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Adenocarcinoma originating from presumed liver ectopic thyroid in a cat

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Abstract

Case summary Ectopic thyroid tissue is rarely reported in dogs and cats in its prediaphragmatic location and has never been described in the liver. A 15-year-old spayed female domestic shorthair cat was diagnosed by ultrasound with a heterogeneous hypoechoic nodular area in the liver at the periphery of the quadrate lobe. A generic diagnosis of carcinoma was made after ultrasound-guided fine-needle aspiration and cytological examination. The patient underwent staging by CT scan and subsequently underwent hepatic lobectomy. Histologically, a diagnosis of thyroid adenocarcinoma was made, confirmed immunohistochemically using positive thyroglobulin staining; the tumour was suspected to be of metastatic origin. CT scans excluded primary thyroid involvement; in addition, lesions at other sites were not detected. Therefore, a final diagnosis of thyroid adenocarcinoma arising from ectopic thyroid tissue in the liver was made. The cat recovered uneventfully from surgery.

Relevance and novel information This report describes an unusual case of an adenocarcinoma originating from presumed thyroid ectopic tissue within the liver of a cat. Ectopic thyroid tissue has been rarely reported in both dogs and cats and, to the authors' knowledge, it has never been described in the liver of a cat.

Keywords: Liver; thyroid; ectopic tissue; adenocarcinoma; thyroglobulin

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Introduction

Hepatic neoplastic lesions, both in their benign and malignant counterparts, may originate primarily from hepatocytes, ductal epithelium or mesenchymal tissues of the stroma (vessels, nerves, connective tissue) or secondarily as metastasis from tumours located in other areas.[1] Neoplasms of the liver arising from ectopic tissue in humans are more infrequent by far.[2]

Ectopia can potentially affect any body tissue. An ectopic thyroid is defined as the presence of thyroid tissue in locations other than the pretracheal region. It is considered an embryologic aberrant localisation that can occur during migration of the tissue along the midline from the primitive tongue to the base of the heart.[3] For this reason, thyroid heterotopia, although rare, is most commonly observed along the midline of the neck, head and thorax in both humans and animals,[2,4,5] while it is extremely rare to find thyroid tissue caudal to the diaphragm. At the ectopic site, thyroid tissue may have a physiological structure, characterised by thyroid follicles, with or without parafollicular C-cells, may be hyperplastic and, more rarely, transform both into benign or malignant neoplasia, in this latter eventuality with or without metastasis. The table in the supplementary material lists the locations of ectopic thyroid tissue

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in its various manifestations (normal, hyperplastic, neoplastic tissue) in humans, dogs and cats, with the corresponding scientific literature (see the References supplement 1 in the supplementary material). From the existing literature, the most common sites for ectopic thyroid in cats appear to be the thorax (mediastinum, caudal mediastinal thyroglossal duct, pericardium) and the tongue. The present case report describes the occurrence of a feline thyroid carcinoma arising from ectopic tissue in the liver.

Case description

A 15-year-old spayed female domestic shorthair cat was examined for a routine checkup. Both the physical examination and the results of the complete blood count and a standard serum biochemistry panel were unremarkable. However, an abdominal ultrasound examination revealed a heterogeneous hypoechoic nodule measuring 9×7 mm at the periphery of the quadrate lobe (Figure 1a). Ultrasound-guided fine-needle aspiration was performed, and cytological examination revealed few mixed inflammatory cells and numerous grouped epithelial cells with moderate to marked anisocytosis and anisokaryosis, round nuclei, reticular to coarse chromatin, prominent nucleoli and poorly basophilic cytoplasm.

Based on the ultrasound and cytological findings, a presumptive diagnosis of epithelial neoplasia (carcinoma) was made and the possibility of a metastatic lesion was considered.

