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Intravitreal *Onchocerca* sp. With Concomitant Cerebral MRI Lesion: A Case Report

Authors' Contribution:
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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Patient: Male, 24-year-old
Final Diagnosis: Intravitreal onchocerciasis
Symptoms: Blurred vision • headache
Clinical Procedure: Vitrectomy
Specialty: Ophthalmology

Objective: Rare disease

Background: *Onchocerca lupi* is a zoonotic filarial nematode that primarily infects canids. Human infection is rare and typically involves the eye or subcutaneous tissue. *O. lupi* infection should be considered in cases of unresolved uveitis or neurological symptoms. We report a diagnostically challenging case of human ocular *O. lupi* infection with possible neurological involvement.

Case Report: A 24-year-old man from Jakarta, Indonesia, presented with a 1-month history of blurred vision, floaters, left ocular discomfort, and intermittent headaches. He did not respond to initial treatment for uveitis. Further examination revealed a mobile, thread-like, whitish worm in the left vitreous. Pars plana vitrectomy enabled removal of an intravitreal worm morphologically most consistent with adult male *O. lupi*, although definitive species-level confirmation was not possible in the absence of molecular testing. The patient's ocular inflammation resolved postoperatively, but his visual acuity remained poor. Due to persistent headaches, brain magnetic resonance imaging (MRI) was performed; a T1-hypointense and T2-weighted fluid-attenuated inversion recovery (FLAIR)-hyperintense white matter lesion was evident in the left parietal lobe. The lesion persisted on 9-month follow-up MRI, and its etiology was uncertain; a causal relationship with the parasitic infection could not be established.

Conclusions: We describe the first reported case of intravitreal *O. lupi* infection with a concurrent cerebral MRI lesion. This infection should be considered in the differential diagnosis of unresolved uveitis in endemic areas to facilitate timely diagnosis and help prevent irreversible visual damage.

Keywords: Nematode Infections • *Onchocerca* • Onchocerciasis, Ocular

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Introduction

Onchocerca spp. are filarial nematode parasites that primarily infect domestic and wild canids, such as dogs and wolves. Documented cases of human infection are rare [1,2]. These zoonotic parasites typically localize to subcutaneous tissue, connective tissue, or ocular structures; they have particular affinity for periocular and ocular regions, including the conjunctiva, sclera, and retrobulbar space [3]. *Onchocerca* spp. were first identified in a wolf in Georgia in 1967. Since then, they have been reported across Europe, North America, and parts of the Middle East. They have increasingly been detected in areas characterized by close human-animal interaction and suboptimal living conditions, leading to reports involving humans [4,5]. Zoonotic onchocerciasis is an uncommon parasitic infection in humans caused by animal-specific species of the *Onchocerca* genus, including *O. lupi*, *O. dewittei japonica*, *O. jakutensis*, and *O. cervicalis*. These parasites usually infect dogs, wild boar, deer, and horses; they are transmitted to humans by insect vectors such as blackflies (*Simulium* spp.) [6]. Once inside the human body, the larvae can develop into adult worms, resulting in clinical manifestations such as subcutaneous nodules, ocular lesions, dermatitis, and, occasionally, neurological complications (eg, epilepsy). Unlike classical onchocerciasis caused by the non-zoonotic species *O. volvulus*, some zoonotic species can complete their life cycle in humans, producing fertile adult worms and carrying the risk of chronic infection [7].

Clinical manifestations of human zoonotic onchocerciasis range from asymptomatic infection to severe disease. Ocular involvement may present as conjunctivitis, ocular pain, lacrimation, or subcutaneous nodules containing adult worms [8]. If left untreated, severe cases can result in vision impairment or chronic inflammation [9]. Diagnosis is challenging due to the rarity of the condition and its similarity to other filarial infections. Thus, diagnostic confirmation often requires histological examination or molecular testing [10].

Treatment of human zoonotic onchocerciasis typically involves surgical removal of nodules or worms, supplemented by antiparasitic therapy such as ivermectin. However, complete resolution can be difficult to achieve in ocular cases [11]. Given its zoonotic potential, *Onchocerca* infection should be considered in the differential diagnosis of ocular or subcutaneous lesions in endemic regions such as Indonesia, where frequent human-animal contact increases the risk of transmission. Here, we report a case of human intravitreal infection most consistent with *O. lupi*, as well as suspected concomitant involvement of the brain parenchyma. The vitreous is an atypical site for this parasite.

