

Screening for naturally occurring hypothyroidism in adult cats: A prospective multi-center study in Central Europe

F. N. Leuthard¹, A. Carranza Valencia², M. Wenger¹, F. Tschuor¹, F. K. Zeugswetter³

¹Tierklinik Mittelland, Oftringen-Zofingen, Switzerland; ²Division of Small Animal Internal Medicine, Department of Clinical Veterinary Science, Vetsuisse Faculty, University of Bern, Bern, Switzerland; ³Clinical Department for Small Animals and Horses, University of Veterinary Medicine, Vienna, Austria

Diagnostik der Hypothyreose bei adulten Katzen: Eine prospektive multizentrische Studie in Mitteleuropa

Die wissenschaftlichen Berichte zur Hypothyreose bei adulten Katzen beschränkt sich auf 16 gemeldete Fälle in den letzten drei Jahrzehnten, dies unterstreicht die Notwendigkeit umfassenderer Studien. Das Ziel diese prospektiven multizentrischen Studie war die Identifikation von spontaner primärer Hypothyreose (SPH) bei erwachsenen Katzen während eines Jahres.

Mitarbeiter von zwei Universitätskliniken und einer privaten Überweisungsklinik untersuchten Katzen, die älter als ein Jahr waren und klinische Anzeichen einer Hypothyreose, wie Verstopfung, Fettleibigkeit/Gewichtszunahme, Lethargie, Schilddrüsengröße, Hautveränderungen oder leichte Azotämie zeigten. Die Laboranalysen für Gesamt-T4-Konzentrationen (TT4) wurden an zwei Standorten intern und an einer Universitätsklinik extern bestimmt. Bei niedrigen oder unterdurchschnittlichen TT4-Werten wurden das Schilddrüsen-stimulierende Hormon (TSH) und TT4 aus Restserum nachgemessen. Zusätzlich wurden die lokalen Dokumentationssysteme auf niedrige bis niedrig-normale TT4-Konzentrationen überprüft, um zusätzliche Katzen mit möglicher SPH im vorliegenden Untersuchungszeitraums zu rekrutieren.

Niedrige (n = 253, 18,3%) bis niedrig-normale (n = 377, 27,3%) TT4-Konzentrationen wurden bei 630 (45,6%) von 1382 Katzen beobachtet. Von diesen 630 möglichen SPH-Katzen wurden 566 (89,8%) Katzen aus folgenden Gründen ausgeschlossen: TT4 wurde gemessen, um eine Hyperthyreose auszuschließen (299 Katzen, 47,4%), die Patienten wurden mit Arzneimitteln behandelt, die die TT4-Konzentration senken (Anti-Schilddrüsen-Medikamente: 155 Katzen, 24,6%; andere Medikamente: 95 Katzen, 15,1%), oder Folgeuntersuchungen konnten nicht durchgeführt werden (17 Katzen, 2,7%).

Summary

Research on naturally occurring hypothyroidism in adult cats is limited to 16 reported cases in the last three decades, highlighting the need for more comprehensive studies. This prospective multicenter study aimed to identify cases of spontaneous primary hypothyroidism (SPH) in adult cats presented over a one-year period.

Staff members of two university hospitals and one private referral clinic screened for cats aged older than one year showing clinical signs suggestive of feline hypothyroidism including obstipation, obesity/weight gain, lethargy, goiter size, skin changes or mild azotemia. They were instructed to proceed with endocrine investigations if low or low-normal total T4 (TT4) concentrations were detected, using in-house analyses at two locations and external analyses at one university hospital. The continuative diagnostic investigations consisted primarily of thyroid-stimulating hormone (TSH) measurements using leftover samples and TT4 reevaluation. Additional cats with possible SPH were recruited by screening the local documentation systems for low to low-normal TT4 concentrations recorded during the study period.

Low (n = 253, 18,3%) to low-normal (n = 377, 27,3%) TT4 concentrations were observed in 630 (45,6%) of 1382 cats. Of these 630 possible SPH cats, 566 (89,8%) cats were excluded for the following reasons: TT4 was measured to rule out hyperthyroidism (299 cats, 47,4%), they were treated with drugs that lower TT4 concentrations (anti-thyroid medications: 155 cats, 24,6%; other drugs: 95 cats, 15,1%), or follow-up investigations could not be conducted (17 cats, 2,7%).

In 64 (10,2%) cats of the 630 cats with low or low-normal TT4 concentration, SPH was considered a realistic differential diagnosis based on clinical signs and further endocrine investigations were recommended. SPH was excluded by TSH (n=55) or repeated TT4-measurements (n=8). Hypothyroidism was diagnosed in one cat with palpable bilateral goiter and suspected congenital dysmorphogenesis.

<https://doi.org/10.17236/sat00346>

Eingereicht: 31.10.2024
Angenommen: 30.12.2024

Screening for naturally occurring hypothyroidism in adult cats: A prospective multi-center study in Central Europe

F. N. Leuthard, A. Carranza Valencia, M. Wenger, F. Tschuur, F. K. Zeugs-wetter

Bei 64 (10,2%) der 630 Katzen mit niedriger oder niedrig-normaler TT4-Konzentration wurde SPH aufgrund klinischer Anzeichen als realistische Differenzialdiagnose angesehen und weitere endokrine Untersuchungen durchgeführt. SPH wurde durch TSH (n=55) oder wiederholte TT4-Messungen (n=8) ausgeschlossen. Bei einer Katze wurde eine Hypothyreose mit tastbarer beidseitiger Vergrößerung der Schilddrüse und Verdacht auf eine angeborene Dyschormonogenese diagnostiziert.

