Internal Medicine

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Title: Ultrasound, CT and FDG PET-CT of Duodenal Granuloma in a Dog

Running Head: CT and FDG PET-CT of duodenal granuloma

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ABSTRACT. A twelve-year-old, spayed female Yorkshire Terrier with intermittent vomiting was diagnosed with regional granulomatous enteritis through histopathological examination. On ultrasonography and computed tomography, a focal thickened duodenal wall showed a mass-like appearance with indistinct wall layers. Marked uptake of $^{18}$F-fluorodeoxyglucose was observed from the mass on positron emission tomography-computed tomography. Regional granulomatous enteritis is a rare form of inflammatory bowel disease and may have similar imaging features with intestinal tumors. This is the first study describing the diagnostic imaging features of ultrasonography, computed tomography and positron emission tomography-computed tomography of regional granulomatous enteritis in a dog.

Key words: computed tomography, dog, duodenum, granuloma, positron emission tomography
In veterinary medicine, the term “inflammatory bowel disease (IBD)” is applied to idiopathic inflammation in the intestinal tissues with no identified underlying causes [8]. Idiopathic IBD is classified depending on predominant cells such as lymphocytic-plasmacytic, eosinophilic, and granulomatous type in small intestine [4, 8]. Among them, regional granulomatous enteritis has been reported in only two dogs. [1, 10] Here, we describe the diagnostic features of ultrasonography, computed tomography (CT) and positron emission tomography-computed tomography (PET-CT) of regional granulomatous enteritis in a dog. To the authors’ knowledge, this is the first report on diagnostic imaging of regional granulomatous enteritis in veterinary medicine.

A twelve-year-old, spayed female, Yorkshire Terrier was presented with intermittent vomiting for 5 days. Six months prior, ovariohysterectomy was performed because of ovarian granulosa cell tumor. On physical examination, abdominal palpation revealed a firm, tubular mass in the left cranial abdomen. Complete blood count was unremarkable. Serum biochemistry demonstrated mildly increased alanine aminotransferase (184 U/l; reference limits, 10-100 U/l), alkaline phosphatase (237 U/l; reference limits, 23-212 U/l), gamma-glutamyl transferase (32 U/l; reference limits, 0-7 U/l) and globulin (4.6 g/dl; reference limits, 2.5-4.5 g/dl).

On abdominal radiographs, there was no remarkable finding. Ultrasonography revealed a heterogeneous hypoechoic mass, about 1.5 cm in diameter, caudolateral to the left kidney (Fig 1A). Blood flow signal was observed within the mass on the color Doppler mode. In the right cranial quadrant, the wall of the descending duodenum was eccentrically thickened at 12 mm, and showed a mass-like appearance with indistinct wall layers. In particular, the muscularis layer looked thicker in this portion
of the duodenum compared to the rest of the duodenum (Fig 1B). The mucosal layer showed heterogeneous hypoechoic change and the serosal layer lost its distinct border. The duodenal lumen was considered to be patent based on the movement of the gas and fluid through the lumen and the lack of duodenal dilation of proximal to the lesion. There were no signs of perforation such as free fluid, regional lymphadenopathy and free air.

CT and PET-CT examination were performed to investigate the characteristics of the left abdominal mass and the duodenal wall thickening, the relationship between two lesions, and to identify metastasis. CT examination using a 16-row multi-detector CT scanner (Somatom Emotion, Siemens, Forchheim, Germany) was performed with 150 mAs and 110 kV in 1 mm slice thickness. Contrast study was performed 3 min after intravenous injection of 880 mgI/kg iohexol (Omnipaque 300, GE Healthcare, Shanghai, China) at a rate of 3 ml/sec through power injector (Medrad Vistron C-T Injector System, Medrad, Inc., Minneapolis, USA). The left abdominal mass was hypoattenuating (48.1 ± 7.9 HU) and caudal to the left kidney. It showed heterogeneously strong contrast enhancement (167.8 ± 8.6 HU), and had a distinct border from the enhanced left kidney (270.6 ± 9.0 HU) (Fig 2). The abdominal mass was not associated with adjacent organs, and the mass was suspected to have originated from mesentery. The descending duodenum mass was isoattenuating (45.1 ± 3.6 HU) with as the adjacent intestinal wall and was approximately 4.2 cm in length and 2.5 cm in height. On the post-contrast CT images, the duodenal mass was markedly enhanced (145.4 ± 14.4 to 161.1 ± 19.2 HU); especially the mucosal layer showed a higher enhancement compared with the muscular layer. There was no evidence of duodenal obstruction, mottling of mesenteric fat and regional lymphadenopathy. The duodenal mass and left abdominal mass seemed to be
connected by a strand of tissue on CT image.

