



## Paracentral acute middle maculopathy following hepatitis B vaccine

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### ABSTRACT

**Purpose:** To report a case of paracentral acute middle maculopathy (PAMM) following Hepatitis B vaccine in a child.

**Observations:** A 12-year-old healthy female presented with a paracentral scotoma in the right eye due to PAMM, likely associated with a recent Hepatitis B vaccine.

**Conclusions:** Despite the great importance of vaccines, it is critical to promptly recognize their rare ocular complications, such as the vaccine associated PAMM described in this report.

### 1. Introduction

Paracentral acute middle maculopathy (PAMM) is an uncommon ocular condition caused by an ischemic insult at the level of the intermediate and deep retinal capillary plexus, clinically resulting in a paracentral scotoma corresponding to the area of ischemia.<sup>1</sup> The typical diagnostic feature observed on cross-sectional optical coherence tomography (OCT) imaging is a hyperreflective band involving the inner nuclear layer (INL).<sup>1</sup> Although PAMM may occur as an isolated condition, it is more commonly associated with other retinal vascular disorders, such as retinal arterial and vein occlusions and diabetic retinopathy.<sup>1,2</sup> Less frequently, PAMM can also be associated with other conditions, including eye compression injury, Purtscher retinopathy, sickle cell retinopathy, and inflammatory occlusive retinal vasculitis.<sup>3</sup> Vaccine-associated PAMM has rarely been described, and, to our knowledge, this is the first reported case of PAMM following Hepatitis B vaccine in a healthy child.<sup>3,4</sup>

### 2. Case report

A 12-year-old healthy female presented with a paracentral scotoma in the right eye for 1 day. She had an unremarkable systemic and ocular history, except for having recently received the first dose of Hepatitis B vaccine 4 weeks prior to the onset of symptoms. She reported no other

adverse reactions to the vaccine. On exam, her best-corrected visual acuity in both eyes was 20/20, anterior segment examination was unremarkable with no signs of inflammation in both eyes, and intraocular pressure was 18 mmHg in the right eye and 20 mmHg in the left eye. Fundus exam of the right eye showed dilated and tortuous vessels, flame-shaped hemorrhages along the temporal arcades and perivenular retinal whitening in the posterior pole (Fig. 1a and b). Fluorescein angiography revealed increased arteriovenous transit time, along with blocked hypofluorescence at the site of the hemorrhages without any associated leakage or staining (Fig. 1c and d). Cross-sectional OCT images illustrated a hyperreflective band involving the INL (Fig. 2a), and the corresponding en face OCT image showed a perivenular fern-like pattern with periarterial sparing (Fig. 3a). OCT angiography of the right eye demonstrated an increased size of the foveal avascular zone and areas of capillary dropout within the deep capillary plexus in the area corresponding to the PAMM lesion (Fig. 3b). Fundus exam, OCT and OCT angiography of the left eye were normal (Fig. 3c and d). The findings in the right eye were consistent with a retinal vascular occlusion associated with PAMM. A thorough systemic work-up was performed in order to exclude any underlying causes, including a physical examination by the family physician, serologies, rheumatological and hypercoagulability factors, complete blood count, erythrocyte sedimentation rate, c-reactive protein, and protein electrophoresis, which were all within normal limits. In addition, the patient had no history of

**Abbreviations:** PAMM, Paracentral Acute Middle Maculopathy; OCT, Optical Coherence Tomography; INL, Inner Nuclear Layer.