Die Ergebnisse deuten darauf hin, dass SPH nach wie vor selten ist und weitere endokrine Untersuchungen, wie TSH-Messungen, erforderlich sind, um weitere Fälle ohne klinischen Verdacht zu diagnostizieren.

Schlüsselwörter: Azotämie, Endokrinologie, Euthyroid-Sick-Syndrom, Katzenmedizin, nicht-Schilddrüsenerkrankung, Schilddrüsenfunktion

Results suggest that SPH remains rare and further endocrine investigations e.g. TSH measurement are needed to find additional cases without any clinical suspicion.

Keywords: azotemia, endocrinology, euthyroid sick syndrome, feline medicine, non-thyroidal illness, thyroid function

Introduction

While spontaneous primary hypothyroidism (SPH) is common in dogs, it is only occasionally diagnosed in cats, and its prevalence in the cat population is poorly quantified. To our knowledge, published cases of naturally occurring primary hypothyroidism in adult cats over the last three decades are limited to eight case reports and one case series, including eight cats.^{1,2,4,7,10,11,21,24} In the case series, Peterson et al. reported the diagnosis of two new cases of SPH per year in their endocrine referral clinic in New York and suggested this to be “the tip of the iceberg”.²¹ As polydipsia and polyuria associated with mild-to-moderate azotemia were common presenting signs, the authors emphasized examining cats with azotemia of unclear origin more closely.²¹ The case series of SPH in the New York area contrasts with the eight isolated cases reported worldwide over the past three decades, suggesting that SPH may be underdiagnosed in veterinary clinics. Conceivable explanations for the underdiagnosis of SPH include a low willingness to investigate cats with a low TT4, a lack of awareness of this condition, and significant challenges in verifying the diagnosis in uncertain cases.^{21,26}

A low TT4 is generally postulated to be due to a non-thyroidal illness (e.g., euthyroid sick syndrome) or administration of drugs such as corticosteroids and phenobarbital. At the same time, hypothyroidism is rarely considered a realistic differential diagnosis.^{6,8,21} In the past, the straightforward diagnostic investigation of cats with suspected hypothyroidism was hampered by the fact that not all hypothyroid cats have a low TT4, the absence of a specific feline TSH assay, the expense of the TSH-stimulation test and the limited availability of thyroid scintigraphy.²¹ The validation of a worldwide available canine TSH assay for use in cats has opened new doors in diagnosing feline thyroid diseases and is currently frequently used to diagnose iatrogenic feline hypothyroidism.^{17,28–30}

The objective of this multi-center study was to specifically search for adult cats with clinical signs suggestive of hypothyroidism and further review cats with low or low-normal TT4 concentration in order to find additional cases with SPH. We hypothesized that hypothyroidism is underdiagnosed in a substantial number of cats. Drawing on data from a North American case series, along with an unpublished case documented at the Small Animal Clinic at the University of Bern in 2017, we anticipated that intensive screening over the one-year study period would allow us to identify previously undiagnosed cases and provide a more detailed characterization of the clinical signs associated with SPH.

Materials and Methods

Data collection

Before initiating the study, conducted from July 2022 to June 2023, all staff members at the Tierklinik Mittelland (Switzerland), the Small Animal Clinic at the University of Bern (Switzerland), and the University Clinic for Small Animals at the University of Veterinary Medicine Vienna (Austria) were educated on the topic of SPH. This included scientific lectures that presented published case studies, outlined expected clinical signs, and discussed potential diagnostic procedures. Lethargy, weight gain, obesity, polyuria/polydipsia, inappetence, seborrhea, poor haircoat or poor regrowth of hair, bradycardia, hypothermia, constipation, palpable bilateral goiter and mild azotemia were considered possible clinical signs of SPH.

Inclusion criteria encompassed cats older than one year with clinical suspicion of hypothyroidism or if they exhibited mild azotemia (creatinine 140–250 µmol/l) without any evidence of underlying kidney disease (normal ultrasonography of the urogenital tract and unremarkable urinalysis). Endocrine investigations were pursued in case of a low TT4

(TT4 <15 nmol/L) concentration or measurements within the lowest 25th percentile of the assay-specific reference ranges (Reference range TT4 10–60 nmol/L). Cats with low-normal TT4 concentrations (TT4 <24 nmol/L) were considered to include cats with «mild» or «partially compensated hypothyroidism», as suggested by Peterson et al.²³

Further, all TT4 analyses carried out at the three clinics during the study period were screened for low TT4 concentrations or measurements in the lowest 25th percentile of the assay-specific reference ranges, and endocrine investigations were pursued if patient history or clinical findings documented in the respective patient sheet included clinical signs suggestive of hypothyroidism.

Exclusion criteria included cats under one year of age to exclude congenital hypothyroidism, cats without any clinical signs or biochemistry changes suggestive of hypothyroidism, cats with severe illness suspected to have nonthyroidal illness syndrome (NTIS), cats with treated hyperthyroidism, and cats that had received thyroid hormone-suppressing substances including glucocorticoids, phenobarbital, sulfonamides, potassium bromide, propranolol, or nonsteroidal anti-inflammatory drugs within the last four weeks. Additionally, cats with a diagnosis of hypoadrenocorticism or on medications potentially leading to hypocortisolism (e.g., trilostane, ketoconazole) were excluded to increase the specificity of TSH measurements.