Monthly liver enzyme monitoring and serial ultrasound of the liver were recommended. An increase in transaminases (aspartate transaminase [AST], alanine transaminase [ALT]) and a progressive growth of the nodule to a size of 1.73×1.34 cm in 4 months were observed (Table 1; Figure 1a–c). At that point, the owner opted to have the cat examined laparoscopically with the aim of undergoing a liver biopsy. After this, a histopathological diagnosis of lymphocytic cholangitis was made. After symptomatic treatment for lymphocytic cholangitis, the transaminases returned to the reference interval, but the liver nodule appeared larger on ultrasound (Figure 1d). At this time, a complete staging of the patient by whole-body CT scan was proposed with the aim of en bloc surgical excision of the liver nodule. The CT examination, using a Toshiba Aquilion 16 strati (120 kV, 200 mAs, slice thickness 1 mm, pitch 1, scan time 1 min, FC13 = soft tissue filter), showed a diffuse

Table 1 Liver enzymology, aspartate transaminase (AST) and alanine transaminase (ALT) sequential variations

Date	Examination	Reference interval
6 May 2022	AST: 19	<25
	ALT: 46	<45
23 July 2022	AST: 33	<25
	ALT: 96	<45
20 September 2022	AST: 179	<25
	ALT: 276	<45
18 October 2022	AST: 17	<25
	ALT: 51	<45
23 December 2022	AST: 21	<25
	ALT: 44	<45

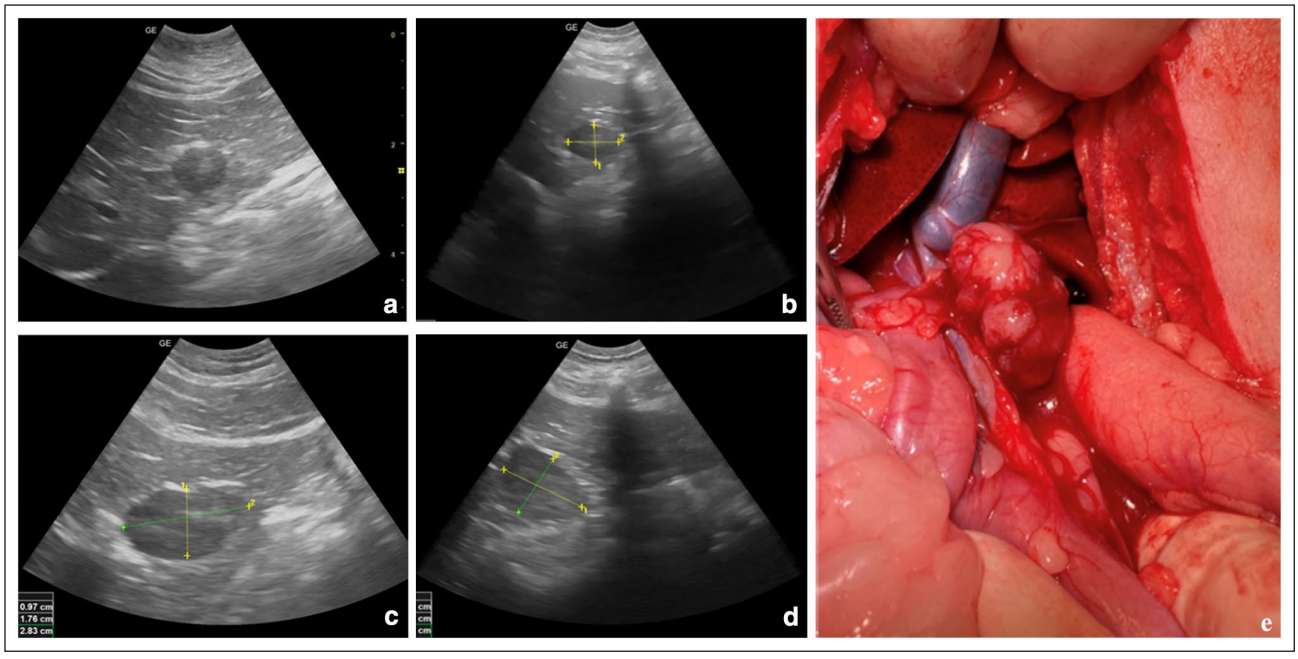

Figure 1 Sequential changes in ultrasound-acquired liver nodule size and view of the liver nodule at surgery: (a) nodule size at time 0: 0.99×0.70 cm; (b) nodule size after 2 months: 0.99×1.33 cm; (c) nodule size after 3 months: 0.97×1.76 cm; (d) nodule size after 4 months 1.73×1.34 cm; and (e) multilobulated discoloured liver mass protruding on the liver surface

