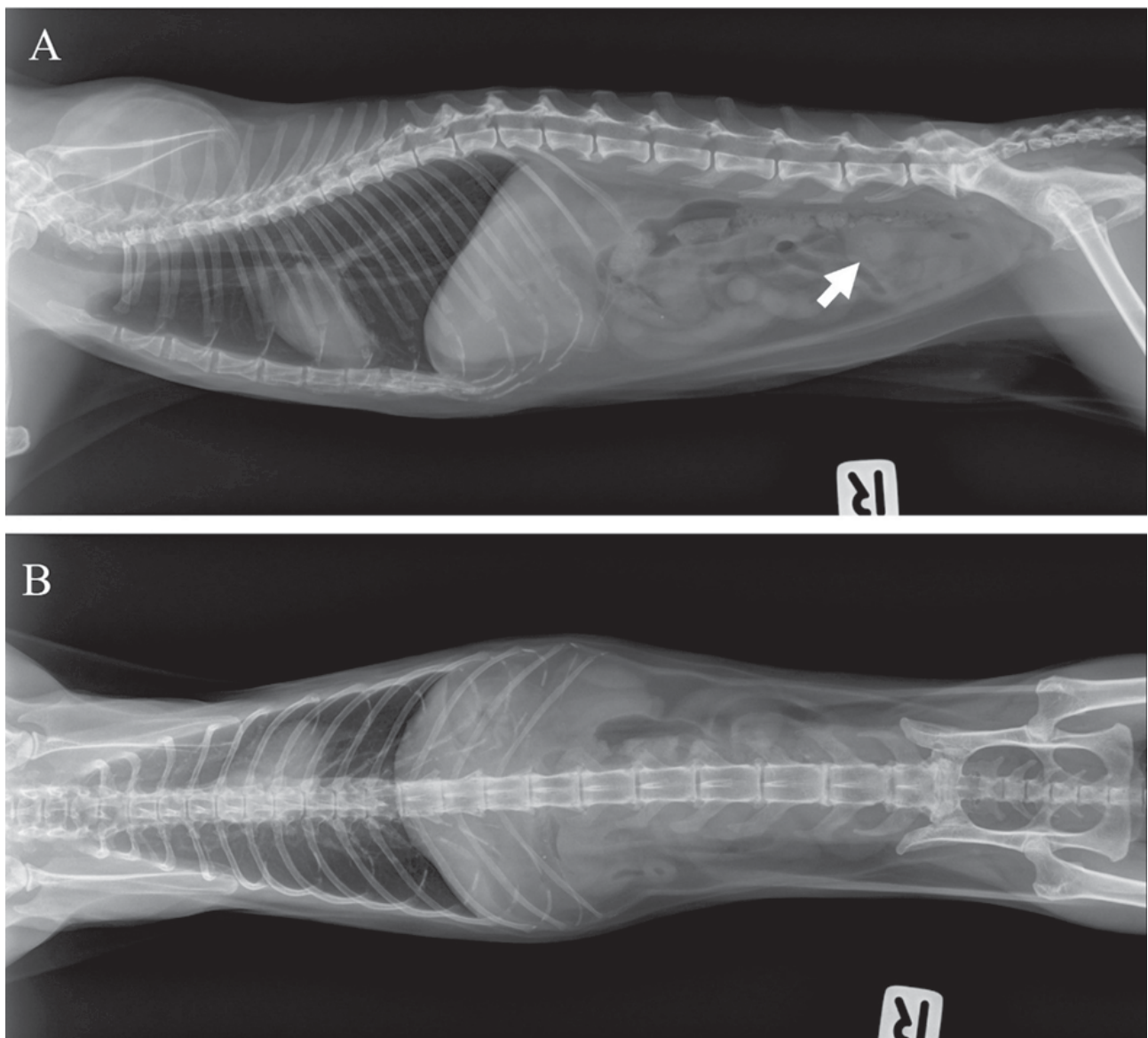
The age at which cats are diagnosed with feline intestinal ACA can vary. One study showed that the average age of diagnosis was 10.7 years (Cribb 1988), while a more recent study reported a median age of 12 years at the time of diagnosis, with an age range from 6-17 years (Czajkowski et al., 2022). The most common clinical signs associated with FIA include weight loss, vomiting, hyporexia, diarrhea, constipation or tenesmus, and hematochezia (Czajkowski et al., 2022). These symptoms are often associated with the tumor's rapid growth, which

can lead to partial or complete blockage of the intestine (Patnaik et al., 1976; Cribb 1988). The factors that increase the risk of developing intestinal neoplasia include predisposing breeds such as Siamese and age greater than 7 years (Czajkowski et al., 2022).