Further endocrine investigations in cats with appropriate clinical signs of hypothyroidism and a low to low-normal TT4 included TSH measurements or TT4 reevaluations. The TSH-stimulation test (Mittelland, Bern) or scintigraphy (Vienna) were restricted to ambiguous cases. Signalment, patient history, presenting problems, known comorbidities, results of physical examinations, blood tests, and diagnostic imaging were recorded.

The study was approved by the Veterinary Inspection Office of the canton of Aargau, Switzerland, by written consent.

Hormone analysis

Serum TT4 concentration was measured using a Catalyst TT4 slide on a Catalyst One Chemistry Analyzer (IDEXX Laboratories, Westbrook, USA) (Mittelland) or a solid phase chemiluminescent competitive immunoassay (Immulite Total T4) on an Immulite 2000 XPI Analyzer (Siemens Healthineers, USA) (Vienna, Bern). For the Immulite total T4, the lower limit of quantification is 12,9 nmol/l and the upper limit of reportable values is 309 nmol/L. The laboratory reference interval for cats is 12–50 nmol/L for the Immulite total T4 and 10–60 nmol/L for the Catalyst One Chemistry Analyzer.^{9,31} Although different laboratories were used, the concentrations provided by all of these measurement methods are considered accurate and no diagnosis of hypothyroidism was made based on just one TT4 mea-

surement.^{5,14,18–20,32} Additionally in cases where further investigation was conducted at the Small Animal Clinic Mittelland (TSH measurement), TT4 concentrations were remeasured using residual samples with the Immulite 2000 XPI analyzer at the external laboratory (laborRvet AG, Reiden, Switzerland).

Feline TSH was measured using a canine TSH CEIA (Immulite 2000 canine TSH; Siemens Healthcare Diagnostic Products Ltd., U.K.) on an Immulite 2000 XPI Analyzer (Siemens Healthineers, USA). The reference interval is 0,02–0,3 ng/ml, the analytical sensitivity is 0,01 ng/mL, the lower limit of quantification is 0,03 ng/mL, and the upper limit of reportable values is 12 ng/mL, respectively.¹⁹ Serum free T4 (fT4) was determined by a CEIA (fT4CEIA; Immulite 2000 Veterinary Free T4; Siemens Healthcare Diagnostics Products).

Analyses were performed by different laboratories depending on the location in which the cat was presented: IDEXX Switzerland, Laborvet Reiden, LABOKLIN Austria, the central laboratory of the Vetmeduni Vienna and the University of Bern, respectively.

Thyroid status

SPH was considered possible in all cats with compatible clinical signs and/or azotemia in combination with a low TT4 or a TT4 concentration in the lowest 25th percentile of the reference range. TSH measurement was performed as the first follow-up test and the diagnosis of primary hypothyroidism was considered unlikely at concentrations < 0,3 ng/ml.¹⁷ SPH was also ruled out if follow-up measurements demonstrated TT4 concentrations in the middle or high reference range (TT4 > 24 nmol/L) of the specific assays. In case of a normal TSH but high clinical suspicion, thyroid scintigraphy (Vienna) or the TSH stimulation test (Mittelland, Bern) were performed.

Thyroid scintigraphy was performed under butorphanol/propofol anesthesia using a low energy high resolution parallel hole collimator (Diacam) gamma camera system (Medical Imaging Electronics, MIE GmbH, Seth, Germany), 30–60 minutes after injecting 150–180 MBq sodium pertechnetate (^{99m}TcO₄) IV. The TSH-stimulation test was performed using recombinant human TSH (Thyrogen 0,9 mg, Sanofi-Aventis, Frankfurt, Germany). TT4 concentrations were determined before and 6 hours after IV administration of 50 ug rhTSH.^{28,29}

Results

Study population

The results of TT4 concentration measurements are presented in Figure 1. A low or low-normal TT4 concentration was measured in 630 (45 %) of 1382 cats. A low-normal TT4

Screening for naturally occurring hypothyroidism in adult cats: A prospective multi-center study in Central Europe

F. N. Leuthard, A. Carranza Valencia, M. Wenger, F. Tschuor, F. K. Zeugswetter

Screening for naturally occurring hypothyroidism in adult cats: A prospective multi-center study in Central Europe

F. N. Leuthard, A. Carranza Valencia, M. Wenger, F. Tschuor, F. K. Zeugs-wetter

was found in 377 cats, and 253 cats had TT4 concentrations below the lower reference limit; hypothyroidism was considered a potential differential diagnosis in 64 cats with low or low-normal TT4 and further endocrine investigations were performed. SPH was excluded by TSH measurement or repeated TT4 measurement in 53 (82,8%) and eight (12,5%) cats, respectively. In two cats (3,2%) with a normal TSH but very high clinical suspicion of hypothyroidism, SPH was finally excluded by scintigraphy (n = 1, normal size, Tc99m uptake, and thyroid background ratio) or TSH-stimulation test (n = 1, basal TT4 20 nmol/L; stimulated TT4 38 nmol/L). SPH was confirmed in one cat with high TSH.