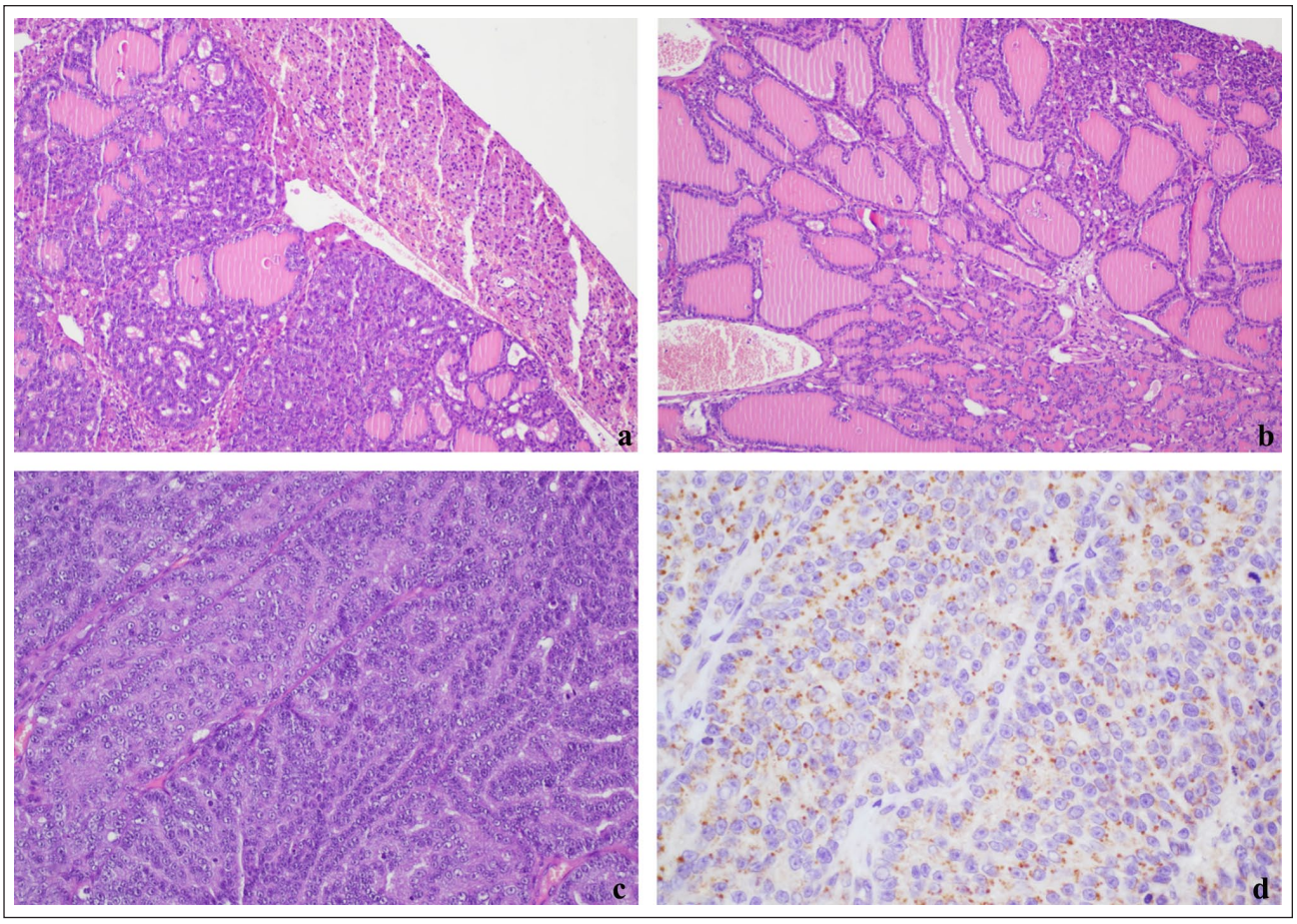

Figure 2 Histology and immunohistochemistry of the liver mass: (a) multilobulated thyroid carcinoma infiltrating the liver parenchima (top, right), thyroid follicles contain colloid; (b) well-differentiated thyroid follicles containing colloid; (c) undifferentiated proliferation of cuboidal cells arranged in trabeculae; and (d) diffuse spot-like immunereactivity to tyreoglobulin of the neoplastic cells. Panels (a–c) haemotoxylin and eosin stain; panel (d) imunohistochemistry with anti-thyreoglobulin

heterogeneous aspect of the liver parenchyma, both in the baseline and in the post-contrast study, especially at the level of the hepatic quadrate lobe. No other changes were found. After a median celiotomy, the mass was isolated from the portal vein and a partial hepatic lobectomy of the quadrate lobe was performed using a single full-thickness 2-0 polydioxanone strangulation suture followed by vascular clips as needed; a minimum of 1 cm of macroscopically normal liver tissue at the excision margin was warranted (Figure 1e).

Histopathological examination revealed a neoplastic nodular lesion occupying the entire surface of the excised tissue, except for a thin compressed rim of hepatic parenchyma (Figure 2a). The neoplasia was multifocally composed of cuboidal epithelial cells with an increased nuclear:cytoplasmic ratio, of homogeneous morphology and small size, laying follicular structures containing a colloid-like dense eosinophilic material (Figure 2b). These areas merged into more tubular or solid epithelial proliferations without secretory accumulation. Atypical features include nuclear crowding, vesicular chromatin and mitotic figures (Figure 2c).

