Short Communication

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Ultrasonographic honeycomb pattern of the spleen in cats: correlation with pathological diagnosis in 33 cases

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Abstract

Objectives The aim of this study was to evaluate the relationship between the ultra sonographic (US) diffuse honeycomb pattern (HCP) of the spleen and a pathological diagnosis in cats, and to assess the influence of transducer type on HCP visualisation.

Methods Abdominal ultrasounds of cats with an HCP were reviewed and splenic size, shape, margination, other parenchymal alterations and splenic hilar lymphadenopathy were recorded. When applicable, images acquired with high-frequency linear and curvilinear transducers were compared to determine if an HCP was more frequently demonstrated on high-resolution images. A retrospective review of the corresponding splenic cyto histopathological samples was also performed.

Results Thirty-three cats met the inclusion criteria. Five cases were diagnosed by histology and 28 by cytology, confirmed by PCR for antigen receptor rearrangements (PARR) in uncertain cases. There were 15 cases of lymphoid hyperplasia, eight cases of lymphoma (four B cell, three T cell and one large granular lymphocytes), six cats with splenitis, three with extramedullary haematopoiesis and one with histiocytic sarcoma. The prevalence of lymphoma in cats with an HCP of the spleen was 24%. Splenomegaly was the most frequent US feature associated with an HCP and was observed in all lymphoma cases. In the images obtained from both high-frequency linear and micro-convex transducers the visualisation of an HCP was enabled in all cases (24/24) and in 62.5% (15/24), respectively.

Conclusions and relevance: Based on our findings, an US HCP of the spleen in cats can be associated with benign and malignant disorders and is infrequently associated with lymphoma in comparison with dogs. Cytological or histological examination, possibly supplemented by PARR, should always be performed for diagnostic support. Use of high-frequency linear transducers is recommended to properly recognise an HCP or subtle changes in splenic parenchyma.

Keywords: Ultrasound; spleen; honeycomb pattern; lymphoma

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Introduction

The honeycomb pattern (HCP) of the spleen is an ultrasonographic (US) feature characterised by a diffuse parenchymal inhomogeneity with multiple small, well-defined hypoechoic foci.[1,2] This feature has been sometimes referred to as having a 'moth-eaten' or a 'Swiss cheese' appearance,[1,3–6] but there is no clarity regarding the size and conspicuity of the disseminated hypoechoic foci contributing to a splenic HCP. Splenomegaly and changes in size and echogenicity of the splenic lymph nodes may be associated with this condition.[1,2] In dogs, a moth-eaten pattern has been primarily associated with lymphoma,[3,7,8] although occasionally observed in benign and other malignant conditions.[2] In cats, a correlation between an HCP and lymphoma has

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been anecdotally reported.[2,4,5] Recently, two reports investigating the association between feline splenic US appearance and cytological diagnosis showed that diffuse inhomogeneity of the spleen with hypoechoic foci, described as moth-eaten or HCP, was not always related to neoplastic disorders.[6,9]

The purpose of this study was to assess the correlation between a splenic HCP and the final cytological or histological diagnosis, and to determine the prevalence of lymphoma in cats with a splenic HCP. In addition, we aimed to establish whether the use of high-frequency linear transducers might increase HCP visualisation.

Materials and methods

Animals

Medical records of cats undergoing abdominal ultrasonography at the Department of Veterinary Medical Sciences, University of Bologna, between March 2009 and April 2017 were retrospectively reviewed for cats with a splenic HCP. Inclusion criteria were complete abdominal ultrasound, evidence of a splenic HCP from retrieved images and US reports, and cytological or histological examination of the spleen performed within 1 week of ultrasound. The splenic HCP was defined by the presence of multiple rounded, well-defined, hypoechoic foci, ranging from 0.5–1 mm in size, disseminated throughout the spleen.