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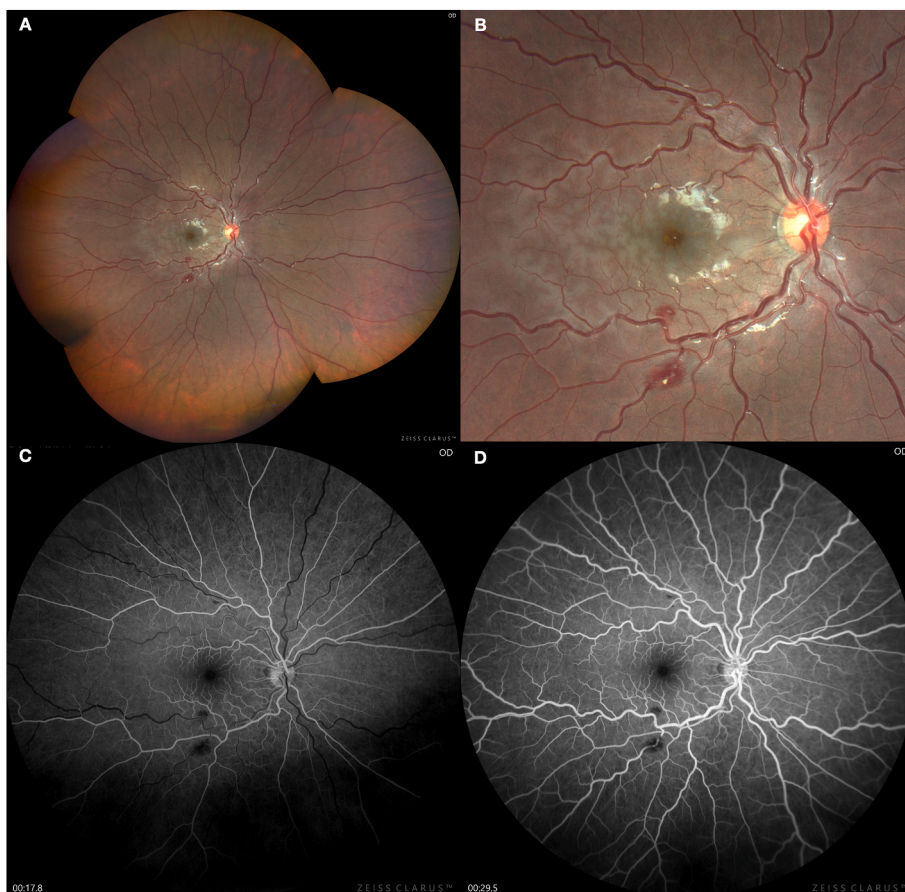
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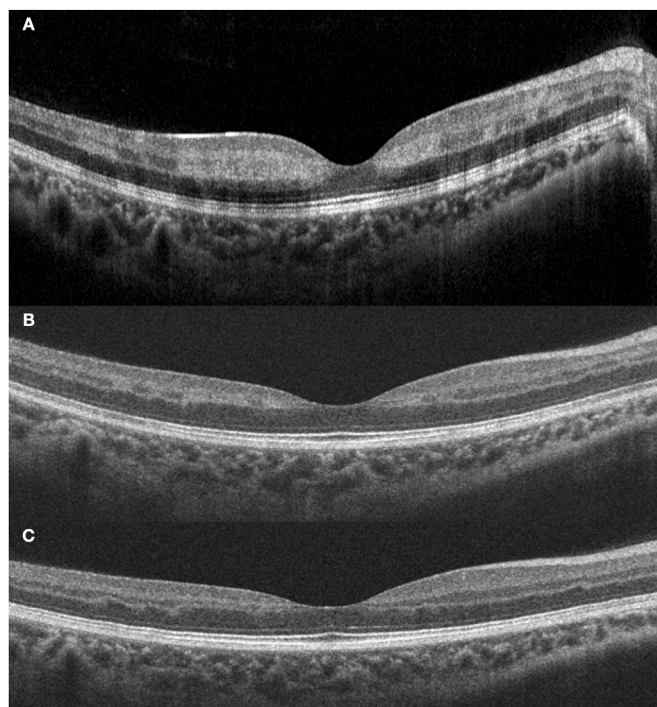
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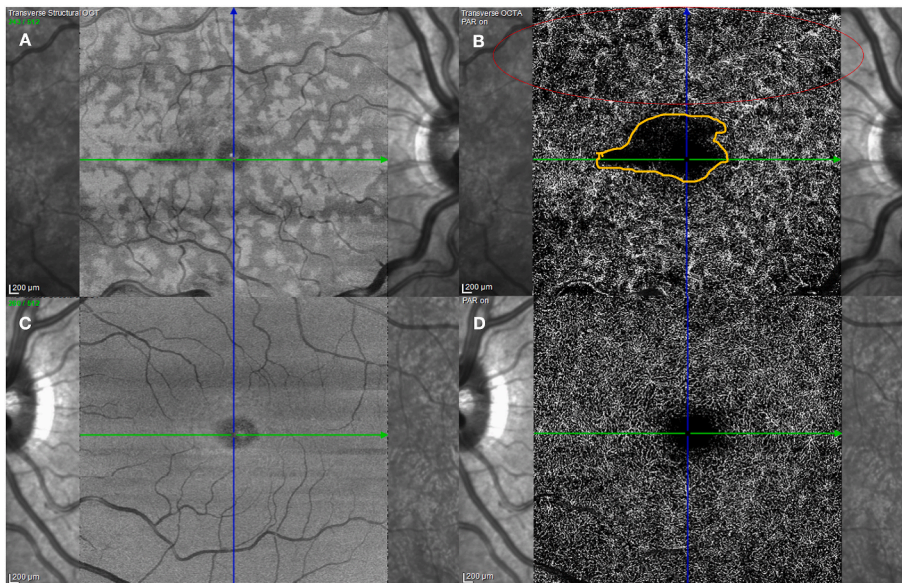


