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Case report

SERIAL MAGNETIC RESONANCE IMAGING FOLLOW-UP OF A CHIHUAHUA WITH MENINGOENCEPHALITIS OF UNKNOWN ORIGIN TREATED WITH PREDNISOLONE AND IMATINIB: A CASE REPORT

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Meningoencephalitis of unknown origin (MUO) is an immune-mediated central nervous system disorder in dogs in which magnetic resonance imaging (MRI) plays a key role in diagnosis and monitoring. This case report describes a five-year-old spayed female Chihuahua (3.9 kg) presented with acute right-sided weakness, anorexia, and vomiting. The initial MRI demonstrated multifocal T2/FLAIR hyperintense lesions in the left frontal lobe with suspected disruption of the blood–brain barrier, consistent with MUO. Immunosuppressive therapy with prednisolone (0.5 mg/kg twice daily, tapered to 0.15 mg/kg once daily) was administered in combination with imatinib (10 mg/kg once daily). Follow-up MRI after seven weeks revealed partial remission of lesions, restoration of blood–brain barrier integrity, and mild ventricular enlargement. At eleven months, chronic gliosis, progressive cerebral atrophy, and further ventricular dilation (39% vs. 29% at 7 weeks) were evident without new lesions. Clinical signs resolved within 25 days, but long-term therapy caused polyphagia, polydipsia, persistent alkaline phosphatase elevation, transient alanine aminotransferase increase, and episodes of hypertriglyceridemia. This case highlights the value of sequential MRI for documenting the transition from acute inflammation to partial remission and chronic structural change in MUO. Prednisolone-based immunosuppression combined with imatinib achieved sustained clinical improvement, while long-term monitoring was essential to detect progressive atrophy and treatment of related adverse effects.

Keywords: brain atrophy, canine, imatinib, meningoencephalitis of unknown origin, prednisolone

INTRODUCTION

Meningoencephalitis of unknown origin (MUO) comprises immune-mediated inflammatory diseases of the canine central nervous system and is diagnosed when no infectious cause can be confirmed by histopathology. It occurs mainly in small-breed dogs and presents with variable neurological signs. Histopathological subtypes

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include granulomatous meningoencephalitis (GME), necrotizing meningoencephalitis (NME), and necrotizing leukoencephalitis (NLE) [1]. Clinical diagnosis relies on magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) analysis, followed by immunosuppressive therapy [2].

Prednisolone (PDS) remains the cornerstone of MUO management. While monotherapy can achieve long-term survival [3], combination protocols with cyclosporine or mycophenolate mofetil have yielded improved outcomes [4,5]. Imatinib, a tyrosine kinase inhibitor originally developed for human oncology, has been reported to improve neurological recovery and reduce lesion burden in dogs with granulomatous meningoencephalitis and meningoencephalitis of unknown origin when used in combination with prednisolone [6,7].

MRI is crucial not only for diagnosis but also for monitoring therapeutic response and prognosis. Lesion improvement within three months is associated with favorable outcomes [2], whereas progressive brain atrophy predicts a poorer prognosis [2,8]. However, long-term sequential MRI assessments in MUO cases treated with combined PDS and imatinib are rarely documented.

The aim of this case report is to describe the clinical course of a Chihuahua with MUO treated with PDS and adjunctive imatinib, using serial MRI examinations to document the transition from acute inflammation to chronic structural changes.

CASE PRESENTATION

A five-year-old spayed female Chihuahua (3.9 kg) was presented with acute weakness of the right fore – and hindlimbs, anorexia, and vomiting. Neurological examination localized the lesion to the forebrain, and magnetic resonance imaging (MRI; 1.5 T, Siemens Magnetom Essenza) was performed.

Clinical findings and diagnostics

The first MRI (day 0, pre-treatment) revealed multifocal T2/FLAIR hyperintense lesions in the left frontal white matter and a smaller right frontal focus with suspected disruption of the blood–brain barrier (BBB). No marked contrast enhancement was detected, and a mild C6–7 intervertebral disc protrusion (<10% compression) was noted. The findings were consistent with MUO.