Cats with splenic diffuse US changes other than an HCP (eg, diffuse hypoechogenicity; heterogeneous appearance with ill-defined areas) and solitary masses or multi-focal nodules >1 mm in size and non-uniform distribution were excluded. Data collected from medical records included signalment, clinical signs, US features, transducer frequency and cytological/histological diagnosis.

Ultrasonography

Ultrasonography was performed using three real-time ultrasound machines (iU22 ultrasound system, Philips Healthcare; Epiq5 ultrasound system, Philips Healthcare; DC 8 ultrasound system, Mindray Bio-medical Electronics Co.) equipped with high-frequency linear transducers (7–15 MHz, 5–18 MHz and 3–11 MHz, respectively) and/or micro-convex transducers (5–8 MHz, 5–8 MHz and 3–12 MHz, respectively).The images and cine loops were evaluated by an experienced radiologist (AD) to describe the splenic appearance. The presence of an HCP was subjectively assessed and described as detectable or not. Furthermore, when an HCP was detectable on both images obtained with micro-convex and high-frequency transducers, a subjective evaluation on whether it was more obvious on high-frequency images was made.

Size, shape, margin appearance, presence of parenchymal alterations other than an HCP and splenic hilar lymphadenopathy were recorded. Splenic size was determined using electronic calipers on a video frame or a still image as previously described. Splenomegaly was defined when splenic thickness was >7.1 mm at the head, >9.3 mm at the level of the body or >8.7 mm at the tail.[10] Shape was subjectively assessed as normal or altered, and the margins (visceral surface) as smooth or irregular. Splenic lymphadenopathy was established when lymph node diameter was >3.2 mm.[11] Other abdominal abnormalities were also recorded.

Cytological and histological analysis

Ultrasound-guided fine-needle aspirates (FNAs) of the spleen were taken, using 22, 23 or 25 G needles and a non-aspiration technique. The obtained smears, air drained and stained with May-Grünwald Giemsa, were successively reviewed by a pathologist (SS) and a clinical pathologist (CA). The final diagnosis was obtained by consensus. In the presence of a cytological diagnosis or suspicion of lymphoma, PCR for antigen receptor rearrangements (PARR), in the T- or B-cell receptor genes, was performed. When available, histological samples were examined for diagnostic purposes by one pathologist (SS) and immunohistochemistry for lineage markers was performed, if necessary, to assess the phenotype of the lymphoid population.

Statistical analysis

Basic descriptive statistics were used to characterise the study population. Prevalence of lymphoma was calculated as the number of cats with a definitive diagnosis of lymphoma over the total number of cats.

Results

Thirty-three cats met the inclusion criteria. Breeds included 30 domestic shorthairs, one Abyssinian, one Maine Coon and one Scottish Fold. Median age was 9 years (range 0.4–16 years). There were 18 castrated males, eight spayed females, three intact males and four intact females. The median weight was 4.5 kg (range 1.5–9 kg). Clinical signs were non-specific and included decreased appetite (n = 18), lethargy (n = 11), vomiting (n = 11) and weight loss (n = 9).

The US images of the spleen obtained by both a linear and micro-convex transducer were available in 24/33 cases. In 4/33 and 5/33 cases the spleen was imaged only by a micro-convex or a linear transducer, respectively. HCP was evident in all the images acquired with a linear transducer (Figure 1), whereas an HCP was not recognised using a micro-convex transducer in 9/24 cases (37.5%) (Figure 2). Of these cats, two had a final diagnosis of lymphoma, four of lymphoid hyperplasia and one case each of histiocytic sarcoma, neutrophilic splenitis and extramedullary hematopoiesis. In 15/24 cases, an HCP was detectable on both linear and

