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EVALUATING FELINE SERUM AMYLOID A AS A DIAGNOSTIC AND PROGNOSTIC MARKER IN FOUR CASES OF FELINE INFECTIOUS PERITONITIS

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ABSTRACT

The paper describes four clinical cases of feline infectious peritonitis (FIP), highlighting the diagnostic utility of feline serum amyloid A (fSAA) in navigating the complexities of FIP diagnosis. The findings underscore the value of fSAA as a biomarker, not only in establishing a more reliable diagnosis but also in facilitating ongoing case monitoring and providing prognostic insights.

Key words: feline, serum, amyloid A, infectious, peritonitis.

Introduction

The initial response to inflammatory triggers – such as infections, trauma, tumors, and surgical procedures – includes the activation of the acute phase (Ebersole J., Cappelli D., 2000). A hallmark of this response is the liver's enhanced synthesis of plasma proteins, known collectively as acute phase proteins (APPs). Multiple and sequential measurements of APPs provide added advantages, especially in evaluating the effectiveness of treatments. APPs are more sensitive than white blood cell (WBC) counts for detecting early signs of inflammation and can accurately indicate early remission or recurrence of diseases (Rossi G., 2023). The SAA is one of the major APP in several species, important in both humans and cats (Kajikawa T. *et al.*,1999). Modulates the immune response by attracting inflammatory cells to tissues and leading to the production of multiple inflammatory cytokines (Gruys E. *et al.*, 2005; Tizard I.,2013). Its concentration may rise more than 1,000-fold in inflammatory status, consequently perceiving inflammation (Tamamoto T. *et al.*, 2013). FSAA concentrations are higher in cats with inflammatory conditions like upper respiratory tract infections, pneumonia, pyometra, and feline infectious peritonitis (FIP) compared to healthy cats. Therefore, measuring fSAA levels is a valuable marker for detecting inflammation in diseased cats (Yuki M. *et al.*, 2020). APPs and especially fSAA are crucial for diagnosing feline infectious peritonitis (FIP) in cats. Diagnosing Feline Infectious Peritonitis (FIP) is challenging due to the disease's complex pathology, overlapping symptoms with other diseases, and limitations in diagnostic tests. FIP is caused by certain mutations of the feline coronavirus (FCoV), which in most cases, doesn't cause serious illness. However, in a small percentage of cats, FCoV mutates, leading to the severe and often fatal condition known as FIP with significant risk of relaps **(**Felten S., Hartmann K. 2019**).** FSAA testing can be a very useful part of non-invasive methods for the complex diagnosis, monitoring and prognosis of FIP.

Description of clinical cases

Case 1 Presentation

Ochka, a young stray kitten, was presented with a swollen abdomen and an eye infection. Her history as a homeless animal suggested potential exposure to infectious diseases. Initial diagnostic

testing included a triple test for common feline viral diseases (Feline Panleukopenia Virus (FPV), Feline Coronavirus (FCoV), Giardia), which yielded negative results. However, blood tests revealed several abnormalities: thrombocytopenia, elevated total protein (80.3 g/L), low albumin (24.3 g/L), a reduced albumin-to-globulin (A/G) ratio of 0.4, and high bilirubin levels (total bilirubin at 56.7 μmol/L, direct bilirubin at 26.5 μmol/L). Elevated ASAT levels (117 U/L) indicated hepatic dysfunction, and an abdominal ultrasound confirmed hepatic lipidosis with a normal – appearing gallbladder and free abdominal fluid, consistent with FIP-associated effusion. Following the initial blood work, along with a progression of clinical signs, the diagnosis was further supported by additional tests, a rapid antibody test for Feline Infectious Peritonitis (FIP), which returned positive. Feline Serum Amyloid A (fSAA) levels were measured using a Veterinary Immunoassay Analyzer (BIONOTE Vcheck V200), which utilizes fluorescent immunoassay (FIA) technology. The fSAA levels were elevated at 105 μg/ml. Serial Blood tests over the following days confirmed leukocytosis, persistent thrombocytopenia, mild anemia, and eosinophilia – all consistent with FIP pathology.

Treatment and Management

Ochka's initial treatment focused on symptomatic support. Intravenous fluid therapy was implemented to stabilize hydration and support hepatic function**.** Intravenous medications were administered to manage hepatic inflammation and support immune response. Following the confirmed FIP diagnosis, Ochka was started on antiviral nucleoside compound – GS-441524 FipHeal ®, a medication with known efficacy against FIP. This treatment continued for 84 days, during which Ochka responded positively, achieving remission.

Follow-Up and Relapse

One year post-treatment, Ochka presented again with similar symptoms after several days outdoors with limited food intake. Physical examination revealed abdominal effusion, consistent with FIP recurrence**.** Blood work showed leukocytosis, elevated fSAA levels (>200 μg/ml)**,** and a low A/G ratio of 0.5, reaffirming the FIP diagnosis.