Cat with confirmed hypothyroidism

Hypothyroidism was verified in one male-castrated domestic short-haired cat two years of age with low TT4 and high TSH (TT4 < 0,3 mcg/dl; Reference range 0,9–2,9 mcg/dl; TSH 8,85 ng/ml; Reference range 0–0,04 ng/ml). Fructosamine and cholesterol concentrations were increased (fructosamine: 384 µmol/l; Reference range 0–340 µmol/l; cholesterol: 6,4 mmol/l; Reference range 1,8–3,9 mmol/l).¹² This cat was small in body size with a bodyweight of 3 kg, had palpable bilateral goiter and clinical signs typically seen in congenital hypothyroidism, including short limbs, broad head, mental dullness, retained deciduous teeth, and open growth plates and constipation.⁸

Excluded population

549 (87%) of 630 cats with a low or low normal TT4 were excluded as TT4 had been measured to exclude hyperthyroidism (299, 54,5%) and had not any clinical signs or suspicion for hypothyroidism, cats for therapy monitoring of hyperthyroidism (155, 28,2%), or the cats had received medication(s) known to reduce TT4 concentrations (95, 17,3%). Medications applied included glucocorticoids (53%), non-steroidal anti-inflammatory drugs (NSAIDs, 33%), phenobarbital (13%) and a combination of NSAIDs and glucocorticoids (2%). No cat received sulfonamide antibiotics or iodine.

Of the 299 cats suspected of hyperthyroidism, 158 [52,8%] had acute non-thyroidal illness and thus suspected NTIS. Of the remaining 141 [47,2%] cats, 131 cats (93%) had low normal, and 10 cats (7%) TT4 below reference interval. The cause of the low concentrations in these cats exhibiting mild diseases remains obscure. Nevertheless, as none showed clinical signs of hypothyroidism, further endocrine investigations were not recommended.

Another 17/630 (2,7%) cats were excluded due to euthanasia or as the owners declined further investigations.

Discussion

The results of this study indicate that SPH hypothyroidism remains a rare disorder in Central Europe and that the diagnosis is restricted to isolated cases. Despite the intensive search for clinical affected cats over a one-year period in three large, small animal clinics and the systematic endocrine screening of all cats with low and low-normal T4 measurements and compatible clinical signs, hypothyroidism was diagnosed only in one cat. Although this cat was two years of age and weighed 3 kg, clinical signs suggested congenital hypothyroidism. Interestingly, both fructosamine and cholesterol were elevated, despite fasting for 12 hours. Increased fructosamine in dogs with hypothyroidism is well known but in contrast to hypothyroid dogs, hypercholesterolemia seems uncommon in affected cats, and to the authors' knowledge elevated fructosamine concentrations despite euglycemia have not been described in cats with hypothyroidism.^{3,15,21,25} Thyroid palpation revealed bilateral goiter, which is in line with the statement that, in contrast to dogs, most cats appear to develop the goitrous form of hypothyroidism.^{15,21} Iodine deficiency or the uptake of environmental goitrogens was considered unlikely given the fact that the cat was fed variable moist and dry commercial cat foods. As suggested for most cats in the case series of Peterson et al. (2018), the hypothesis that best fits our cat is a hereditary defect of hormone production (dyshormonogenesis).²¹ The varying ability to secrete adequate amounts of TT4 and TT3 in affected cats could explain differences in disease onset, clinical presentation, and severity. Milder

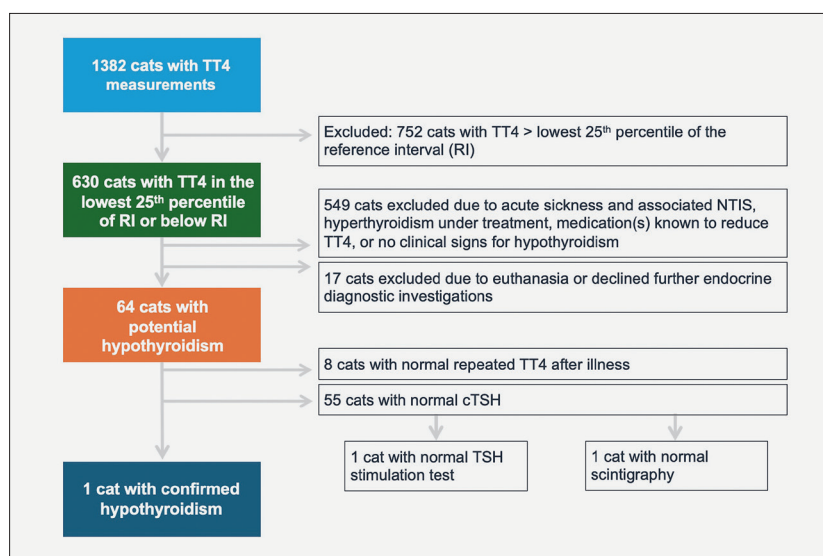


Figure 1: A total of 1,382 cats with TT4 laboratory results were screened for naturally occurring hypothyroidism over one year. Of these, 752 cats were excluded because their TT4 concentrations were >23 nmol/L. Among the 630 cats with TT4 concentrations <24 nmol/L, only 64 were identified as having potential hypothyroidism. Of these, 63 cats were excluded, leaving one cat confirmed with hypothyroidism. NTIS: nonthyroidal illness syndrome; RI: reference interval.

forms or partial defects of dyshormonogenesis likely lead to more subtle signs and later manifestation. The cat showed clinical improvement, with reduced lethargy and increased activity, including play behaviors, following administration of levothyroxine at a dose of 16,7 µg/kg (50 µg per cat) twice daily. Although we excluded cats younger than one year to exclude cats with congenital hypothyroidism, we ended up with a cat suggestive of congenital hypothyroidism. By excluding congenital cases, we aimed to ensure that our study explicitly addresses the less common, naturally occurring form of hypothyroidism that arises over time.