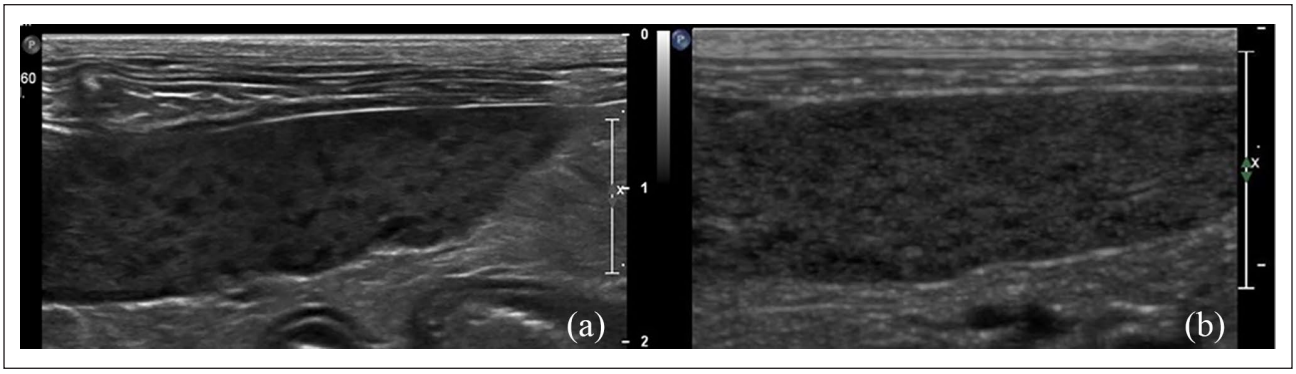

Figure 1 Ultrasonographic images of two feline spleens showing a honeycomb pattern with multiple small hypoechoic foci with a final diagnosis of (a) pyogranulomatous splenitis and (b) lymphoid hyperplasia

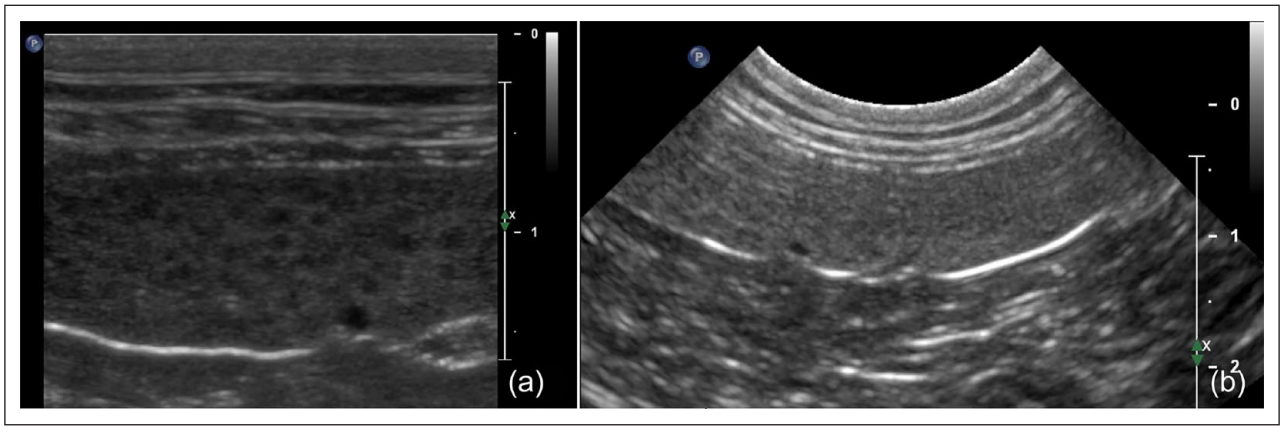

Figure 2 Comparison between US images of a feline spleen obtained with (a) linear and (b) curvilinear arrays. Honeycomb pattern is well recognisable on the (a) high-frequency image in contrast with the image obtained with the (b) micro-convex probe, where only a slight inhomogeneity of the splenic parenchyma is visible. Final diagnosis was lymphoid hyperplasia

micro-convex images; however, in the majority of these (n = 11/15), an HCP was subjectively more evident on the high-frequency images.