In three days after CT examination, PET-CT (Discovery 600 PET/CT system, GE Healthcare, Milwaukee, USA) was performed at 50 min after intravenous injection of 11 MBq/kg $^{18}$F-fluorodeoxyglucose (FDG). The patient was anesthetized before injection of FDG. On PET-CT, non-contrast enhanced CT (Helical, 8 slice, 120 kVp, 80 mAs, 3.79-mm slice thickness) was performed for attenuation correction and then, emission scan was performed with duration time of 3 min per bed (totally 5 beds). Acquired data were reconstructed using ordered subset expectation maximization reconstruction (128×128 matrix, 3.27-mm slice thickness, subset: 21, iteration: 2).

There was a strong FDG uptake by the duodenal mass as well as by the left abdominal mass (Fig 3). The maximal standardized uptake value of each mass was 11.0 and 7.3, respectively. There was no metabolic evidence of malignancy in whole body other than duodenal and left abdominal masses. The combined imaging studies defined a diagnosis of pathologically active duodenal and mesenteric masses. The differential list for the duodenal mass included primary intestinal neoplasia and, less likely, granulomatous inflammation. The left abdominal mass was suspected to be a granuloma due to the history of recent surgery, with neoplasia as a second differential diagnosis.

Because of the progressive vomiting, a partial obstruction of the duodenum was suspected, and surgical excision of both masses was planned. At laparotomy, the duodenal mass arose from the wall of descending duodenum, and was expanded by about 3 cm. It was an intramural mass, which ran through the circumference of the wall, with pink to red color and was palpated firm. The left abdominal mass was located caudal to left kidney and adhered to it. The mass also had pink to reddish
color, and indistinct border with adjacent mesentery tissues. There was no connection
between the abdominal mass and duodenal mass in contrary to CT image. Intestinal
resection and anastomosis were performed, and the abdominal mass was removed.
After surgery, the dog recovered and was fed semi-liquid diets for 3 days. The dog
was rechecked after 1 month without any clinical signs.

The duodenal mass was diagnosed as sterile pyogranuloma histopathologically (Fig 4).
The infectious organisms were investigated by histopathological examination using
special stains including Periodic acid-Schiff, Ziehl-Neelsen acid-fast, Gram and Wright-
Giemsa stains and found to be negative. The left abdominal mass was diagnosed as
pyogranulomatous and lymphocytic nodular steatitis, and infectious organisms were
also ruled out using special stains. Non-absorbable sutures used in the previous
ovariohysterectomy were identified and those were suspected as the cause of steatitis.
Regional granulomatous enteritis, one of idiopathic IBDs, has been reported in only
two dogs [1, 10]. The ileum, jejunum and pylorus were affected in the two dogs.
Regional granulomatous enteritis is consistent with Crohn’s disease, major type of
IBD, in human. Crohn’s disease is characterized by a transmural granulomatous
inflammation of the intestine [11]. This disease mainly affects both colon and
terminal ileum, even though it can affect any portion of the gastrointestinal tract [16].
Regional granulomatous enteritis in dogs and Crohn’s disease in humans have
common histological features, characterized by predominant neutrophilic inflammation
with granuloma formation [6, 17]. In some patients with Crohn’s disease, intestinal
perforation or bowel obstruction due to granuloma formation has been reported [2, 7].
In this case, the histopathological findings were consistent with the previous report
[17], however, granuloma arose from the descending duodenum and there was no
evidence of intestinal obstruction or fistula formation.

Although the etiology of the regional granulomatous enteritis is unclear, the pathogenesis of this condition is reported as the breakdown of immunological tolerance to luminal antigens [3, 6]. The non-idiopathic inflammation is more common in dogs, however, and various etiologies including *Yersinia* and mycobacterial infections, foreign-body reactions, and fungal disease can cause the intestinal granuloma [4, 5, 14, 15, 19]. Therefore, the underlying causes should be ruled out before diagnosis of idiopathic intestinal granuloma. In this dog, infectious organisms and foreign bodies were ruled out using Periodic acid-Schiff, Ziehl-Neelsen acid fast, Wright-Giemsa, and Gram stains and diagnostic imaging.

The extent of wall thickening and integrity of wall layering are useful parameters in distinguishing inflammation from tumor on ultrasonography [21]. Integrity of the intestinal wall layering is normal or reduced in enteritis, and most intestinal tumors lose the normal wall layering [21]. However, granulomatous enteritis can have an extensively thickened intestinal wall with loss of wall layering [5, 14]. In this dog, the thickened duodenum showing a mass-like appearance was found on ultrasonography, and therefore, we include only intestinal tumor but also a granulomatous enteritis into the differential lists.