**Fig. 1.** Color fundus photos of right eye demonstrating dilated and tortuous vessels, flame-shaped hemorrhages and perivenular retinal whitening in the posterior pole (A and B). Fluorescein angiography of the right eye illustrates prolonged arteriovenous transit time and blocked hypofluorescence in areas of retinal hemorrhages (C and D). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)



**Fig. 2.** Cross-sectional optical coherence tomography of the right eye reveals patchy hyperreflective bands involving the inner nuclear layer 1 day after the onset of symptoms (A), followed by gradual resolution of the hyperreflective bands 1 month later (B), and thinning of the inner nuclear layer 3 months later (C).





**Fig. 3.** En face optical coherence tomography (OCT) of right eye shows perivenular fern-like pattern with periarterial sparing (A). OCT angiography demonstrates an increased size of the foveal avascular zone (highlighted in yellow) and areas of capillary dropout within the deep capillary plexus (highlighted in red) (B). En face OCT and OCT angiography of left eye are normal (C and D). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

dehydration. The only association encountered was a recent history of Hepatitis B vaccine. The patient reported a gradual improvement of the paracentral scotoma with a complete resolution over 9 months, with visual acuity remaining at 20/20. Furthermore, cross-sectional OCT images showed a gradual resolution of the hyperreflective band followed by INL thinning (Fig. 2a and b).

### 3. Discussion

Hepatitis B virus is a substantial global burden. Vaccination has had a great impact in reducing the case load of chronic infections.<sup>5</sup> Ocular side effects following Hepatitis B vaccine are rare events, with retinal vascular occlusion,<sup>6</sup> uveitis,<sup>7,8</sup> and optic neuritis<sup>9</sup> having been previously described. In the pre-OCT era, Devin et al. reported a case of a young, healthy male with an impending central retinal vein occlusion following a first dose of Hepatitis B vaccine and then a central retinal artery occlusion following the second dose.<sup>6</sup> Although we cannot definitively determine that the clinical presentation of PAMM in our patient was caused by the vaccine, the recent history of having received the first dose of Hepatitis B vaccine and the thorough negative work-up and review of systems suggest a possible association. Our case along with the one reported by Devin et al.<sup>6</sup> may indicate that an ischemic insult to the retinal vasculature can occur following an autoimmune response to the vaccine. It has been shown that the main pathogenic mechanism for the development of uveitis following systemic infections is the deposition of immune complexes with subsequent complement activation.<sup>10</sup> In addition, it has been proposed that a delayed type of hypersensitivity or immunogenic response to the vaccine carrier (adjuvants added to vaccine to potentiate their immunogenicity) could be a potential mechanism of uveitis following Hepatitis B vaccine.<sup>7</sup>

Vaccine-associated PAMM is a rare event but has been previously described following H1N1, meningococcal, and yellow fever vaccines.<sup>3,11</sup> However, the presence of other risk factors may confound the determination of a causal link between the vaccine and the retinal disorder. In the previously reported case of PAMM following H1N1 vaccine, the patient was older than 50 years and had comorbidities, including hypertension and hypothyroidism.<sup>3</sup> Similarly, in the case of PAMM following meningococcal and yellow fever vaccines, the patient was a smoker and had a first-degree atrioventricular block.<sup>11</sup> McKay et al.<sup>4</sup> described the only case similar to ours of a healthy, young patient with no other risk factors who developed a globular pattern of PAMM after meningococcal vaccine. Fortunately, our patient presented with a

perivenular fern-like pattern of PAMM, known to have a better prognosis, where the ischemic insult remains closer to the perivenular pole at the level of the intermediate and deep retinal capillary plexus, with no further progression of the ischemic cascade.

### 4. Conclusions

We present a case of PAMM in a healthy child with a recent Hepatitis B vaccine and an otherwise negative work-up for various other potential underlying etiologies. This suggests a possible temporal association of the PAMM with the vaccine.

#### Patient consent

The patient(s)/patient's legal guardian consented to publication of the case in writing/orally.

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#### Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

#### Declaration of competing interest

All authors have no financial disclosures.

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