As a result of the presence of a follicular structure containing dense colloid-like secretion, the most likely diagnosis was thyroid carcinoma metastasis. Consequently, the lesion was further evaluated using immunohistochemistry. Almost all neoplastic cells showed mild but diffuse cytoplasmic positivity for thyroglobulin; in 30% of them, the staining was a cytoplasmic brown coarse granulation (Figure 2d). The results of the immunohistochemical study confirmed the thyroid origin of the neoplasm and prompted the search for the primary tumour site. In addition, thyroxine (T4) and thyroid-stimulating hormone (TSH) were within the normal range. In view of these results, a re-evaluation of the previous CT study ruled out primary thyroid involvement as well as any nodular lesions elsewhere. Consequently, all these elements led to a diagnosis of a malignant neoplasm (thyroid adenocarcinoma) arising from ectopic thyroid tissue in the liver.

The cat recovered uneventfully from surgery, and serial ultrasound scans at 7 months postoperatively showed no recurrence of the mass.

Discussion

To the authors' knowledge, this case report is the first complete description of a case of thyroid carcinoma originating from presumed ectopic thyroid tissue within the liver. Ectopic thyroid tissue is a rare condition with a prevalence of approximately one per 100,000 to 300,000 people.[6] When originating from the tongue (the most common site of occurrence), it has been found to be clinically relevant in 1:10,000 to 1:100,000 people, although subclinic microscopic ectopic thyroid may be present in 10% of people.[7,8] In addition, the cancer rate of the lingual thyroid is very low, at approximately 1%.[9]

According to the veterinary scientific literature, different from human medicine, in which liver ectopia is seldom reported, no cases of liver ectopia in the feline and canine species has been found (see the References supplement 1 in the supplementary material).