Revised Treatment Plan

Ochka's treatment was updated to include combination antiviral therapy with GS-441524 and molnupiravir Lagevrio ®, aimed at increasing efficacy against FIP. Supportive therapy was also administered to maintain immune function and manage inflammation. Serial fSAA tests monitored inflammatory response, showing improvement with fSAA levels reduced to 54.5 μg/ml, and white blood cell count normalized.

Case 2 Presentation

Sima, a 9-year-old mixed breed cat living with five other cats, presented at the clinic with concerning symptoms approximately 10 days after her latest vaccination. Regularly vaccinated and dewormed, Sima's recent symptoms included lethargy, two episodes of vomiting, and a noticeable anorexia. On examination, she had a high fever of 40°C, prompting further investigation. Initial blood work indicated suspected pancreatitis, marked by eosinophilia and white blood cell abnormalities. The biochemical profile showed total protein at 64.2 g/L, low albumin at 22.1 g/L, an A/G ratio of 0.5, and elevated fSAA (68 μg/ml). While her Feline Pancreatic Lipase (FPL) level was within the normal range, further testing revealed feline coronavirus (FCoV) antibodies. A PCR test from Laboclin was positive, and an antibody level of 15.76 was recorded, indicating an infection consistent with dry FIP. An abdominal ultrasound showed no effusion, aligning with dry FIP.

Treatment and Management

Sima's initial treatment focused on symptomatic management. However, as her symptoms persisted, treatment with the antiviral GS-441524 was initiated. Over the following three weeks, Sima responded positively: her appetite improved, and repeat blood work showed a reduction in FSAA levels to 29 μg/ml, though still elevated.

Follow-Up and Relapse

Approximately 10 days after her initial improvement, Sima experienced a recurrence of symptoms, including lethargy and vomiting. Her FSAA level increased to 40.5 μg/ml. Continued GS-441524 and symptomatic therapy stabilized her condition.

Long-Term Follow-Up

Seven months after completing her FIP treatment, Sima presented with a mild recurrence of symptoms, including a fever of 40.2°C. Blood work revealed a normal FSAA level of 14 μg/ml. Symptomatic therapy managed the fever, and Sima's condition improved.

Outcome

Sima's case demonstrated a positive response to GS-441524 for FIP. Ongoing management and adjustments to therapy stabilized her health, reflecting resilience and recovery.

Case 3 Presentation

Petkan, a 12-year-old male cat that had not been neutered, presented for examination due to persistent vomiting and loss of appetite over the past three days. Despite regular deworming, Petkan had been experiencing sporadic vomiting and constipation. His owners reported he had vomited food followed by gastric juices and had lost 300 grams in weight over the past 10 days. On clinical examination, Petkan exhibited pale pink mucous membranes, and his left eye showed no pupillary reaction. There was inflamed tissue growth around the lower left canine. Blood tests revealed several abnormalities: a low platelet count of 53 G/L, slightly elevated AST at 27 U/L, decreased albumin at 26.3 g/L, and a low albumin-to-globulin (A/G) ratio of 0.5. Additionally, the FSAA (Feline Serum Amyloid A) level was elevated at 55.5 μg/ml, indicating inflammation.

Treatment and Management

Symptomatic therapy was initiated for vomiting, and a coronavirus antibody test returned positive. Suspected neoplastic growth in the gum area was also noted. Two weeks later, follow-up tests showed slight platelet improvement and normalized fSAA levels. Antiviral treatment with molnupiravir was initiated, with additional vitamin supplementation.

Follow-Up and Deterioration

Unfortunately, despite the initiation of antiviral therapy, Petkan's condition continued to deteriorate significantly over the next two months. He exhibited increased lethargy, persistent vomiting, and further weight loss, which prompted additional evaluations and adjustments to his treatment regimen. The fSAA levels increased over 200 μg/ml. However, the response to therapy remained inadequate.

Outcome

After careful consideration and consultation with the owners, the difficult decision was made to euthanize Petkan due to his declining quality of life and lack of improvement despite aggressive treatment efforts. This case highlights the challenges in managing FIP, especially in older cats with concurrent health issues such as suspected neoplasia.

Case 4 Presentation

Mazzoni, a 7-year-old male neutered mixed-breed cat, was presented with a history of diarrhea lasting four days. Mazzoni also experienced vomiting of stomach contents, anorexia and increased vocalization. He drank more water than usual but showed little interest in toys or junk food. Mazzoni was regularly dewormed, vaccinated and lived indoors with two other outdoor cats. On examination, Mazzoni had a normal body temperature of 38.8°C and normal mucous membranes. His abdomen was soft but distended, with slight intestinal hypermotility. Blood tests revealed eosinophilia (7.8%) but were otherwise within normal limits. Biochemical tests indicated slightly elevated ALP at 136 U/L, low albumin at 20.5 g/L, and a low albumin-to-globulin (A/G) ratio of 0.5. Both T4 and FPL levels were normal.