After seven weeks of therapy (day 55), MRI demonstrated partial remission with decreased lesion intensity, restored BBB integrity, and mild enlargement of the left lateral ventricle (29% of hemispheric height).

At nearly eleven months (day 343), MRI showed residual hyperintense lesions without enhancement, progressive cerebral atrophy, and further ventricular dilation (39% vs. 29% at seven weeks), compatible with chronic gliosis and compensatory enlargement (Figures 1–9).

Ventricular diameter was measured on transverse T2-weighted images at the level of the interthalamic adhesion and expressed as a percentage of total hemispheric height to allow quantitative monitoring of ventricular size over time.

Table 1. Sequential MRI findings in a Chihuahua with MUO (1st–3rd follow-up).

Time point	MRI findings	Interpretation
1st MRI (Day 3)	- Multifocal T2/FLAIR hyperintense lesions involving the left frontal, temporal, parietal, and occipital lobes, predominantly affecting the white matter. - Focal lesion also observed in the right frontal lobe. - Partial BBB disruption suspected. - Mild C6–7 intervertebral disc protrusion (<10% compression).	Findings consistent with acute inflammatory lesions; presumptive diagnosis of MUO.
2nd MRI (Day 55)	- Similar distribution of T2/FLAIR hyperintense lesions in the left cerebrum and right cingulate cortex. - No significant contrast enhancement, indicating improved BBB integrity compared to the 1st MRI. - Compensatory enlargement of the left lateral ventricle (29% of hemispheric height). - Occipital hypoplasia with mild cerebellar crowding.	Partial remission with improved BBB integrity; residual lesions persist. Continued medical management recommended.
3rd MRI (Day 343)	- Persistent T2/FLAIR hyperintense lesions in the left cerebral hemispheres (frontal, temporal, parietal, occipital) and focal lesion in the right frontal lobe. - No new lesions identified. - No significant contrast enhancement. - Progressive enlargement of the left lateral ventricle (39% vs. 29% at the 2nd MRI). - Occipital hypoplasia with cerebellar crowding unchanged.	Chronic residual lesions with gliosis and progressive brain atrophy; consistent with long-term sequelae rather than active inflammation.

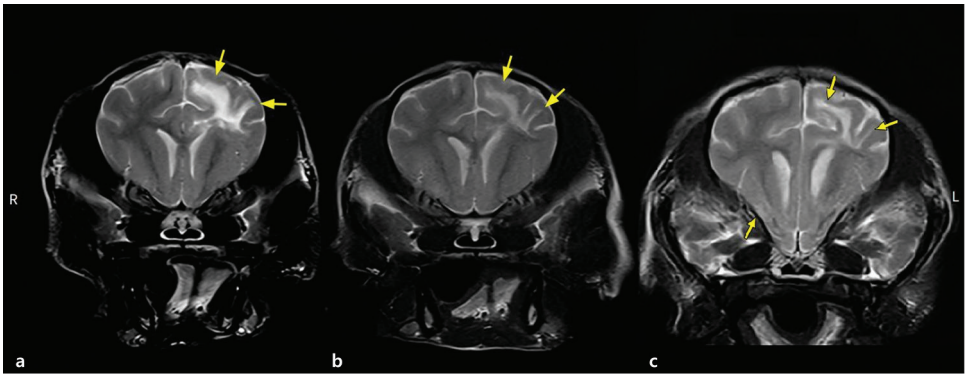

Figure 1. Sequential T2-weighted MR images of the left frontal lobe
(a) Initial MRI (day 0, pre-treatment) shows multifocal T2-hyperintense lesions predominantly in the left frontal white matter, with ill-defined margins (yellow arrows).
(b) Follow-up MRI at 7 weeks (day 55) demonstrates reduction in lesion extent and sharper lesion borders (yellow arrows), consistent with partial remission.
(c) At 11 months (day 343), residual hyperintense areas persist in the left frontal and temporal lobes (yellow arrows), interpreted as chronic gliosis rather than active inflammation.