Generally, ectopic thyroid tissue behaves in the same physiological manner as normal thyroid tissue. However, a pathological behaviour of this condition has also been reported, which rarely leads to hyperplasia or neoplasia, either benign or malignant,[4] with or without metastasis. For these reasons, to further investigate this clinical condition, thyroid function tests were carried out. T4 and TSH, in particular, were tested and the results revealed they were within the normal range. Unfortunately, we tested these parameters only after surgical removal of the mass; however, owing to the extreme rarity of the entity, we arrived at the final diagnosis only after histopathological analysis and by exclusion of the other differential diagnoses. Indeed, in our case, the mass was an incidental finding during a routine checkup and only a multidisciplinary approach to the problem allowed us to focus on the diagnosis. The initial histological diagnosis was suspected metastatic thyroid carcinoma, as no information regarding the examination of other organs was provided to the pathologist. In addition, ectopic thyroid tissue in the liver is exceptionally rare in humans and has never been reported in pets, which led to it not being considered. Only the confirmation of a normal pretracheal thyroid gland and the absence of clinical signs before and after surgery led to this unusual diagnosis. However, it is also reasonable that thyroid function tests were within the normal range even before surgery, as our case was also asymptomatic. Indeed, clinical signs of thyroid dysfunction, including weight loss, polyphagia, polyuria/polydipsia (PU/PD) and nervousness, were present in the case of a hormone-secreting ectopic thyroid tumour in dogs.[10] In humans, non-specific symptoms, including pain, dyspnoea or dull pain below the xiphoid, have also been reported when the ectopic thyroid is located adjacent to the diaphragm.[11]

There are a few reports on the management of thyroid ectopia, mainly focusing on cases of prediaphragmatic thyroid ectopia in dogs and cats. In dogs, only one large case series reported variable, generally long survival times after surgery and medical therapy for sublingual ectopic thyroid adenocarcinoma, with deaths primarily due to local invasiveness or metastasis;[12] in all other reported cases, diagnosis was post mortem, no follow-up was mentioned or the dog died from metastasis (see the Reference supplement 1 in the supplementary material). In a small series of dogs, a partial excision of the hyoid was accomplished with tumour resection.[13] In cats, mainly single case reports are available in the literature, suggesting that surgery may be successful in this species as well.[4,5] However, in one case, the diagnosis was made post mortem, and in another report, only the abstract was available, with no mention of therapy. In an old paper regarding thyroidectomy in 48 cats, recurrence of hyperthyroidism after thyroidectomy was reported in 3/4 cats, followed by ectopic thyroid tissue[14] and this required a second surgery. It can be concluded that surgery should be recommended for ectopic thyroid malignancy, if feasible. In addition, histopathology should assess the surgical margin status to help predict the outcome. In our case, this approach resulted in the patient remaining disease free for over 20 months.

Finally, the authors believe it is worth mentioning that an occult form of thyroid carcinoma, rarely described in humans,[15] cannot be excluded in this cat. In human cases, the primary tumour can be difficult or impossible to detect, or it may disappear, leaving the metastasis as the only remaining tumour site. The CT scan in this cat (with all the limits of this imaging procedure) excluded the presence of a thyroid microcarcinoma. Even though a total thyroidectomy for histological examination of the entire, apparently healthy thyroid gland was not performed for ethical reasons, both the normal thyroid function tests and the long disease-free period made the hypothesis of metastasis from an occult thyroid carcinoma unlikely.

Conclusions

Ectopic thyroid tissue has rarely been reported both in dogs and cats in its prediaphragmatic location and it appears to be exceptional in other localisations. To the authors' knowledge, it has never been described within the liver of a cat. Because of its rarity and absence of nonspecific clinical manifestations, it may be misdiagnosed. This case report emphasises the need to combine several diagnostic tools for diagnostic accuracy, such as imaging, laboratory tests (even though not very useful in this

specific case), cytology and pathologic evaluation (including histology and immunohistochemistry). In this case, biopsy alone was not sufficient, and the final diagnosis of ectopic thyroid adenocarcinoma was only confirmed after complete surgical excision and the exclusion of malignancy in both normotopic thyroid glands.

Supplementary material The following file is available as supplementary material:
References supplement 1: Survey of the scientific literature (1970–2023) on the occurrence of ectopic thyroid tissue in humans, dogs and cats; case reports are organised by antomic location and relative pathology.

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Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognised high standards ('best practice') of veterinary clinical care for the individual patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*. Although not required, where ethical approval was still obtained, it is stated in the manuscript.

Informed consent Informed consent (verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (experimental or non-experimental animals, including cadavers, tissues and samples) for all procedure(s) undertaken (prospective or retrospective studies). No animals or people are identifiable within this publication, and therefore additional informed consent for publication was not required.

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