Treatment and Management

Initial treatment included probiotics and a therapeutic diet. Further testing, including coproovoscopy and a coronavirus antigen test, returned negative results, although an antibody test was positive**.** The diagnosis of FIP was suspected and was further supported by additional tests- antibodies for feline coronavirus were measured- 37.22. fSAA levels were measured at 92 μg/ml, supporting a suspected FIP diagnosis. GS-441524 therapy began, initially in combination with molnupiravir. After 10 days, GS-441524 was discontinued, and treatment continued with molnupiravir alone. Over one month, Mazzoni showed improvement: appetite returned, vomiting ceased, and normal urination/defecation patterns resumed. Blood tests showed improved fSAA (<5 μg/ml) and slightly improved A/G ratio (0.6).

Follow-Up

On day 84 of therapy, Mazzoni was in good general condition and fSAA levels remained normal (<5 μg/ml), and an antibody test revealed levels of 11.21, prompting a two-week extension of molnupiravir.

Outcome

One year later, Mazzoni recovered fully, with fSAA levels consistently under 5 μg/ml, demonstrating resilience through the treatment course.

Discussion

Currently, no single test can conclusively diagnose FIP in living cats. Diagnosis often relies on a combination of clinical signs and physical examination findings, laboratory tests (e.g., blood tests showing high protein levels, white blood cell counts, and changes in globulin levels), Imaging (e.g., ultrasound) to check for organ abnormalities and PCR tests (Addie K. *et al.*, 2009). Obtaining a definitive diagnosis of FIP based on non-invasive approaches is difficult. Confirmation of the disease relies on finding appropriate cytological or histopathological changes in association with positive immunostaining for FCoV antigen (Tasker S., 2018). In most cases, these invasive tests are only done after other diagnostic methods fail, as they pose risks to the cat. Therein lies the importance of using a complex of non-invasive methods to confirm the diagnosis and elevated fSAA levels help support the suspicion of FIP, especially in cases where other clinical signs align with FIP (Hazuchova K. *et al.*, 2017). In each of the documented FIP cases, elevated fSAA values were consistently observed. Following therapeutic intervention and subsequent clinical improvement, amyloid levels demonstrated a marked reduction. Conversely, in instances of relapse, indicator values rose once again. In Case 3, the patient did not respond to treatment, and a progressive

worsening of the condition was noted, accompanied by fSAA levels surpassing the initial baseline measurements. These findings underscore the significance of this diagnostic test in enhancing disease diagnosis, relapse detection, and prognostic assessment. In Case 3, where levels exceed 200 μg/ml, disease progression and prognosis appear notably poor. These clinical data highlight the critical role of this laboratory test in improving disease diagnosis, relapse detection, and prognosis assessment. In Case 3, where levels surpass 200 μg/ml, the disease demonstrates a poor progression and prognosis. Fluctuations in these values can also serve as indicators of treatment efficacy, offering valuable guidance for ongoing disease monitoring. As reported in the study by Krentz *et al.* (2021)**,** the use of antiviral therapy resulted in a fast and persistent drop in fSAA levels in feline FIP cases. This rapid decline in fSAA concentration suggests that it might indicate superior virucidal activity, implying a positive response to antiviral treatment in cats with FIP. Research has highlighted further diagnostic applications for this indicator, identifying key benefits including its effectiveness in distinguishing between cats with FIP and those with comparable clinical signs but without FIP. According to Rossi G., (2023), measuring acute phase proteins (APPs) can be instrumental for this purpose. Giordano *et al.* (2004) found that SAA levels were persistently higher in cats with FIP, in contrast to temporary rises seen in cats only exposed to FCoV. Achieving a definitive FIP diagnosis remains difficult, especially with its differing clinical forms like wet and dry FIP. Many diagnostic tests cannot accurately differentiate between feline enteric coronavirus and the FIP virus, and a pre-mortem diagnosis is often challenging in cats lacking body cavity effusions (Felten & Hartmann, 2019). Acute phase proteins (APPs) are therefore essential for diagnosing FIP, serving as vital indicators in clinical settings (Felten & Hartmann, 2019).

Conclusion

The study demonstrates the significant diagnostic and prognostic value of fSAA as a biomarker in feline infectious peritonitis (FIP) cases. Across four distinct cases, elevated fSAA levels reliably indicated inflammation associated with FIP, while fluctuations in these levels mirrored responses to antiviral therapy and helped to monitor disease progression or recurrence. This underscores the utility of fSAA testing as part of a comprehensive, non-invasive approach to FIP diagnosis and management, providing essential guidance in therapeutic planning and outcome assessment for affected cats.

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