Case Report

We present the case of a 24-year-old man from Jakarta, Indonesia, who resided in an apartment and reported no regular contact with animals. While living in Solo, Central Java, he developed ocular symptoms in his left eye over the course of 1 month, including blurred vision, hair-like floaters, and ocular discomfort. Concurrently, he began experiencing intermittent headaches. He reported no ocular pain, redness, or discharge and had no history of ocular trauma or inflammation. He was otherwise medically fit and well.

Despite a prior diagnosis of uveitis and treatment at multiple clinics, the patient's ocular symptoms progressively worsened, prompting him to seek a second opinion at our institution. Comprehensive ophthalmic examination revealed severely reduced visual acuity in the left eye (6/60, without improvement on pinhole testing), a positive relative afferent pupillary defect, and retinal and subretinal lesions. A mobile, whitish, thread-like parasite was identified in the vitreous of the left eye, prompting urgent surgical intervention.

Pars plana vitrectomy was performed to remove the parasite, followed by postoperative antibiotic prophylaxis. Microscopic examination of the extracted parasite using an Olympus light microscope (CX21FS1, Olympus Corp, Tokyo, Japan) revealed a mature white worm measuring 12 mm × 320 µm. Examination with an Olympus binocular microscope (CX23, Olympus Corp) at 40 × objective magnification demonstrated cuticular ridges and striae, the absence of a buccal cavity, and a short posterior spicule. These morphological features were most consistent with adult male *O. lupi* (**Figure 1**), although species-level identification could not be confirmed because the formalin-fixed specimen precluded molecular analysis. Specifically, formalin fixation prevented DNA extraction using the available methods. After parasite removal, ocular inflammation substantially improved; however, visual acuity remained unchanged, and no systemic antiparasitic therapy was administered.

Given the patient's history of chronic headaches, brain magnetic resonance imaging (MRI) was performed. This imaging investigation revealed a hyperintense white matter lesion in the left parietal lobe on T2-weighted fluid-attenuated inversion recovery (FLAIR) sequences, with corresponding hypointensity on T1-weighted images (**Figure 2A**). Consultations with Neurology and Infectious Disease specialists were conducted to evaluate the need for further intervention and the possible clinical significance of the *O. lupi* infection.

Based on the MRI findings, cerebral vasculitis and cytomegalovirus (CMV) infection were considered in the differential diagnosis. CMV encephalitis was considered unlikely given the absence of systemic or ophthalmic manifestations of CMV

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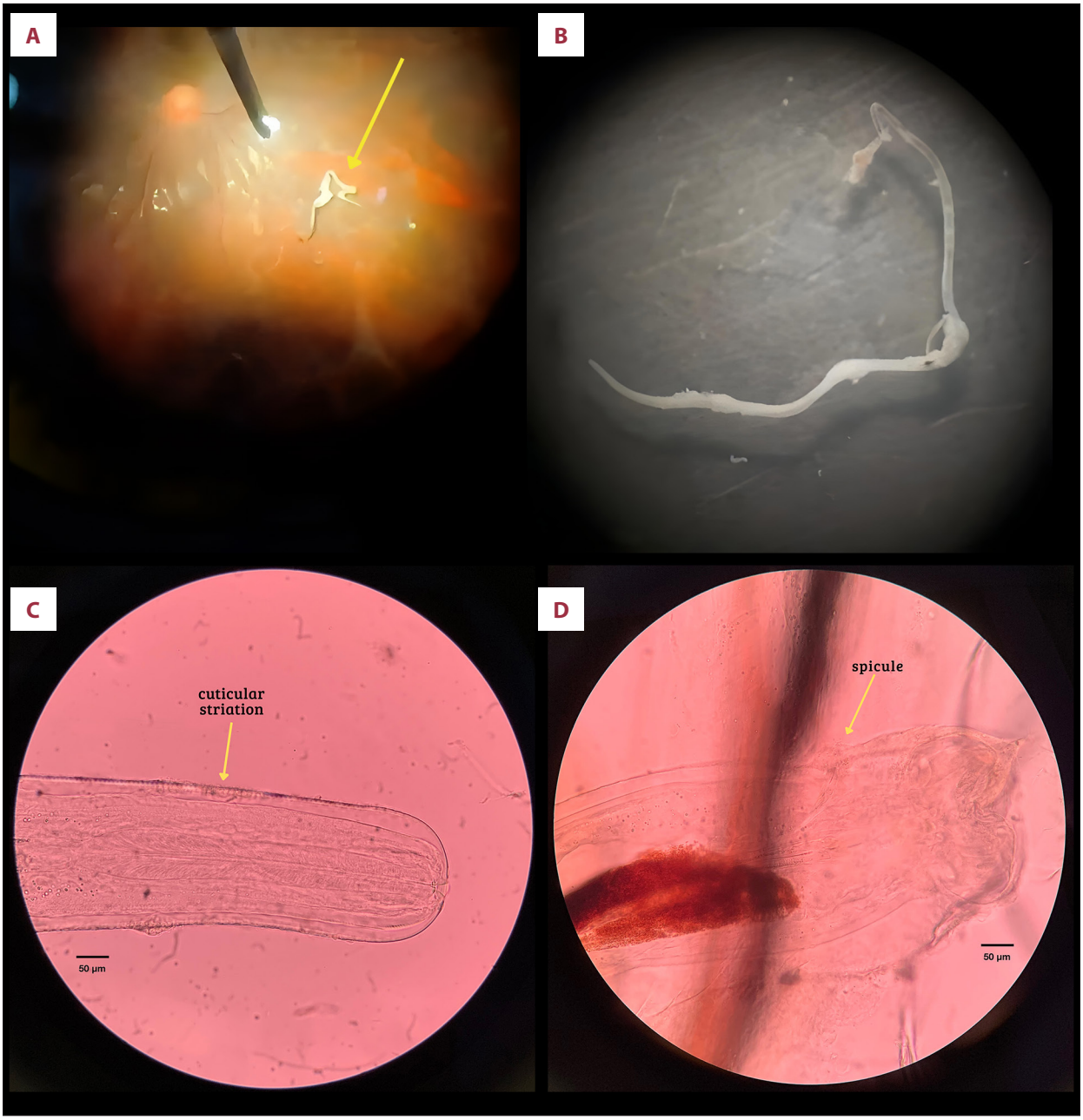