Case description

A 15-year-old spayed female domestic shorthair cat weighing 2.7 kg was presented to Prasu-Arthorn Animal Hospital, Faculty of Veterinary Science, Mahidol University, with a history of weight loss, decreased appetite and chronic vomiting for more than 3 months. The cat was fed commercial and home-cooked diets. For the history of the health program, a cat only received the rabies vaccination. Physical examination showed that the cat had normal vital signs. No abdominal discomfort was perceived on abdominal palpation. Internal parasite was also not detected on direct fecal examination.
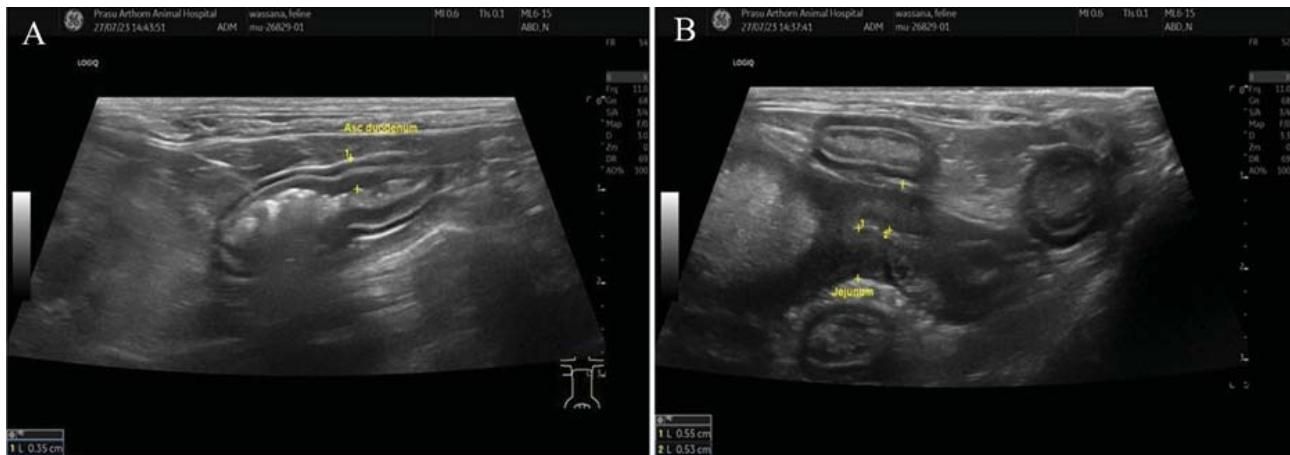
Hematological profiles revealed mild leukocytosis, neutrophilia with left shift and mild thrombocytopenia with adequate platelet numbers on the blood smear. Normal biochemical profiles were observed. Feline pancreatic lipase (fPL), serum folate, and serum cobalamin were still within normal limits. Abdominal radiograph indicated a mass-like lesion located cranially to the urinary bladder (Figure 1). Abdominal ultrasonography revealed diffuse thickening of the small intestinal wall. The jejunum was typically thickened with prominent muscularis layers (0.3-0.4 cm thickness). The most severe lesions showed segmental thickening (0.5 cm thickness) with loss of intestinal wall layers. The most thickened lesion was approximately 5 cm. in length. Duodenum and ileum were also mildly thickened to 0.35 cm. and 0.3-0.4 cm, respectively, with a prominent muscularis layer. Jejunal lymph nodes were enlarged with homogeneous
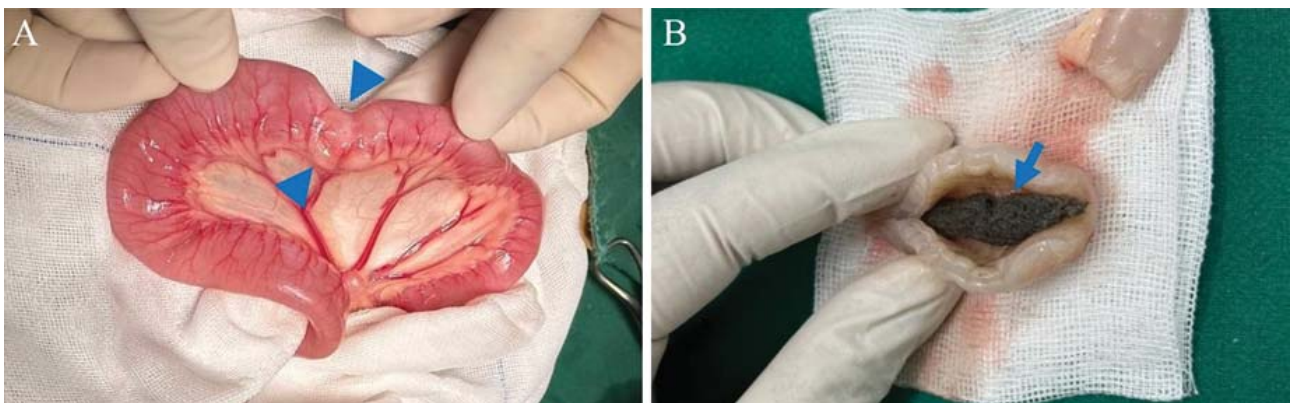
Figure 1. Radiographic imaging of thorax and abdomen. A) The right lateral view revealed a soft tissue opacity mass-like lesion cranially to the urinary bladder (arrow). B) Radiographic imaging of dorsoventral view.