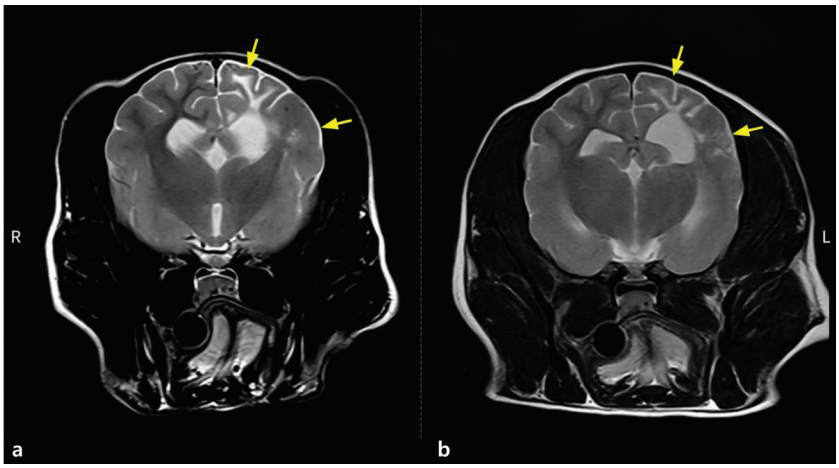

Figure 2. Serial T2-weighted MR images of the left parietal and temporal lobes
(a) Initial MRI (day 0, pre-treatment) shows hyperintense lesions with poorly defined borders in the left parietal and temporal lobes (yellow arrows).
(b) Follow-up MRI at 7 weeks (day 55) demonstrates a decrease in lesion size and clearer margins (yellow arrows), consistent with partial remission.

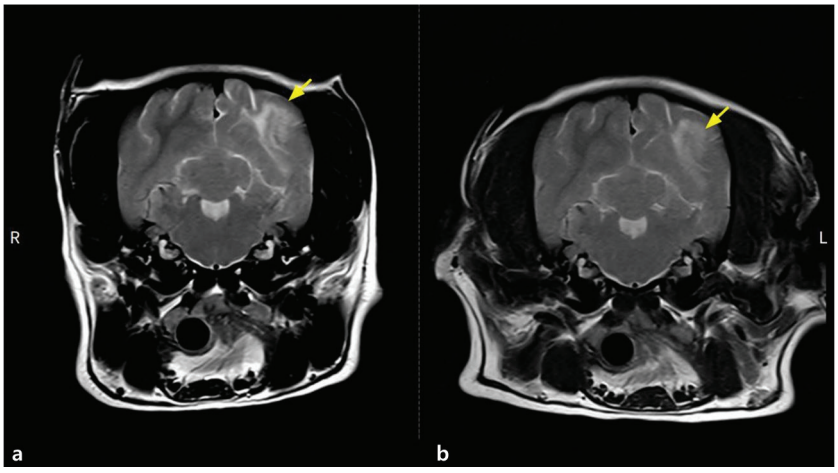

Figure 3. Serial T2-weighted MR images of the left occipital lobe
(a) Initial MRI (day 0, pre-treatment) reveals a hyperintense lesion in the left occipital lobe (yellow arrow) with indistinct borders.
(b) At 7 weeks (day 55), the lesion is reduced in size and more clearly defined (yellow arrow), consistent with remission.