Table 1 summarises the descriptive US features of the spleen with the corresponding final diagnosis. The thickness of the splenic body and the head was measured in 33/33 and 3/33 cases, respectively, while measurement of the tail was not feasible. Splenomegaly was the most frequent US feature associated with an HCP (69.7% of cases). In all cases in which the spleen was of normal size (n = 10/33), the final diagnosis was consistent with a non-neoplastic disorder (lymphoid hyperplasia [n = 6], splenitis [n = 4]).

In addition to an HCP, four cats had focal splenic lesions: one had multiple ill-defined hypoechoic nodules (approximately 7 × 4 mm) bulging from splenic margins; the remainder had solitary or multiple small hyperechoic nodules. FNAs of those nodules were not available.

Ultrasonographic findings in other abdominal organs included diffuse changes in echogenicity or relative thickness of the intestinal wall layers (n = 6), diffuse or focal variations in echogenicity and echotexture of the liver (n = 7) and kidneys (n = 12), and focal thickening of the small intestine with a loss of layering associated with jejunal lymphadenopathy (n = 4). Of the cases with small intestinal thickening and regional lymphadenopathy, two had a diagnosis of splenic lymphoma and the other two of neutrophilic splenitis and extramedullary haematopoiesis. Among the group of cats with renal US changes, four exhibited increased cortical echogenicity, one had a focal hyperechoic nodule and five showed a diffuse parenchymal hyperechogenicity with loss of cortico medullary distinction. Chronic kidney disease was diagnosed in four cats, while an additional cat was diagnosed with multicentric lymphoma involving the kidneys and spleen.

In five cases, surgical (n = 1) or post-mortem (n = 4) histological samples allowed a final diagnosis. The remaining 28 cases underwent cytological examination (n = 9; 32%) or cytological examination and PARR (n = 19; 68%). Final diagnoses are reported in Table 1.

Overall, a diagnosis of lymphoma was obtained in 8/33 cases, corresponding to a 24.2% prevalence.

Table 1 Descriptive ultrasonographic features of the spleen and final diagnosis of the 33 cats with a splenic honeycomb pattern

Final diagnosis		Diagnosis			Size		Shape		Margins		Splenic hilar lymphadenopathy	
	No. of cases (%)	H	C	C + P	Normal	Enlarged	Normal	Altered	Smooth	Irregular	Yes	No
Lymphoma	8 (24.2)	1	1	6	NA	8	6	2	4	4	3	5
Lymphoid hyperplasia	15 (45.4)	2	0	13	6	9	14	1	7	8	2	13
Histiocytic sarcoma	1 (3.0)	1	0	0	NA	1	1	NA	1	NA	NA	1
Extramedullary haematopoiesis	3 (9.1)	0	3	0	NA	3	3	NA	2	1	NA	3
Splenitis	6 (18.2)	1	5	0	4	2	5	1	5	1	2	4

H = histology; C = cytology; C+P = cytology + PCR for antigen receptor rearrangements (PARR); NA = not available

Discussion

In the present study, lymphoproliferative disorders accounted for nearly 70% of cats with an HCP. Among them, two-thirds were represented by lymphoid hyperplasia and one-third by lymphoma (24.2% of all cases). The remaining conditions observed included splenitis, extramedullary haematopoiesis and one case of histiocytic sarcoma. These findings are consistent with previous studies showing a lack of agreement between a US diffusely inhomogeneous appearance of the spleen and a cytological diagnosis of malignant neoplasia, and the frequent association of this US pattern with benign splenic lesions in cats.[6,9,12] Therefore, when a US splenic HCP is observed in cats, multiple differential diagnoses should be considered, including benign lymphoproliferative, inflammatory and reactive diseases, although lymphoma is still a likely option.