hypoechoic parenchyma (Figure 2). A part of the jejunal wall was markedly thickened and obstructed, leading to a jejunal resection and anastomosis. Grossly, the resected sec-tion was obstructed by a hairball (Figure 3). The jejunal tissue was submitted for fungal culture and histopathologic examination.

Figure 2. An abdominal ultrasonography (linear probe 11MHz). A) mild thickening of duodenal and jejunal wall. B) A marked thickening of the jejunal wall with a loss of the intestinal wall layer.

Figure 3. Exploratory laparotomy. A) The jejunal segment that is thickened and obstructed (arrowhead). B) The resected jejunal segment that appears to be obstruction by the hairball (arrow).

Microscopically, the tissue section exhibited an extensive growth of neoplastic cells mostly pronounced in the mucosal layer with multiple small numbers in submucosal and muscular layers. The lateral margin of the neoplasm was considered poor. There was a lake of mucin-like particles observed within the submucosal layer. The neoplastic cells were arranged in irregular glands to solid nests pattern on the dense fibrous tissue. Cell shapes were mainly 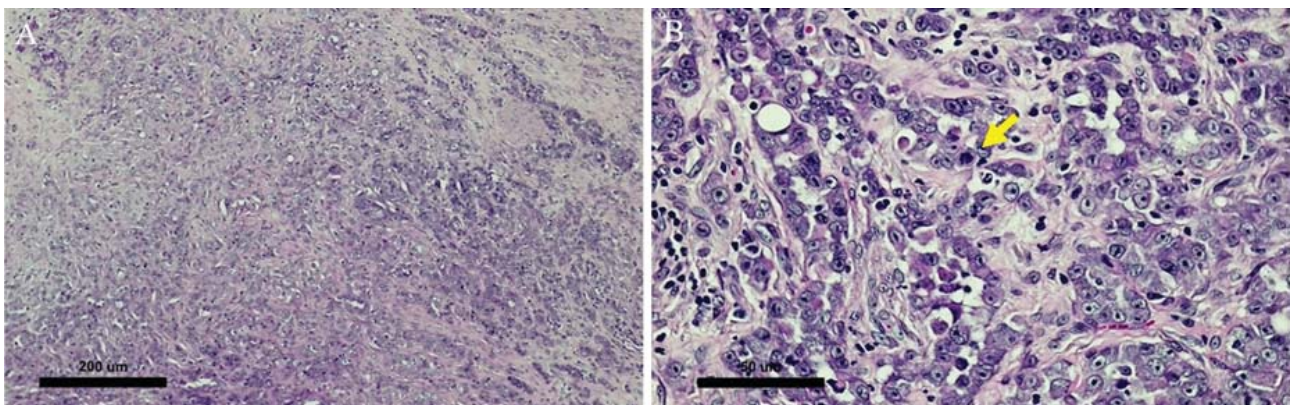cuboidal with conspicuous cell border in glandular area and polygonal in solid area. Small to moderate amount of eosinophilic cytoplasm was noted with round to oval shaped nuclei, finely granulated chromatin and often with single prominent nucleolus. Anisocytosis and anisokaryosis were marked. Mitotic figures were 10 cells/2.37 mm^2. The cells in the subjacent layers and in other sections were poorly differentiated; however, few granulated, plumped cells were seen. These cells were considered related to goblet cells that they

reacted with PAS staining similar to goblet cells in non-affected mucosal epithelium. Neutrophils and lymphocytes infiltration were spontaneously observed in the vicinity of neoplastic areas. Vascular invasion was not observed (Figure 4). The neoplasm was diagnosed as intestinal adenocarcinoma. Mold and yeast excluding dermatophytes conventional culture on Sabouraud dextrose agar (SDA^+) was identified as *Aspergillus* sp. Based on macroscopic and microscopic morphology, *A. fumigatus* was the most suspected species. However, histopathology detected no fungal elements, and Periodic Acid Schiff (PAS) staining was negative. As a result, the fungal infection could be ruled out.