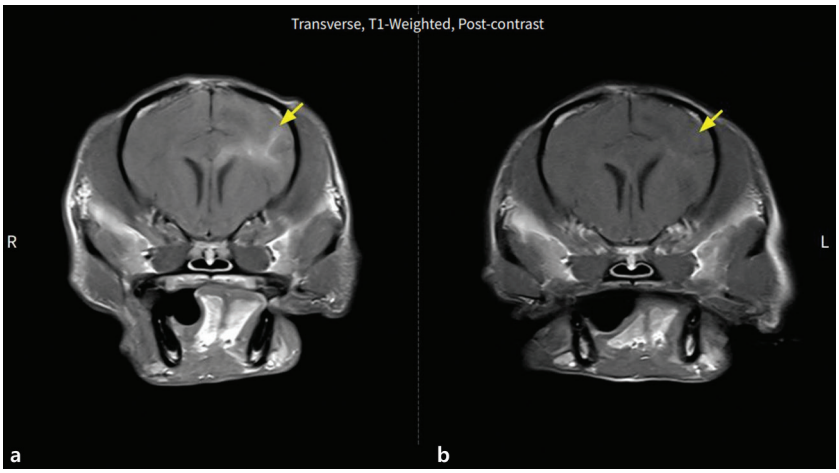

Figure 4. Post-contrast T1-weighted MR images of the left frontal lobe
(a) Initial post-contrast MRI (day 0, pre-treatment) shows a left frontal lesion without marked enhancement (yellow arrow), despite suspected BBB disruption.
(b) At 7 weeks (day 55), no abnormal enhancement is visible (yellow arrow), indicating recovery of BBB integrity.

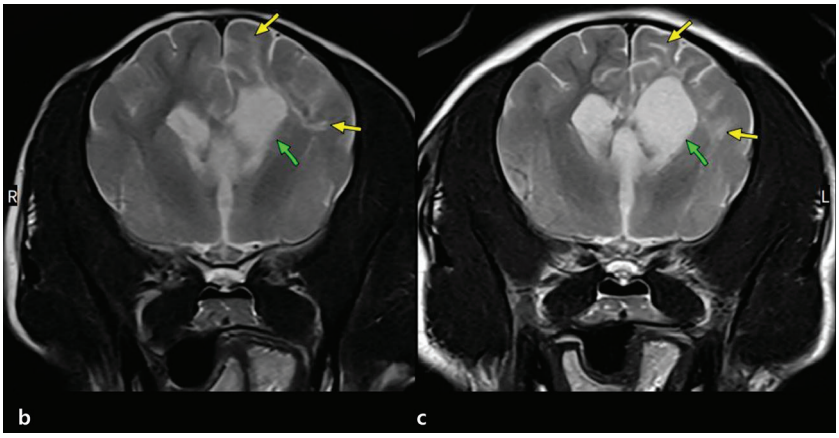

Figure 5. Progressive ventricular enlargement with chronic residual lesions
(b) At 7 weeks (day 55), T2-hyperintense lesions in the left parietal and temporal lobes remain (yellow arrows). The left lateral ventricle is mildly enlarged (green arrow, ~29%).
(c) At 11 months (day 343), residual lesions persist (yellow arrows), while the left lateral ventricle is further dilated (green arrow, ~39%), consistent with progressive brain atrophy.

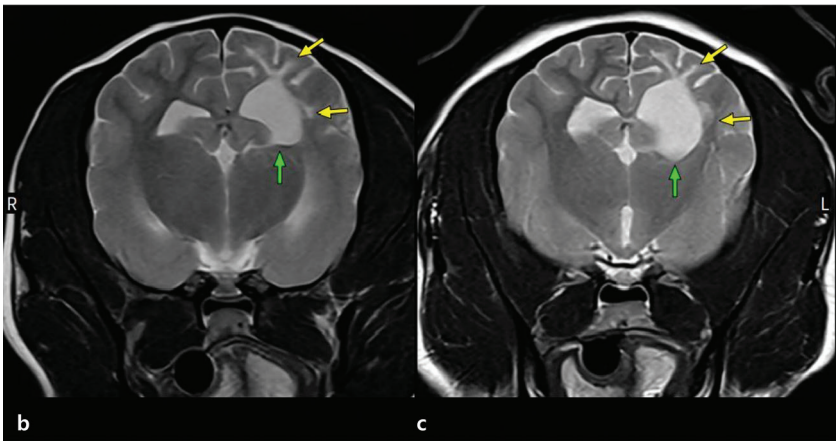

Figure 6. Chronic residual lesions with progressive ventricular enlargement
(b) At 7 weeks (day 55), residual hyperintense lesions remain in the left parietal and temporal lobes (yellow arrows). The left lateral ventricle shows compensatory enlargement (green arrow, 29%).
(c) At 11 months (day 343), lesions persist (yellow arrows) with further ventricular dilation (green arrow, 39%).