The most common US feature associated with an HCP in the present study was splenomegaly, observed in 100% of the cats with lymphoma and in 60% of the cats with other splenic disorders. All cases with normal splenic size had a final diagnosis of a benign disorder, suggesting that an HCP is more likely to be associated with benign conditions when splenic size is normal. However, as splenomegaly was observed in 10 cats with benign splenic disorders, this finding must be interpreted with caution. The low specificity of splenomegaly may be a consequence of the feline non-sinusoidal splenic capillary architecture making the spleen of cats less capable of storing large blood volumes and splenomegaly a common feature of splenic pathology, regardless the aetiology.[10,13,14]

The remaining US features, including altered splenic shape and irregular margins, were rather nonspecific. Although these evaluations were made according to the veterinary literature, it must be considered that their US assessment is subjective; hence, the diagnostic accuracy could be affected by the operator's experience.

We chose not to evaluate relative splenic echogenicity compared with left renal cortex and hepatic parenchyma because many patients in our study showed US and haematological abnormalities of the kidneys and liver, which potentially prevents a correct judgement from being made. Moreover, it has been demonstrated that a mild increase in renal cortex echogenicity can be found in neutered male cats without any underlying renal disorders.[15] Splenic lymphadenopathy was infrequent in this study, even in the lymphoma group.

In addition, abnormalities of other abdominal structures were found both in cats with lymphoma and reactive and inflammatory diseases.

When the effect of the transducer type on the HCP visualisation was evaluated, considerable differences were noted comparing linear with micro-convex arrays. The HCP was always consistently visible on the high-frequency linear images, while it was not recognisable in nine of the cases when the spleen was imaged with a micro-convex probe. Even when detectable on images acquired with both types of transducer, in the majority of cases the HCP was more evident on images obtained with a linear transducer. A similar result was found in a previous retrospective study,[6] where an HCP appearance of the splenic parenchyma was more frequently recognised in images acquired by a linear transducer.[6] These results support the hypothesis that high-frequency linear arrays enable a better visualisation of a subtle diffuse inhomogeneous appearance of splenic parenchyma, making the HCP more apparent. Linear arrays allow a better axial resolution than curvilinear transducers;[16] therefore, disseminated hypoechoic foci ranging from 0.5–1 mm are more easily detected by high-frequency linear transducers.

The present study has some limitations owing to its retrospective nature. The ultrasounds were performed by different ultrasonographers, and their different skills and experience may have affected image quality. A standard protocol/setting for image acquisition (eg, focus position, depth, time-gain compensation, harmonic mode and number of scan planes) was not established, influencing the possibility of detecting an HCP using a micro-convex transducer and correctly assessing splenic size. Finally, histological samples were available only in five cats, while in the majority of cases the diagnosis was based on cytology and PARR, which are not considered a gold standard for the diagnosis of splenic disorders. Indeed, PARR has the potential to be very sensitive and specific; however, false-positive and false-negative results occur for a variety of reasons, and results should always be interpreted in conjunction with histopathology. In addition, PARR is substantially less sensitive in cats than it is in dogs, and it has been estimated that currently available protocols detect 60–65% of feline neoplastic lymphocyte samples.[17]

Conclusions

In this study, the prevalence of splenic lymphoma in cats with an HCP was low (24%). HCP was observed in cats with benign lymphoproliferative disorders and other reactive conditions. Given the wide spectrum of splenic diseases potentially associated with an HCP in cats, cytological or histological examination, possibly supplemented by PARR, is always recommended.

High-frequency transducers are valuable in the detection of an HCP and should always be used in the US assessment of the splenic parenchyma.

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Ethical approval This work involved the use of non-experimental animals only (owned or unowned), and followed established internationally recognised high standards ('best practice') of individual veterinary clinical patient care. Ethical approval from a committee was not necessarily required.

Informed consent Informed consent (either verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work for the procedure(s) undertaken. No animals or humans are identifiable within this publication, and therefore additional informed consent for publication was not required.

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