Of the 630 cats with TT4 concentrations in the lowest 25th percentile of reference interval, hypothyroidism was considered a potential differential diagnosis in 64 cats. TSH measurement revealed hypothyroidism in only one single case, and the majority were presumed to have nonthyroidal illness syndrome (NTIS). NTIS, previously called sick euthyroid syndrome, is a secondary thyroid disorder associated with low thyroid hormone concentrations, despite the thyroid gland being structurally and functionally normal.^{16,22} NTIS is likely an adaptive process to non-thyroidal diseases that aims to reduce energy expenditure and minimize metabolic demands.^{22,27} NTIS was only confirmed in cats in this study who were not in severe condition and potentially had naturally occurring hypothyroidism. Confirmation of NTIS and further blood workups did not seem ethical for severely clinically ill patients; therefore, the diagnosis of NTIS was unconfirmed for many cases in this study. The clinician in charge made the decision not to perform further diagnostics, usually when a cat was in a severe condition such as organ failure. Also, our study aimed to look for spontaneous adult-onset primary hypothyroidism and not evaluate the prevalence of cats with NTIS. Only cats that may have had a suspicion of hypothyroidism were provided with confirmation for NTIS to exclude the diagnosis of spontaneous hypothyroidism.

In contrast to primary hypothyroidism, TSH concentrations are usually normal or low in NTIS, but slightly elevated values may also occur. In one study including 222 cats with NTIS, mild increases in TSH were observed in 7 (3,2%) patients independent of disease severity.¹⁶ Elevated TSH concentrations in cats with low TT4 concentrations are thus not 100% specific for hypothyroidism, and elevations have to be interpreted cautiously. Noteworthy, TSH is usually >2 ng/ml in SPH, whereas concentrations above 0,5 ng/ml are very unusual in NTIS.^{16,22} TSH ranged from 2,1 to 20 ng/ml (median 10,1 ng/ml) in the case series from New York and was 8,85 ng/ml in the hypothyroid cat of this study.²¹ As TSH concentrations are very high in hypothyroid cats, new feline-optimized canine TSH assays with a very low analytic sensitivity will undoubtedly improve the differentiation between low and low-normal TSH concentrations but likely not bring any advantage to verify hypothyroidism.

Aside from TSH determination, scintigraphy and the TSH stimulation test, a potential further test to diagnose hypothyroidism is the measurement of free T4.¹⁶ Published cases of SPH suggest that this test has improved sensitivity compared to TT4 measurement.²⁷ Nevertheless, fT4 can be lowered as well as elevated in cats with NTIS, and TSH is considered more reliable.^{16,27} While serum fT4 measurements in this study were obtained via chemiluminescence and may be less accurate than those performed using the modified equilibrium dialysis technique, fT4 concentrations were never interpreted in isolation.

Based on the diagnosis rate observed in a recent study at a referral clinic in New York, which reported approximately two new cases of SPH per year, along with an unpublished case documented at the Small Animal Clinic at the University of Bern in 2017 (ESH, male castrated, four years old, showed bilateral goiter, lethargy, bradycardia, weight loss despite good appetite; TT4 17,3 nmol/l, fT4 (RIA) 5,7 pmol/l, TT3 3,4 pmol/l, TSH 3,3 ng/ml) we anticipated diagnosing more cats during the twelve-month intensive screening period. During the writing of this study, the sixteenth case of SPH in a private clinic in Germany was published, underscoring the existence of affected cats and highlighting the necessity for ongoing surveillance of this condition.¹

Our primary objective was to identify cats displaying clinical signs suggestive of hypothyroidism, which may have led to the exclusion of asymptomatic cases. Out of 64 cats with suspected SPH, only one was confirmed to have SPH. Given our focus on clinically apparent SPH, it is likely that we missed some cases without visible clinical signs and only laboratory changes, due to subjective judgement by clinicians. Measuring TSH in all 630 cats with TT4 concentrations in the lowest 25th percentile of the reference interval – even in those without clinical signs of SPH – might have increased case detection.¹³

This study has several limitations. First, TSH measurement was used as the main test to verify hypothyroidism in cats with low or low-normal TT4 concentrations. Although TSH measurement using a canine assay is considered a sensitive test to diagnose hypothyroidism, and all published cases so far exhibited excessive concentrations, it is possible that some patients were missed.^{5,13} It is not known whether a subset of cats with SPH exhibit normal TSH concentrations, similar to what is observed in canine hypothyroidism.¹⁵ Further endocrine investigations excluded SPH in two cats with high clinical suspicion and a normal TSH concentration in this study. Therefore, some cats classified as NTIS in this study may have been SPH cases that were misclassified. Second, follow-up examinations were only recommended in cats with consistent clinical signs and/or azotemia. As clinical signs can be very subtle in affected cats, some SPH patients may have been incorrectly excluded. Third, many TT4 measurements were analyzed using