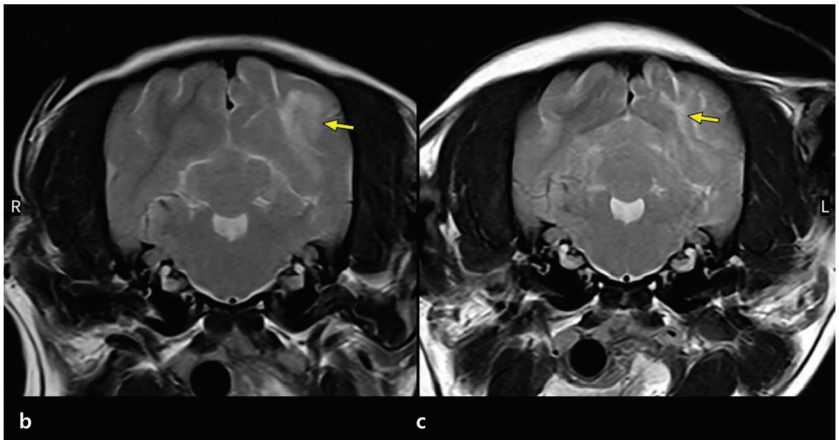

Figure 7. Serial T2-weighted MR images of the left occipital lobe
(b) At 7 weeks (day 55), a small residual occipital lesion is present with clearer borders (yellow arrow).
(c) At 11 months (day 343), the lesion remains stable (yellow arrow), consistent with chronic gliosis.

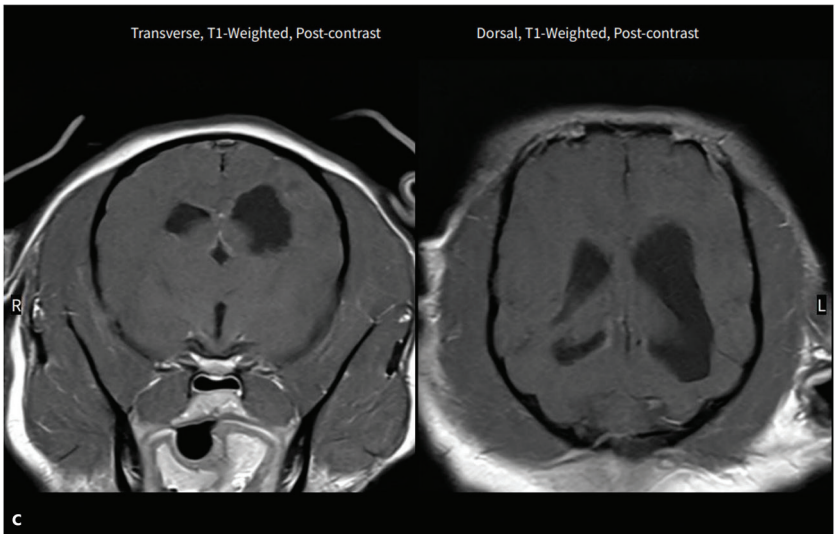

Figure 8. Post-contrast T1-weighted MR images at long-term follow-up
(c) Transverse (left) and dorsal (right) post-contrast T1-weighted images at 11 months (day 343) show no abnormal enhancement. These findings indicate absence of active inflammation and support chronic residual changes.

