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Case report

# Acute posterior multifocal placoid pigment epitheliopathy and granulomatous uveitis following influenza vaccination

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ABSTRACT

*Purpose:* To report a case of acute placoid multifocal posterior pigment epitheliopathy (APMPPE) following influenza vaccination. The patient exhibited granulomatous uveitis during the recovery phase.
*Observations:* A woman in her thirties developed flu-like symptoms seven days after receiving an influenza vaccination. Approximately 2 weeks later, the patient reported with conjunctival injection, blurred vision, and pain in her left eye. She was examined in our clinic, and the best-corrected visual acuity was 20/15 OD and 20/20 OS. Multiple whitish spots were observed bilaterally in the deep retinal layer along with edema of the left optic disc. Both indocyanine green and fluorescein angiographic findings suggested a diagnosis of APMPPE. Although APMPPE lesions were gradually resolved after one month, keratic precipitates, anterior chamber and vitreous cellular infiltration, iris and angle nodules, and macular edema were observed and were treated with topical steroid eye drops. No systemic disorders including sarcoidosis, tuberculosis, and Wegener's granulomatosis were present.
*Conclusion and importance:* As influenza vaccinations are administered worldwide, ophthalmologists should be aware of the ocular side effects following vaccination. Although rare, the possibility of APMPPE occurrence following influenza vaccination should be considered; additionally, the recovery phase of APMPPE may be associated with granulomatous uveitis that requires steroid therapy.


## 1. Introduction

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) was first reported in a study by Gass;[1] it mostly exhibits a self-limited benign clinical course. Its precise pathogenesis has not been described. Although it usually occurs in otherwise healthy young adults, it may occur in association with severe systemic disorders, including tuberculosis,[2] Wegener's granulomatosis,[3] cerebral vasculitis,[4] Lyme disease,[5] and sarcoidosis.[6] In addition, it rarely occurs following vaccination for hepatitis B virus,[7] meningococcus C,[8] varicella zoster virus,[9] and influenza virus.[10]

To our knowledge, only one case of APMPPE following human influenza virus vaccine was reported,[10] and this case reportedly demonstrated a benign clinical course. Accordingly, we report the first case of APMPPE following influenza vaccination that later developed into granulomatous uveitis.

## 2. Case report

A woman in her thirties developed flu-like symptoms including fever, cough, and nausea 7 days after a subcutaneous administration of influenza vaccine. Approximately 10 days after the onset of initial symptoms, the patient noticed redness and blurred vision in her left eye. Three days later, she developed pain in the same eye. As these symptoms did not resolve, she consulted an ophthalmologist. Following a clinical examination, the best-corrected visual acuity (BCVA) was 20/15 OD and 20/20 OS. The intraocular pressure was 19 mmHg OD and 15 mmHg OS. The slit-lamp biomicroscopic examination revealed cellular infiltration (1 + cell) in the left anterior chamber, and the fundus examination revealed optic disc edema in the same eye. The patient was treated with systemic and topical non-steroid anti-inflammatory drugs (NSAIDs). For the observed signs of uveitis, she was referred to the Department of Ophthalmology at Hirosaki University Hospital on the following day. On examination, it was observed that the ocular injection had resolved, and the BCVA was 20/15 OD and 20/20 OS. The intraocular pressure was 14 mmHg OD and 11 mmHg OS. Although there were no

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abnormal findings in the anterior segment and ocular media, the fundus examination revealed multiple whitish spots present bilaterally in the deep layer of the retina along with optic disc edema in the left fundus (Fig. 1A and B). The indocyanine green angiography (IA) exhibited multiple hypofluorescent spots bilaterally (Fig. 1C). Fluorescein angiography (FA) initially showed bilateral presence of hypofluorescent spots that gradually turned hyperfluorescent. Extensive fluorescent dye leakage from the left optic disc was observed (Fig. 1D). Laboratory examinations revealed that the blood cell counts, kidney function, liver function, and serum electrolyte levels were within the normal range. The C-reactive protein level was less than 0.020 mg/dl, angiotensin-converting enzyme level was 15.2 U/l, soluble IL-2 receptor level was 156 U/l, and CD4/8 ratio was 2.92. Tests for serologic antinuclear antigens were negative. Although the patient tested positive for cutaneous tuberculin reaction, the T-spot test showed negative results. No acute elevation of anti-viral antibodies against varicella zoster virus, herpes simplex virus, EB virus, and cytomegalovirus were observed. Since these findings suggested a diagnosis of APMPPE, we decided to carefully observe the patient following continued treatment with topical bromofenac sodium hydrate eye drops only. Systemic NSAID treatment was discontinued. One month after the initial examination, although the BCVA was 20/15 OD and 20/20 OS, fine keratic precipitates were observed and cells (1 + cell) were detected bilaterally in both the anterior chamber and anterior vitreous space. In addition, there were bilateral iris and angle nodules (Fig. 2A). Since these findings suggested a diagnosis of granulomatous uveitis, bromofenac sodium treatment was discontinued and treatment with 0.1% fluorometholone eye drops was started. Two weeks later, although the bilateral keratic precipitates, anterior chamber cells (1 + cell), and left optic disc edema were still present, the iris and angle nodules disappeared. However, there was macular edema in the left eye (Fig. 2B). The BCVA was 20/15 OD and 20/25 OS. Treatment with 0.1% fluorometholone was replaced with 0.1% betamethasone eye drops. In order to evaluate the possibility of presence of sarcoidosis or other systemic disorders, the patient was further referred to internists. Chest radiography and CT findings did not exhibit bilateral hilar lymphadenopathy and alveolar biopsy and bronchoalveolar cytological examination did not detect any evidence of pathologic lesions, including those of sarcoidosis and tuberculosis. Electrocardiography showed normal findings. No other systemic signs suggestive of sarcoidosis and other systemic disorders, including tuberculosis, Lyme disease, Wegener's granulomatosis and other cerebral diseases were observed. The fundus lesions gradually disappeared after another month (Fig. 2C and D). The final BCVA was 20/15 OU.