Figure 1. Parasite identification. (**A**) Intravitreal worm observed during the vitrectomy procedure; (**B**) cuticular striations at the anterior end of *Onchocerca lupi*; (**C**) short posterior spicule of *O. lupi*; (**D**) thin, thread-like, white adult *O. lupi* worm (12 mm × 320 µm).

infection, the patient's immunocompetent status, and spontaneous clinical improvement without antiviral therapy. However, formal serological testing was not performed, and CMV infection could not be definitively excluded. Immune-mediated vasculitis was also considered less likely because there were no focal neurological deficits, systemic features suggestive of vasculitis, or history of immunosuppressive therapy; the lesion improved without specific immunosuppressive treatment.

At the 9-month follow-up, the patient reported gradual improvement in his headaches. Repeat brain MRI demonstrated that the hyperintense white matter lesion in the left parietal lobe on T2-FLAIR sequences persisted but had substantially decreased in size (**Figure 2B**). Because the patient's clinical presentation was inconsistent with ischemic stroke, we considered the possibility that the brain lesion reflected migration of the worm or its metabolites across the blood-brain barrier (BBB); however, such migration remains speculative and was not supported by direct evidence. Although the lesion may

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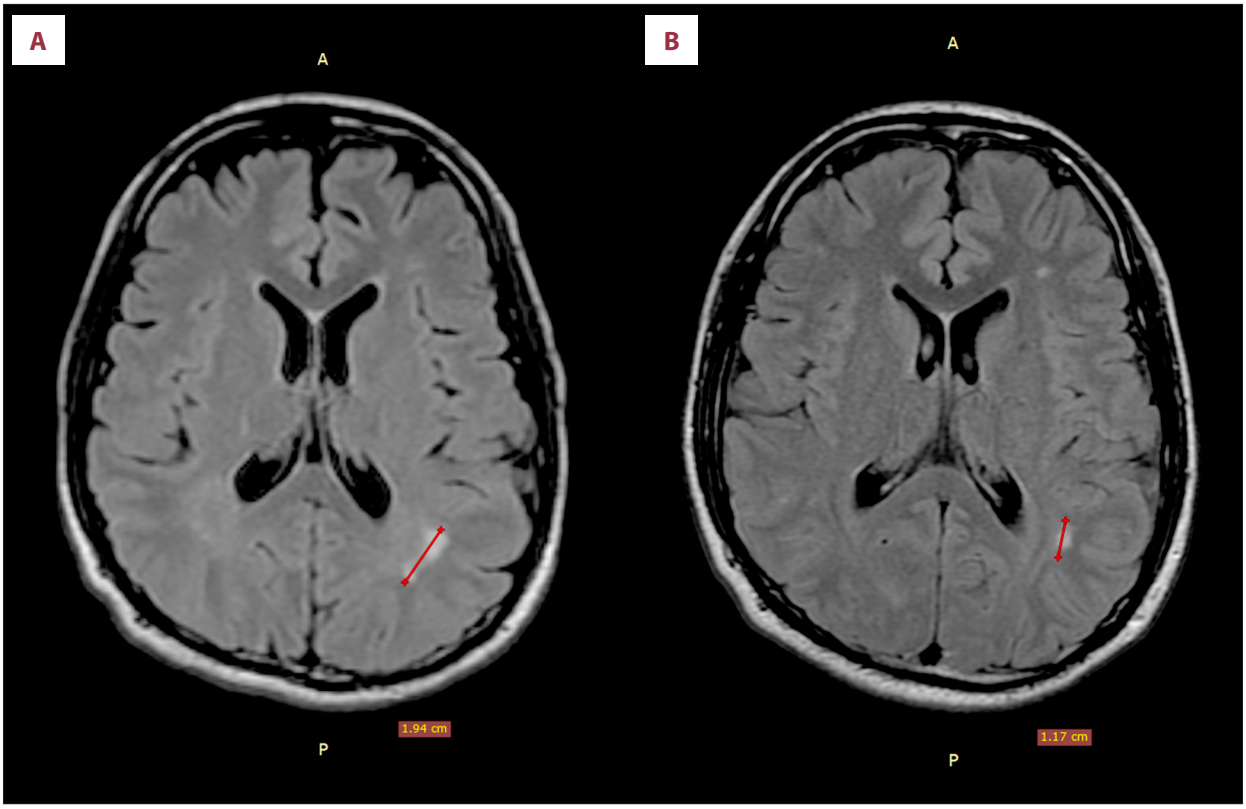