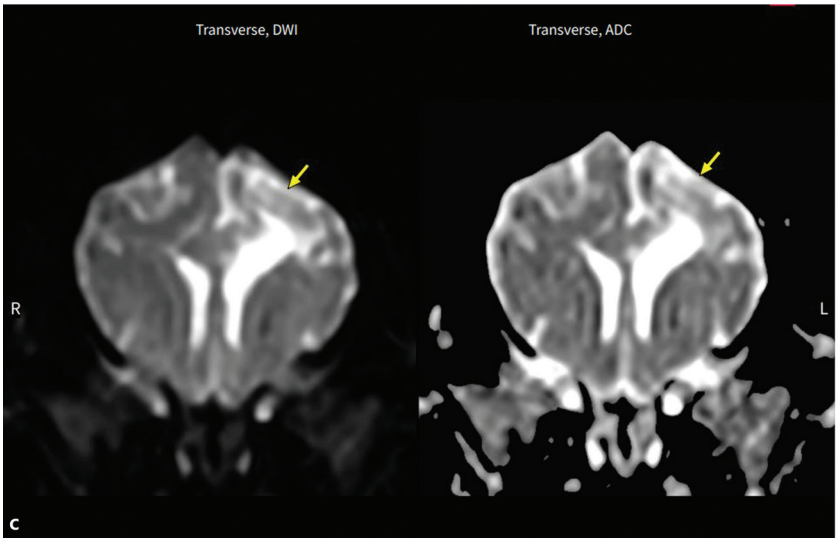

Figure 9. Diffusion-weighted and ADC images of the left frontal lesion
(c) Diffusion-weighted imaging (DWI) shows a hyperintense lesion in the left frontal lobe (yellow arrow). **(d)** The corresponding ADC map demonstrates no restricted diffusion (yellow arrow), suggesting chronic gliosis rather than acute ischemia.

Cerebrospinal fluid obtained from the cerebellomedullary cistern contained 5–11 nucleated cells per low-power field, predominantly mononuclear cells, without erythrocytes or infectious microrganisms. Protein concentration was within the normal range, supporting a presumptive diagnosis of MUO in conjunction with imaging and clinical findings (Figure 10).

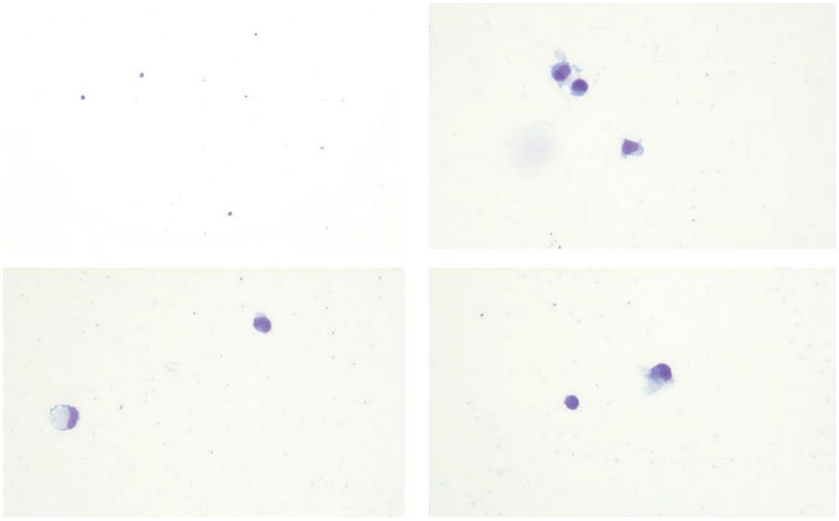

Figure 10. Cerebrospinal fluid cytology from the cerebellomedullary cistern CSF sample (300 μL) collected from the cerebellomedullary cistern, centrifuged and stained with Diff-Quik. **(a–d)** Microscopy (×10–40) shows 5–11 nucleated cells per field, predominantly mononuclear cells with few small lymphocytes. No erythrocytes or infectious organisms were observed. Diagnosis: within normal limits or mild mononuclear pleocytosis ("grey zone"), suggestive of possible early inflammatory changes.

Treatment and follow-up

Prednisolone (0.5 mg/kg twice daily) was initiated immediately after the first MRI and tapered gradually to 0.15 mg/kg once daily by day 201 of treatment. Concurrent medications included imatinib (10 mg/kg once daily), famotidine (0.5 mg/kg once daily), and omeprazole (0.5 mg/kg once daily). By day 25, gait had normalized and neurological deficits had resolved. During long-term treatment, polyphagia and polydipsia developed but improved with steroid tapering.