## 3. Discussion

Influenza vaccination is performed worldwide and is especially recommended for older people and/or people with chronic diseases. Therefore, ophthalmologists should be aware of the ocular side effects of influenza vaccine as well as other vaccines. In addition, as this vaccination is required for health care providers and associated personnel, they might also be at risk. Although ocular

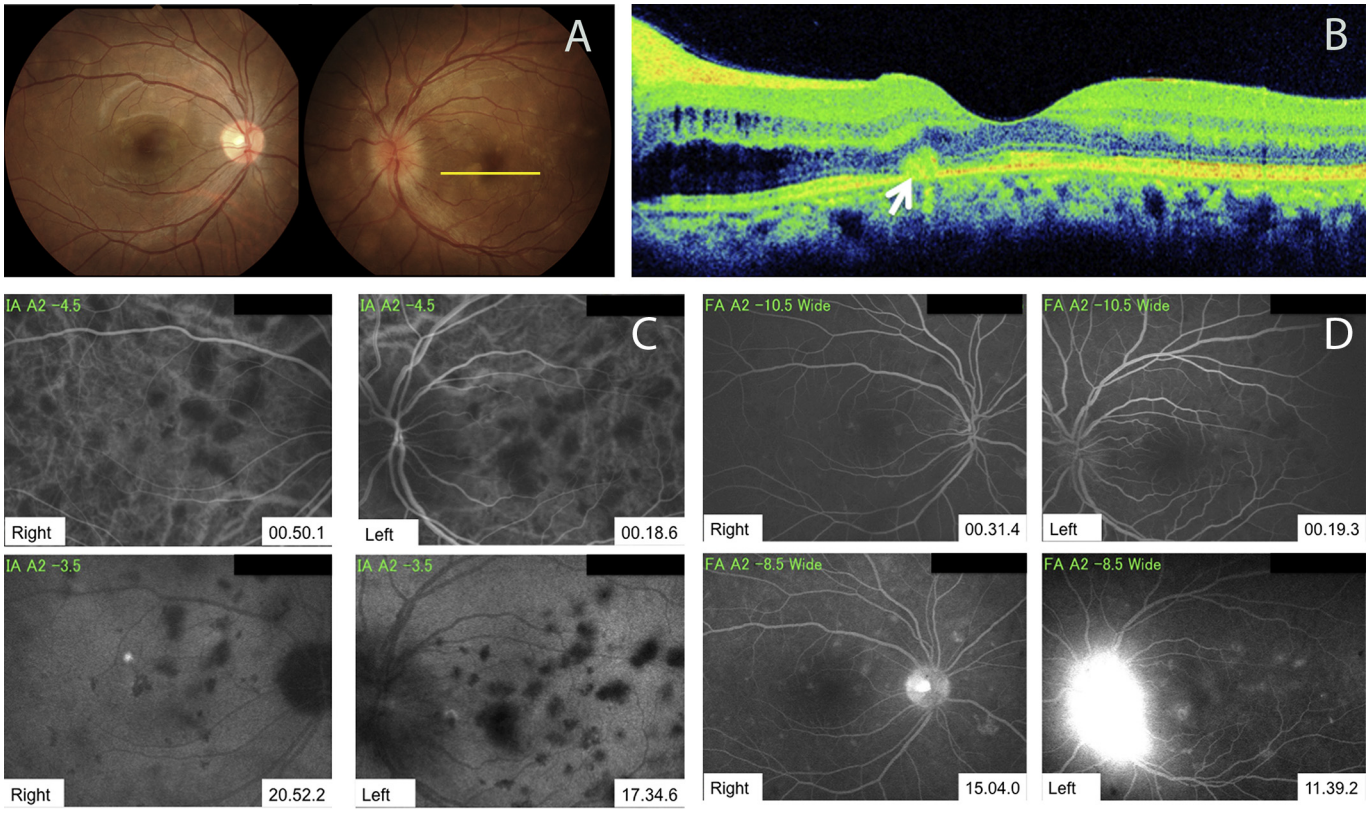


**Fig. 1.** Fundus images of a patient with acute posterior multifocal placoid pigment epitheliopathy. Multiple whitish spots are observed bilaterally and optic disc edema is present in the left eye (A). At the initial examination, optical coherence tomography at the horizontal section indicated in the fundus image (a yellow line in A) demonstrates retinal edema associated with optic disc edema and swelling of retinal pigment epithelium corresponding to a whitish spot in the left eye (arrow) (B). Indocyanine green angiography findings show multiple hypofluorescent spots exhibited bilaterally (C). Fluorescein angiography findings show bilaterally present hyperfluorescent spots in the early phase, development into hypofluorescent spots in the late phase, and fluorescein dye leakage from the left optic disc (D). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)