Figure 2. Brain magnetic resonance images of a 24-year-old man with vitreous *Onchocerca lupi* infection. (**A**) Hyperintense lesion in the white matter of the left parietal lobe on T2-weighted fluid-attenuated inversion recovery (FLAIR) sequences; (**B**) follow-up magnetic resonance image at 9 months demonstrating persistence of the lesion, with a decrease in size.

have contributed to the patient's headaches, a definitive causal relationship could not be established. The patient's headaches improved with nonsteroidal anti-inflammatory drugs.

Discussion

This case report describes a severe and novel presentation of zoonotic *O. lupi* infection. Identification of an adult worm within the vitreous cavity, accompanied by radiological evidence of an intracranial lesion, suggested possible systemic dissemination and neurotropic activity. This unusual presentation warrants careful consideration and further investigation. Among *Onchocerca* species, *O. lupi* is most strongly associated with ocular involvement. This zoonotic filarial parasite has a particular affinity for periocular and ocular regions, including the conjunctiva, sclera, and retrobulbar space. In both canine and human hosts, *O. lupi* has been reported to cause subconjunctival and episcleral nodules, presenting with ocular discomfort, swelling, and—in some cases—visual impairment. Localization of the parasite to ocular tissue has also been confirmed by histopathological and molecular analyses, making it an important pathogen in both veterinary and human ophthalmic parasitology [6,7].

Human infection with *O. lupi* is exceedingly rare and was first documented in Turkey in 2011 [10]. Although cases have been reported involving various tissues, including ocular structures [11], the rarity of reported infections likely reflects—at least in part—the diagnostic challenges associated with this parasite. Many cases may be misdiagnosed due to nonspecific clinical manifestations and the limited availability of laboratory methods for definitive diagnosis [12]. Consequently, *Onchocerca* spp. may be overlooked in the differential diagnosis.

Our patient provides a pertinent illustration of these diagnostic challenges. His blurred vision and floaters were consistent with recognized ocular manifestations of *O. lupi* infection [8,11,13]. However, the absence of more typical findings, such as conjunctival injection, ocular pain, or subcutaneous nodules, contributed to an initial misdiagnosis of uveitis. The key diagnostic finding was a motile worm within the vitreous cavity, indicating migration to a deep ocular structure. Such localization represents an unusually severe manifestation of infection. The associated retinal and subretinal lesions likely resulted from a combination of direct mechanical injury and inflammation induced by parasitic metabolites [8,14]. The absence of direct animal contact in the present case contrasts with the typical epidemiological pattern of transmission. Instead,

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the patient's frequent travel throughout Java Island suggests exposure to infected blackfly (*Simulium* spp.) vectors outside his urban residence, highlighting travel history as an important and potentially overlooked risk factor [15].

A key finding in the present case was the lack of visual improvement after successful pars plana vitrectomy and worm extraction. This finding suggests that the pathological process, including mechanical injury and presumed toxic or inflammatory metabolite-induced chorioretinitis [10,11], had caused irreversible retinal damage before surgery. Such an outcome underscores the potentially devastating consequences of intraocular nematode infection and the importance of early intervention.