Following abdominal ultrasonography conducted three days post-operation revealed no dilation, normal thickness of the small intestine, and a standard peristalsis rate of six times per minute. There was no evidence of ascites or peritonitis. No signs of recurrence were detected 78 days post-operation. Regrettably, the cat returned with ascites. A subsequent abdominal ultrasonography showed diffuse thickening across all sections of the small intestine, with a prominent muscularis layer. Anechoic peritoneal fluid was observed, earning an AFAST score of 4/4. The cat passed away 21 days after the initial detection of ascites. Fluid cytology samples revealed a high protein concentration and a moderate nucleated cell count. Numerous small clusters of papillary projections consisting of oval to polygonal tumor cells were observed, along with a significant number of neutrophils and macrophages. The tumor cells exhibited large oval nuclei, prominent multiple nucleoli, and abundant vacuolated cytoplasm. The cytologic diagnosis pointed towards neoplastic effusion, with carcinoma being the most suspected condition.

Figure 4. Histopathological findings. A) Hematoxylin and eosin stain of jejunal section at 100x, 200 µm scale bar (left). B) Hematoxylin and eosin stain of jejunal section at 400x, 50 µm scale bar showed neoplastic cells appeared as poorly arranged glands. Small to moderate amount of eosinophilic cytoplasm was noted with round to oval shaped nuclei, finely granulated chromatin and often with single prominent nucleolus. Mitotic figure is presented (arrow)

Discussion

Feline intestinal adenocarcinoma (FIA), the most common non-hematopoietic gastrointestinal tumor, accounts for 8% of all non-hematopoietic tumors (Turk et al., 1981; Rissetto et al., 2011). Adenocarcinoma (ACA), a malignant tumor resulting from unregulated cell growth within glandular tissue, is generally locally invasive and often metastasizes to local or distant sites, with rates of local and distant metastases reported to range from 55-76% (Patnaik et al., 1976; Czajkowski et al., 2022). FIA represents 7-27% of gastrointestinal neoplasia in cats (Patnaik et al., 1976; Turk et al., 1981; Cribb 1988; Rissetto et al., 2011). Cats diagnosed with intestinal adenocarcinoma typically fall within the middle to old age bracket, with affected individuals ranging from 5 to 17 years old and an average age of 11.3 years (Patnaik et al., 1976). A more recent study suggests an older age trend, with a median age of 14 years and mean ages spanning 8.7 to 11.3 years (Green et al., 2011). The most comprehensive case series on feline intestinal neoplasia, which include 1,129 cases, also highlights that Siamese cats and those over the age of 7 are at increased risk for developing this condition. Specifically, Siamese cats have a 3.7-fold higher risk of developing any form of intestinal neoplasia (Rissetto et al., 2011). While a male predominance is commonly reported in the literature, some studies have found an equal gender distribution (Patnaik et al., 1975, 1976; Turk et al., 1981; Cribb 1988; Kosovsky et al., 1988; Rissetto et al., 2011). In the present case, the 15-year-old cat falls into the high-risk category for developing intestinal tumors.

In this case report, the cat exhibited clinical signs consistent with feline intestinal adenocarcinoma (FIA), including weight loss, reduced appetite, and chronic vomiting over a three-month period. These symptoms are among the most common clinical signs associated with small intestinal adenocarcinoma, as reported in the literatures (Green et al., 2011; John et al., 2017; Czajkowski et al., 2022). Such symptoms often result from the rapid growth of the tumor, which can lead to a partial or complete intestinal obstruction due to its annular stenosing growth pattern (Patnaik et al., 1976; Cribb 1988). The most frequent physical examination findings include a palpable abdominal mass, emaciation, and dehydration (Cribb 1988; Kosovsky et al., 1988; Green et al., 2011). The absence of abdominal discomfort upon palpation and the lack of internal parasites in fecal examination further support a neoplastic diagnosis. The hematological profile revealed mild leukocytosis and neutrophilia, which were common in cats with systemic inflammation or stress. The presence of left shift and mild thrombocytopenia could be indicative of an ongoing inflammatory response (Rivers et al., 1997; Czajkowski et al., 2022). The normal biochemistry profile, fPL, serum folate, and serum cobalamin ruled out other potential causes, such as pancreatitis and malabsorption syndromes (Zoran 2006; Watanabe et al., 2012). The radiographic and ultrasonographic findings provided further evidence towards a neoplastic condition. The mass-like lesion observed cranially to the urinary bladder and the diffuse thickening of the small intestinal wall, particularly the jejunum, were indicative of a localized neoplastic process. The enlargement of the jejunal lymph nodes could suggest a possible cancer cells invasion. However, only 9% of cats have imaging results that indicate intrathoracic metastases (Czajkowski et al., 2022).