Screening for naturally occurring hypothyroidism in adult cats: A prospective multi-center study in Central Europe

F. N. Leuthard, A. Carranza Valencia, M. Wenger, F. Tschuor, F. K. Zeugswetter

Screening for naturally occurring hypothyroidism in adult cats: A prospective multi-center study in Central Europe

F. N. Leuthard, A. Carranza Valencia, M. Wenger, F. Tschuur, F. K. Zeugs-wetter

an in-house analyzer rather than a reference laboratory method using reference limits provided by the manufacturer. Furthermore, different assay techniques were used based on the location of the cat. Noteworthy the in-house TT4 assay shows strong agreement in classification with a standard laboratory method at serum TT4 concentrations between 12–50 nmol/L.¹⁹ Additionally, TT4-determination was intended as a first screening test, and no diagnosis was based on TT4 measurement alone.

Conclusion

Naturally occurring hypothyroidism is an uncommon condition in adult cats in central Europe and its diagnosis can be difficult due to nonspecific clinical signs. Measuring TSH in adult cats should probably not be limited to those with a clinical suspicion of hypothyroidism but also include asymptomatic cats with low TT4 concentrations, to help identify potential cases that might otherwise be missed. Slightly elevated TSH concentrations, even in combination with a low TT4, should be interpreted cautiously to avoid misdiagnoses.

Dépistage de l'hypothyroïdie naturelle chez les chats adultes : une étude prospective multicentrique en Europe centrale

La recherche sur l'hypothyroïdie naturelle chez les chats adultes se limite à 16 cas rapportés au cours des trois dernières décennies, ce qui souligne la nécessité d'études plus complètes. Cette étude prospective multicentrique visait à identifier les cas d'hypothyroïdie primaire spontanée (HPS) chez les chats adultes présentés sur une période d'un an.

Le personnel de deux hôpitaux universitaires et d'une clinique privée de référence a examiné les chats âgés de plus d'un an présentant des signes cliniques évocateurs d'hypothyroïdie féline, notamment la constipation, l'obésité/la prise de poids, la léthargie, la taille du goitre, les altérations cutanées ou une légère azotémie. Il leur a été demandé de procéder à des examens endocriniens si des concentrations de T4 totale (TT4) faibles ou normales étaient détectées, en utilisant des analyses internes sur deux sites et des analyses externes dans un hôpital universitaire. Les examens diagnostiques continus consistaient principalement en des mesures de l'hormone thyroïdienne stimulante (TSH) à partir des échantillons restants et en une réévaluation de la TT4. D'autres chats susceptibles d'être atteints de SPH ont été recrutés en recherchant dans les systèmes de documentation locaux les concentrations de TT4 faibles ou normales enregistrées pendant la période de l'étude.

Acknowledgement

The authors would like to thank the owners of the patients that were enrolled in this study for their consent and participation. The authors received no financial support for the research, authorship and/or publication of this article.

Conflict of Interest

The authors have no conflict of interest to declare.

Screening per l'ipotiroidismo naturale nei gatti adulti: uno studio prospettico multicentrico nell'Europa Centrale

La ricerca sull'ipotiroidismo naturale nei gatti adulti è limitata a 16 casi riportati negli ultimi tre decenni. Questa situazione necessita di studi più approfonditi. Questo studio prospettico multicentrico ha come obiettivo di identificare i casi di ipotiroidismo primario spontaneo (SPH) nei gatti adulti presentati nell'arco di un anno.

Lo staff di due ospedali universitari e di una clinica di rinvio privata hanno sottoposto a screening i gatti di età superiore a un anno che mostravano segni clinici che potevano suggerire un ipotiroidismo felino, tra cui costipazione, obesità/aumento di peso, letargia, dimensioni del gozzo, alterazioni cutanee o lieve azotemia. Sono stati istruiti a procedere con indagini endocrine se venivano rilevati dei livelli di T4 totale (TT4) bassi o bassi-normali, utilizzando analisi interne in due sedi e analisi esterne in un ospedale universitario. Le indagini diagnostiche successive consistevano principalmente nella misurazione dell'ormone stimolante la tiroide (TSH) utilizzando campioni residui e nella rivalutazione del TT4. Altri gatti con possibile SPH sono stati reclutati esaminando i sistemi di documentazione locali per concentrazioni di TT4 basse o basse-normali registrate durante il periodo di studio.

Des concentrations de TT4 faibles (n = 253, 18,3 %) à faibles normales (n = 377, 27,3 %) ont été observées chez 630 (45,6 %) des 1 382 chats. Sur ces 630 chats potentiellement atteints de SPH, 566 (89,8 %) ont été exclus pour les raisons suivantes : La TT4 a été mesurée pour exclure une hyperthyroïdie (299 chats, 47,4 %), ils étaient traités avec des médicaments qui diminuent les concentrations de TT4 (médicaments antithyroïdiens : 155 chats, 24,6 % ; autres médicaments : 95 chats, 15,1 %), ou les examens de suivi n'ont pas pu être effectués (17 chats, 2,7 %).

Chez 64 (10,2 %) des 630 chats présentant une concentration de TT4 basse ou basse-normale, le SPH a été considéré comme un diagnostic différentiel réaliste sur la base des signes cliniques et des examens endocriniens complémentaires ont été recommandés. Le SPH a été exclu par la TSH (n=55) ou des mesures répétées de TT4 (n=8). Une hypothyroïdie a été diagnostiquée chez un chat présentant un goitre bilatéral palpable et suspecté de dysmorphogénèse congénitale.