Our parasitological examination indicated that the worm was most consistent with adult male *O. lupi* based on key morphological features, including cuticular ridges, a filiform body, and a short posterior spicule. However, because the posterior end was partially damaged and the specimen had been preserved in formalin, definitive species-level confirmation by molecular sequencing was not possible. Thus, the diagnosis should be regarded as most consistent with *O. lupi*, rather than conclusively confirmed [16]. This diagnostic limitation is a common challenge in resource-limited settings.

Onchocerca spp. are primarily parasites of canids, and in cases of human infection, they should be distinguished from other nematodes (eg, *Thelazia* spp.). In our patient, *Thelazia* infection was considered less likely because these worms typically lack structural characteristics associated with deep intraocular migration; the observed cuticular ridges, body dimensions, and short posterior spicule were more consistent with *Onchocerca* spp. [17]. Conversely, previous reports of *Onchocerca* spp. in subconjunctival and intraocular locations [10,12] support their capacity for the deep tissue migration observed in our patient.

The most intriguing aspect of the present case was the possible neurological involvement. After parasite removal, the patient's headaches gradually improved over 9 months, accompanied by a reduction in lesion size on follow-up MRI. The hyperintense MRI lesion suggested possible central nervous system involvement. We cautiously hypothesize that either the parasite or its inflammatory metabolites may have crossed the BBB and contributed to lesion formation; however, this interpretation remains speculative in the absence of histopathological or cerebrospinal fluid confirmation.

Neurotropic behavior has been documented in other nematodes, including *Toxocara* spp. and *Angiostrongylus* spp. [4,18]. Hematogenous dissemination of third-stage larvae (L3) to various tissues is consistent with the pathophysiology of filarial infections [19]. However, any proposed route of dissemination in the present case remains theoretical; our discussion of possible hematogenous spread and BBB disruption should be regarded as a hypothesis, rather than established pathophysiology. One possible mechanism is that larvae entered through the gastrointestinal tract, accessed the lymphatic system, and subsequently disseminated via systemic circulation to the eye and central nervous system [11]. They may then have crossed the BBB through inflammation-induced disruption of Virchow-Robin spaces [9].

Definitive diagnosis of neuroparasitic infection typically requires histopathological examination or cerebrospinal fluid analysis [20]. However, these invasive investigations were not feasible in the present case. Although the clinical and radiological findings support possible central nervous system involvement, they are insufficient to establish a causal relationship. Accordingly, long-term neurological follow-up is warranted.

Other potential causes of a solitary white matter lesion, including demyelinating disease and alternative infectious etiologies, were also explored. Demyelinating disease was considered less likely because there was no history of transient neurological episodes, no multifocal lesions on MRI, and no clinical course typical of multiple sclerosis or related disorders. Furthermore, there were no clinical or laboratory findings suggestive of other neurotropic infections, such as tuberculosis, toxoplasmosis, or fungal disease. Nevertheless, in the absence of cerebrospinal fluid analysis or brain biopsy, these alternative diagnoses cannot be definitively excluded, and the lesion etiology remains uncertain.

Some limitations of this case should be acknowledged. Given the lack of molecular confirmation of species identification and the absence of histopathological or cerebrospinal fluid evidence of cerebral infection, any suggestion of neurotropic dissemination or BBB crossing remains speculative. Additionally, serological testing for CMV infection was not performed, and neither cerebrospinal fluid analysis nor brain biopsy was undertaken, both of which would have been necessary to definitively exclude infectious and inflammatory causes of the intracranial lesion.

Despite these limitations, this case broadens the recognized spectrum of ocular involvement in human *O. lupi* infection. It highlights the importance of including *O. lupi* infection in the differential diagnosis of atypical uveitis or neuro-ophthalmic symptoms in patients from endemic regions. Such infection should not be excluded solely based on the absence of direct animal contact, given that travel within endemic areas can represent an important risk factor.

Future research should focus on developing accessible diagnostic assays for rare pathogens. Additional clinical and experimental studies are also needed to clarify the neurotropic

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potential of *Onchocerca* spp., elucidate underlying pathophysiological mechanisms, and establish evidence-based treatment guidelines for complex ocular and neurological presentations.

Conclusions

We report the first case of intravitreal infection most consistent with *O. lupi* accompanied by a cerebral MRI lesion. Although the abnormal finding on brain MRI was associated with chronic headaches, a causal relationship with the ocular parasitic infection or any putative larval migration or metabolite dissemination could not be established and remains hypothetical. *O. lupi* infection should be considered in the differential diagnosis of persistent or atypical uveitis to facilitate timely intervention and help prevent irreversible ocular damage.

Department and Institution Where Work Was Done

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Informed Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Patient anonymity has been preserved.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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