The characteristic CT findings of Crohn’s disease have been reported as mural contrast-enhancement, intestinal wall thickening and stratification, obstruction due to wall thickening, enhanced fistulae and engorged vasa recta, correlated with active mucosal inflammation [7, 20]. In veterinary medicine, there is no report of the CT features of regional granulomatous enteritis. In this case, the CT examination demonstrated duodenal wall thickening with marked contrast enhancement, however,
there were no obstructive lesions and fistulae. In addition, the engorged vasa recta were not seen on CT images.

The PET-CT examination enables quantifying and precisely localizing FDG uptake in the body [12]. Inflammatory cells (e.g., macrophage, lymphocyte), like cancer cells could also express glucose transporters. In inflammatory conditions, both the number of inflammatory cell and expression of glucose transporters increase. These factors could contribute to increased FDG uptake [13]. Therefore, PET-CT findings should be correlated with other information which includes clinical history, other imaging findings and histologic examination if the patient was suspected of both inflammation and neoplasm. In this case, the dog underwent previous surgery and the differential diagnosis of inflammation such as granuloma was needed for the left abdominal mass in light of increased FDG uptake. On the basis of the previous history of this dog, the left abdominal mass was suspected as a suture granuloma. Suture granuloma, in human, have been reported to lead to FDG accumulation within the lesion [9, 18, 23], and this case was consistent with these previous reports. Apart from the limitations to distinguish inflammation from neoplasm, PET-CT is a promising modality in the diagnosis of infection or inflammation [13]. Especially, PET-CT is helpful to assess the extent and severity of the inflammatory lesions and to evaluate the result after treatment in Crohn’s disease [12]. Though this dog did not undergo follow up PET-CT examination due to recovery without clinical signs.

The treatment of idiopathic IBD usually involves a combination of dietary control, antibiotics, and immunosuppressive agents, regardless of the histological type [6]. In human Crohn’s disease, surgical resection is usually indicated for patients who fail to respond to drug or dietary therapy [22]. In regional enteritis in a dog, the surgical
resection of the affected portion of the bowel loops palliates the clinical signs [1].

This dog did not undergo long term follow up but recovered completely after surgical resection of the duodenal granuloma.

In the present case, it was not possible to distinguish granulomatous enteritis from intestinal tumor by diagnostic imaging in spite of the multiple modalities. Few cases of regional granulomatous enteritis have been reported in the veterinary literature and the human literature indicates that regional granulomatous enteritis may have similar imaging features to that of intestinal tumors. Ultrasonography, CT and PET-CT were helpful to determine the shape, location, and extension of the duodenal mass, and to exclude metastasis.

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Fig 1. (A) Ultrasonography of the mass caudal to the left kidney. The hypoechoic mass (m) had ill-defined margin and was surrounded hyperechoic mesentery (arrows). (B) Ultrasonography of the duodenal mass (d). The thickened duodenal wall (*) in the far field was seen to involve mucosal and muscular layers compared to the normal wall layers in the near field. The hyperechoic adjacent mesentery (arrows) was consistent with edema or inflammation. The hyperechoic line (arrow heads) was the duodenal lumen with small volume of gas.
Fig 2. Computed tomography of left abdominal mass and the duodenal mass. In pre-contrast (A) CT image, left abdominal mass (*) and the duodenal mass (short arrows) had homogeneously attenuated similar to normal small intestine density. After contrast injection (B), the left abdominal mass (*) showed heterogeneous contrast enhancement, and the thickened duodenal wall exhibited contrast enhancement of the mucosal layer and muscular layer, markedly at mucosal layer (black arrowheads). Heterogeneously enhancing region with irregular margin at the dorsal duodenal wall surface (white arrowheads) was distal region of normal pancreatic right limb. A strand of soft tissue attenuating tissue connecting the left mass to the duodenal mass was shown on pre- (A) and post-contrast (B and D) images. The strand was suspected peritoneal adhesion (long arrows). In reformatted dorsal plane (C and D), the left abdominal mass (*) was located caudal to the left kidney (k), and the duodenal mass showed marked mucosal enhancement (black arrowhead). Note: s = stomach, d = duodenum. Left of the image is the right side of the dog.
Fig 3. Positron emission tomography and computed tomography images using FDG.

(A) Maximum intensity projection view showed two focal FDG uptakes in abdominal cavity and several physiologic uptakes (esp. brain, heart, kidneys, urinary bladder). (B-C) Fusion PET-CT images showing abnormal FDG uptakes. (B) On dorsal plane, there were focal FDG uptakes in duodenum (arrow head) and in left abdominal cavity (arrow). (C) The same findings were noted on transverse plane. Note: B = brain, H = heart, K = kidney, U = urinary bladder, S = injection site. Left of the image is the right side of the dog.
Fig 4. Microscopic findings of the duodenal mass. The multiple pyogranulomas consist mainly of macrophages with some lymphocytes and neutrophils. Hematoxylin and eosin. 50x