The most accurate diagnosis of Feline Intestinal Adenocarcinoma (FIA) is typically achieved through a surgical biopsy. For cats undergoing ultrasonography-guided fine needle aspiration cytology, less than half of

the cases showed results that were consistent with histopathology (Czajkowski et al., 2022). Adenocarcinomas are classified into four groups based on histologic characteristics include adenocarcinomas with a solid group of cells (carcinoid), adenocarcinomas with both solid and acinar cells, papillary adenocarcinoma, and mucinous adenocarcinoma (Patnaik et al., 1976). In this case, In this case, the histopathological examination confirmed the diagnosis of intestinal adenocarcinoma. Three months following intestinal mass resection, a cat developed a neoplastic abdominal effusion, which was suspected to be carcinoma. As a result, this cat possibly had FIA at a metastatic stage. FIA metastasizes rapidly, with 72-84% reported to have detectable metastases at diagnosis. Rates of local and distant metastases have been reported with range from 55-67% (Turk et al., 1981; Green et al., 2011; Czajkowski et al., 2022). Regional lymph nodes, peritoneum, liver, and lungs have been reported to be the most frequent sites of ACA metastases (Turk et al., 1981; Cribb 1988; Kosovsky et al., 1988; Green et al., 2011).

In this report, *Aspergillus* sp. was identified by fungal culture. Based on macroscopic and microscopic characters, *A. fumigatus.* was suspected. The standard diagnostic techniques for identifying species were matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) and polymerase chain reaction (PCR) (Arastehfar et al., 2022). A metagenomic study has revealed that fungi constitute between 0.02% and 0.3% of the feline gastrointestinal microbiota. Among these, Aspergillus and Saccharomyces are reported to be the most abundant fungal genera (Barry et al., 2010; Handl et al., 2011; Minamoto et al., 2012; Tun et al., 2012). However, the absence of fungal elements in histopathology and

negative PAS staining suggest that this could be a contamination rather than a true infection in this cat. Therefore, it is crucial to consider the results of the fungal culture identification in conjunction with the histopathological findings to confirm the diagnosis.

Surgical resection is the treatment of choice for malignant non-hematopoietic intestinal tumors in cats regardless of the presence or absence of metastasis. Cats diagnosed with ACA and subsequently treated with surgery demonstrated a significantly extended survival time, with a median survival duration of 365 days. Obtaining clean margins following the surgical resection of an intestinal mass is widely recognized to lead to improved outcomes (Bakaeen et al., 2000). In order to achieve a comprehensive removal of intestinal tumors, it has been suggested that the surgical boundaries should range from a minimum of 2 cm to a maximum of 8 cm (Vail 2011). In contrast, cats suspected of having ACA but did not undergo surgical removal had a median survival time of only 22 days. Moreover, cats showing no signs of metastatic disease at the time of surgery had a median survival time of 843 days, compared to 358 days for those with metastatic disease (Green et al., 2011). However, it's important to note that complete mural margins were only present in 15% of cats, and local lymph node metastases were identified in 52% of cats. A recent study revealed that the administration of adjuvant chemotherapy was not significantly associated with improved disease-free or overall survival. However, it is possible that a selection bias was present, which the adjuvant chemotherapy is more likely administered in cats with more advanced disease. (Czajkowski et al., 2022).

After the intestinal resection and anastomosis were performed, all previous clinical signs, including weight

loss, vomiting, and anorexia, were resolved. Post-operative abdominal ultrasonography revealed a normal thickness throughout the small intestine. This improvement may be attributed to the cat having concurrent intestinal adenocarcinoma and food-responsive enteropathy; the intestinal thickening was resolved as a result of a food trial with a hydrolyzed protein diet. (Heilmann et al., 2024). However, the cat's owner was lost to a follow up thereafter. Regrettably, 78 days post-surgery, the disease relapsed with neoplastic abdominal effusion, and the cat died four months after the operation.

In conclusion, this case report provides valuable insights into the clinical, radiographic, ultrasonographic, and histopathological findings in a cat diagnosed with intestinal adenocarcinoma. It highlights the importance of a comprehensive diagnostic approach to ensure an accurate diagnosis. Additionally, complete surgical resection with adequate margins is crucial and directly affects the disease-free and overall survival time.

Acknowledgments

Conflict of interest

The author has no conflicts of interest to declare.

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