Les résultats suggèrent que le SPH reste rare et que des investigations endocriniennes supplémentaires, comme la mesure de la TSH, sont nécessaires pour trouver d'autres cas sans suspicion clinique.

Mots clés: azotémie, endocrinologie, hypothyroïdie fonctionnelle, médecine féline, maladie non thyroïdienne, fonction thyroïdienne

Concentrazioni basse (n = 253, 18,3%) o basse-normali (n = 377, 27,3%) di TT4 sono state osservate in 630 (45,6%) dei 1382 gatti esaminati. Di questi, 630 con possibile SPH, 566 (89,8%) sono stati esclusi per i seguenti motivi: il TT4 era stato misurato per escludere l'ipertiroidismo (299 gatti, 47,4%), erano stati trattati con farmaci che abbassano le concentrazioni di TT4 (farmaci antitiroidei: 155 gatti, 24,6%; altri farmaci: 95 gatti, 15,1%) o non è stato possibile effettuare indagini di follow-up (17 gatti, 2,7%).

In 64 (10,2%) dei 630 gatti con concentrazioni basse o basse-normali di TT4, l'SPH è stato considerato una diagnosi differenziale realistica sulla base dei segni clinici ed è stato raccomandato di effettuare ulteriori indagini endocrine. L'SPH è stato escluso attraverso il TSH (n = 55) o misurazioni ripetute del TT4 (n = 8). L'ipotiroidismo è stato diagnosticato in un gatto con gozzo bilaterale palpabile e sospetta disormonogenesi congenita.

I risultati suggeriscono che l'SPH rimane raro e che ulteriori indagini endocrine, come la misurazione del TSH, sono necessarie per individuare altri casi senza sospetti clinici.

Parole chiave: azotemia, endocrinologia, sindrome del malato eutiroideo; medicina felina, malattie non tiroidee; funzione tiroidea

Screening for naturally occurring hypothyroidism in adult cats: A prospective multi-center study in Central Europe

F. N. Leuthard, A. Carranza Valencia, M. Wenger, F. Tschuor, F. K. Zeugs-wetter

Literaturnachweis

- Atrissi N. Primäry Hypothyreose bei einer Katze – Fallbericht. Tierärztliche Umschau Kleintiermedizin. 2024; 3: 20–24.
- Blois SL, Abrams-Ogg AC, Mitchell C, Yu A, Stowen D, Lillie BN, Kiupelel M. Use of thyroid scintigraphy and pituitary immunohistochemistry in the diagnosis of spontaneous hypothyroidism in a mature cat. J Feline Med Surg. 2010; 12(2): 156–160.
- Boretti, F. S., Breyer-Haube, I., Kaspers, B., & Reusch, C. E. (2003). Klinische, hämatologische, biochemische und endokrinologische Aspekte bei 32 Hunden mit Hypothyreose [Clinical, hematological, biochemical and endocrinological aspects of 32 dogs with hypothyroidism]. Schweiz. Arch. Tierheilkd. 2003; 145(4): 149–159.
- Cobucci GC. Cintilografia de tireoide e radioiodoterapia com dose individualizada em gatos com doenças tireoidianas. 2024; p 97. Tese (Doutorado em Ciências Veterinárias)–Universidade Federal de Lavras, Lavras.
- Fernandez Y, Puig J, Powell R, Seth M. Prevalence of iatrogenic hypothyroidism in hyperthyroid cats treated with radioiodine using an individualised scoring system. J Feline Med Surg. 2019; 21(12): 1149–1156.
- Fliers E, Boelen A. An update on non-thyroidal illness syndrome. J Endocrinol Invest. 2021; 44(8): 1597–1607.
- Balgano M, Spalla I, Callegari C, Patruno M, Auriemma E, Zanna G, Ferro S, Zini E. Primary hypothyroidism and thyroid goiter in an adult cat. J Vet Intern Med. 2014; 28(2): 682–686.
- Greco DS. Diagnosis of congenital and adult-onset hypothyroidism in cats. Clin Tech Small Anim Pract. 2006; 21(1): 40–44.
- IDEXX. Total T4 testing guide: canine hypothyroidism <https://www.idexx.com/files/total-t4-testing-guide-cat-unified.pdf> (2017, accessed 1 December 2022).
- Kent A, Constantino-Casas F, Herrtage ME. Naturally occurring acquired primary hypothyroidism in a cat due to lymphocytic thyroiditis. Vet Rec Case Rep 2016; 4: e000282. DOI:10.1136/vetreccr-2015-000282
- Koral E, Ek M. Primary hypothyroidism in an adult cat. Cocatepe Veterinary Journal 2022; 15: 507–511.
- LABOKLIN. Reference values: https://laboklin.com/wp-content/uploads/2024/09/Referenzwerte_Dog_Cat_Rabbit_Pig__EN_07.2024.pdf (2024, accessed 27.12.2024)
- Lin J, Schwens C, Schaub S, et al. Large-scale screening for cases of suspected spontaneous hypothyroidism in adult cats and description of clinical, laboratory, scintigraphic features and treatment in four affected cats, Proceedings, 34th ECVIM-CA Annual Congress Lyon, France, 2024 (available from: European Veterinary Endocrinology Society)
- Lucy JM, Peterson ME, Randolph JF, Scrivani PV, Rishniw M, Davignon DL, Thompson MS, Scarlett JM. Efficacy of Low-dose (2 millicurie) versus Standard-dose (4 millicurie) Radioiodine Treatment for Cats with Mild-to-Moderate Hyperthyroidism. J Vet Intern Med. 2017; 31(2): 326–334.