Laboratory findings

Serum biochemistry revealed transient alanine aminotransferase elevation during high-dose prednisolone administration that normalized with tapering, while alkaline phosphatase remained persistently increased. Triglyceride fluctuations and transient neutrophilia (peak WBC 23.9 × 10^3/μL; 91% neutrophils) were consistent with corticosteroid-associated effects rather than imatinib toxicity (Table 2).

Table 2. Serial hematological and biochemical changes in relation to prednisolone tapering and imatinib treatment.

Treatment phase	Days after treatment	Prednisolone dose	Imatinib	ALT (17-78 U/L)	ALP (47-254 U/L)	Triglyceride (30-133 mg/dL)	WBC (6-17×10³/μL) / Neutrophil (52-81 %)	Key observations
Initial	Day 0–14	0.5 mg/kg BID	10 mg/kg SID	287–388	608–2264	228	WBC 15.4, Neu 77%	Acute ALT spike, marked ALP elevation, hypertriglyceridemia
Early taper	Day 15–30	0.5 mg/kg SID	10 mg/kg SID	34–54	600–620	295–330	WBC 7–10, Neu 73–83%	ALT improved, ALP persistently high, mild neutrophilia
Stable treatment	Day 60–150	0.5 mg/kg SID	10 mg/kg SID	~38	622	330	WBC 10.9, Neu 83%	Stable values, ALP still elevated, CRP within normal
Dose reduction	Day 180	0.35 mg/kg SID	10 mg/kg SID	~54	1026–1248	~126	WBC peaked 23.9, Neu 91%	Transient leukocytosis & neutrophilia, likely steroid-related
Maintenance	Day 200+	0.15 mg/kg SID	10 mg/kg SID	45–51	762–872	120–335	WBC 8–9.7, Neu ~70%	ALT stabilized, ALP chronically high, hypertriglyceridemia episodes

DISCUSSION

This case represents a rare description of a Chihuahua presumptively diagnosed with meningoencephalitis of unknown origin (MUO), treated with prednisolone-based immunosuppression combined with imatinib, and monitored by serial magnetic resonance imaging (MRI) examinations over nearly one year. The clinical and imaging findings were discussed in the context of previous reports, highlighting therapeutic strategies, monitoring approaches, and the importance of long-term follow-up in MUO.

MUO comprises non-infectious inflammatory diseases of the canine central nervous system, including granulomatous meningoencephalitis (GME), necrotizing meningoencephalitis (NME), and necrotizing leukoencephalitis (NLE) [1]. Because histopathological confirmation is often not feasible, clinical diagnosis relies on MRI, cerebrospinal fluid (CSF) analysis, and empirical immunosuppression [2]. Prednisolone remains the cornerstone of therapy and has proven effective both as monotherapy and in multi-agent protocols. Reported median survival with prednisolone alone is approximately 600 days [3], while combinations with cyclosporine or mycophenolate mofetil have achieved longer survival and higher response rates [4,5]. In this case, neurological improvement and MRI evidence of blood–brain barrier recovery were observed shortly after initiating prednisolone, consistent with its anti-inflammatory effects.

Imatinib, a tyrosine-kinase inhibitor originally developed for human oncology, has been explored in veterinary neurology and shown to enhance neurological recovery and reduce lesion burden in dogs with GME and MUO [6,7]. In the present case, adjunctive imatinib led to gait normalization by day 25 and stabilization of lesions on follow-up MRI. These outcomes align with previous reports and support its potential role as an adjunctive therapy [6,7]. However, persistent alkaline phosphatase elevation and transient alanine aminotransferase increases raise concern for hepatotoxicity. As imatinib is known to cause hepatic and myelosuppressive toxicity in humans [9], regular biochemical and hematological monitoring is essential during long-term administration.

MRI was indispensable for documenting disease progression. Sequential examinations demonstrated the transition from acute inflammation to partial remission and chronic atrophy. These findings are consistent with previous reports indicating that lesion improvement within three months predicts a favorable prognosis [2] and that progressive brain atrophy represents a negative prognostic indicator [8,10,11]. Repeat MRI is therefore valuable for assessing therapeutic efficacy and anticipating relapse.

Chronic immunosuppression carries well-recognized risks. Reported adverse effects include polyphagia, polydipsia, elevated liver enzymes, and hypertriglyceridemia [12]. The current case showed similar findings that improved after steroid tapering. Although imatinib-related hepatotoxicity could not be completely excluded, the biochemical

changes were consistent with corticosteroid effects. These observations emphasize the need for careful dose adjustment and routine monitoring of hepatic and metabolic parameters during prolonged therapy.

In conclusion, this case confirms the efficacy of prednisolone and suggests the potential benefit of adjunctive imatinib in MUO. Sequential MRI provided a valuable insight into disease progression, from acute inflammation to chronic structural changes. Clinically, neurological signs improved markedly with normalization of gait by day 25 of treatment, although long-term prednisolone therapy caused reversible metabolic effects. Comprehensive MUO management should therefore include serial MRI follow-up, consideration of multi-agent immunosuppressive regimens, and vigilant monitoring for treatment-related complications to ensure a safe and effective therapy.

Ethical Approval

This clinical case did not involve experimental procedures. Ethical approval was waived by the Institutional Animal Care and Use Committee of Pet in Zoo Animal Medical Center.

Authors' contributions

WDP conceived the study, collected and analyzed the clinical data, drafted and revised the manuscript, with MRI interpretation provided by Ian Veterinary Imaging Center.

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Declaration of conflicting interests

The author declares no conflict of interest.

Statement of informed consent

Written informed consent was obtained from the owner for the use of clinical data and MRI images in this publication.

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MENINGOENCEFALITIS NEPOZNATOG POREKLA LEČEN PREDNIZOLONOM I IMATINIBOM: PRIKAZ SLUČAJA

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Meningoencefalitis nepoznatog porekla (MNP) je imunološki posredovana bolest centralnog nervnog sistema kod pasa kod koje magnetna rezonanca (MR) igra ključnu ulogu u dijagnozi i praćenju. Ovaj izveštaj opisuje petogodišnju sterilisanu ženku čivave (3,9 kg) koja je ima akutnu slabost desne strane tela, anoreksiju i povraćanje. Prva MR je pokazala multifokalne T2/FLAIR hiperintenzivne lezije u levom frontalnom režnju sa sumnjom na poremećaj krvno-moždane barijere, što je u skladu sa MNP. Imunosu-

presivna terapija prednizolonom (0,5 mg/kg dva puta dnevno, postepeno smanjena na 0,15 mg/kg jednom dnevno) primenjena je u kombinaciji sa imatinibom (10 mg/kg jednom dnevno). Kontrolna magnetna rezonanca nakon sedam nedelja otkrila je delimičnu remisiju lezija, obnavljanje integriteta krvno-moždane barijere i blago uvećanje komora. Nakon jedanaest meseci, hronična glioza, progresivna cerebralna atrofija i dalja dilatacija komora (39% naspram 29% nakon 7 nedelja) bile su evidentne bez novih lezija. Klinički znaci su se povukli u roku od 25 dana, ali je dugotrajna terapija izazvala polifagiju, polidipsiju, perzistentno povišenje alkalne fosfataze, prolazno povećanje alanin aminotransferaze i epizode hipertrigliceridemije. Ovaj slučaj ističe vrednost sekvencijalne magnetne rezonance za dokumentovanje prelaska sa akutne upale na delimičnu remisiju i hronične strukturne promene kod MUO. Imunosupresija usled upotrebe prednizolona u kombinaciji sa imatinibom postigla je održivo kliničko poboljšanje, dok je dugoročno praćenje bilo neophodno za otkrivanje progresivne atrofije i neželjenih efekata povezanih sa lečenjem.