Screening for naturally occurring hypothyroidism in adult cats: A prospective multi-center study in Central Europe

F. N. Leuthard, A. Carranza Valencia, M. Wenger, F. Tschuor, F. K. Zeugs-wetter

- ¹⁵ Mooney CT. Canine Hypothyroidism. In: Côté E. Textbook of Veterinary Internal Medicine. 9th ed. Elsevier – OHCE, 2024:1920–1931.
- ¹⁶ Peterson ME, Melián C, Nichols R. Measurement of serum concentrations of free thyroxine, total thyroxine, and total triiodothyronine in cats with hyperthyroidism and cats with nonthyroidal disease. *J Am Vet Med Assoc* 2001; 218: 529–536.
- ¹⁷ Peterson ME. Feline focus: Diagnostic testing for feline thyroid disease: hypothyroidism. *Compend Contin Educ Vet* 2013; 35: E4.
- ¹⁸ Peterson ME. More Than Just T4: Diagnostic testing for hyperthyroidism in cats. *J Feline Med Sur* 2013; 15: 765–777.
- ¹⁹ Peterson ME, Guterl JN, Nichols R, Rishniw M. Evaluation of Serum Thyroid-Stimulating Hormone Concentration as a Diagnostic Test for Hyperthyroidism in Cats. *J Vet Intern Med.* 2015; 29(5): 1327–1334.
- ²⁰ Peterson ME, Rishniw M, Bilbrough GE, Cote KB. Comparison of in-clinic point-of-care and reference laboratory total thyroxine immunoassays for diagnosis and post-treatment monitoring of hyperthyroid cats. *J Feline Med Surg.* 2018; 20(4): 319–324.
- ²¹ Peterson ME, Carothers MA, Gamble DA, Rishniw M. Spontaneous primary hypothyroidism in 7 adult cats. *J Vet Intern Med.* 2018; 32(6): 1864–1873.
- ²² Peterson ME, Davignon DL, Shaw N, Dougherty E, Rishniw M, Randolph JF. Serum thyroxine and thyrotropin concentrations decrease with severity of nonthyroidal illness in cats and predict 30-day survival outcome. *J Vet Intern Med.* 2020; 34(6): 2276–2286.
- ²³ Peterson ME, Rishniw M. Urine concentrating ability in cats with hyperthyroidism: Influence of radioiodine treatment, masked azotemia, and iatrogenic hypothyroidism. *J Vet Intern Med.* 2023; 37(6): 2039–2051.
- ²⁴ Rand JS, Levine J, Best SJ, Parker W. Spontaneous adult-onset hypothyroidism in a cat. *J Vet Intern Med.* 1993; 7(5): 272–276.
- ²⁵ Reusch CE, Gerber B, Boretti FS. Serum fructosamine concentrations in dogs with hypothyroidism. *Vet Res Commun* 2002; 26: 531–536.
- ²⁶ Scott-Moncrieff JC. Feline Hypothyroidism. In: Côté E. Textbook of Veterinary Internal Medicine. 9th ed. Elsevier – OHCE. 2024: 1935–1939.
- ²⁷ Vandermeulen E, Duchateau L, Van de Maele I, Daminet S. Comparison of free thyroxine measurement by chemiluminescence and equilibrium dialysis following 131I therapy in hyperthyroid cats. *J Feline Med Surg.* 2020; 22(12): 1114–1120.
- ²⁸ Stegeman JR, Graham PA, Hauptman JG. Use of recombinant human thyroid-stimulating hormone for thyrotropin-stimulation testing of euthyroid cats. *Am J Vet Res* 2003; 64: 149–152.
- ²⁹ Van Hoek IM, Vandermeulen E, Peremans K, Daminet S. Thyroid stimulation with recombinant human thyrotropin in healthy cats, cats with non-thyroidal illness and in cats with low serum thyroxin and azotaemia after treatment of hyperthyroidism. *J Feline Med Surg.* 2010; 12(2): 117–121.
- ³⁰ Wakeling J, Hall T, Williams TL. Correlation of thyroid hormone measurements with thyroid stimulating hormone stimulation test results in radioiodine-treated cats. *J Vet Intern Med* 2020; 34: 2265–2275.
- ³¹ Williams TL, Archer J. Validation of an automated enzyme immunoassay for the measurement of serum total thyroxine in cats. *Vet Clin Pathol.* 2016; 45(1): 148–153.
- ³² Wolff EDS, Bilbrough G, Moore G, Guptill L, Scott-Moncrieff JC. Comparison of 2 assays for measuring serum total thyroxine concentration in dogs and cats. *J Vet Intern Med.* 2020; 34(2): 607–615.

Korrespondenzadresse

Dr.med.vet. Fabienne Leuthard
Tierklinik Mittelland
Kieferstrasse 2
CH-Oftringen-Zofingen 4665
Telefon: +41 62 922 789 70 70
E-Mail: fleuthard@tierklinik-mittelland.ch