Anterior Uveitis and Cataract After Rubella Vaccination: A Case Report of a 12-Month-Old Girl

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abstract

Many reports associating uveitis after vaccination have been reported, including 2 cases after measles, mumps, and rubella (MMR) vaccine. We report the case of a 12-month-old girl who developed a unilateral anterior uveitis with rubeosis and cataract 3 months after an MMR vaccination at 9 months of age. Aqueous humor analysis showed the presence of more rubella-specific immunoglobulin G in the affected eye than in the unaffected one. This is the second report showing an association between MMR vaccine and anterior uveitis and the first supported by the presence of intraocular rubella antibodies. Pediatrics 2013;132:e1035–e1038

KEY WORDS
rubella vaccine, uveitis, cataract

ABBREVIATIONS
AU—anterior uveitis
FHUS—Fuchs heterochromic uveitis syndrome
HLA-B51—human leukocyte antigen restriction element
HSV—herpes simplex virus
IgG—immunoglobulin G
MMR—measles, mumps, and rubella
RV—rubella virus
VZV—varicella zoster virus

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Anterior uveitis (AU) is idiopathic in >50% of cases.1 Herpes simplex virus (HSV) and varicella zoster virus (VZV) are the most common infectious etiologic agents of AU, accounting for 5% to 10% of all uveitis cases seen at tertiary referral centers in the western world and are the most common cause of infectious AU.2,3 Fuchs heterochromic uveitis syndrome (FHUS) accounts for 2% to 11% of all cases of anterior uveitis.4 This entity has been associated with intraocular evidence of rubella virus (RV).5–8 HSV, VZV, and RV AU are characterized by unilateral involvement in >80% of cases. AU associated with RV is characterized by a young age at onset and more common cataract and iris heterochromia, consistent with the clinical appearance of FHUS.9

Many reports relating to uveitis and vaccines have been published, including reports on bacillus Calmette–Guérin10–12; measles, mumps, and rubella (MMR);13,14 diphtheria, tetanus, and pertussis15; measles, mumps, and rubella (MMR);13,14 diphtheria, tetanus, and pertussis15; influenza16,17; smallpox18; varicella19; and hepatitis B immunization.20,21 The MMR vaccine, a combination of 3 live attenuated viruses, was licensed in 1971. Each year in the United States nearly 10 million doses of this vaccine are distributed, and >200 000 a year are distributed in Switzerland. The Advisory Committee on Immunization Practices recommends administering the first dose at age 12 to 15 months and the second dose at age 4 to 6 years. During outbreaks, vaccination of infants between 6 and 12 months of age may be recommended despite the fact that the safety and effectiveness of mumps and rubella vaccine in infants of <12 months have not been established (US Food and Drug Administration, www.fda.gov/downloads/BiologicalBloodVaccines/ApprovedProducts/ucm123789.pdf).

We present a case of unilateral anterior uveitis with cataract and iris heterochromia that developed 3 months after the first dose of MMR vaccine administered to a 9-month-old infant.

**CASE**

A 12-month-old Caucasian girl presented at our clinic with an 11-day history of left-eye redness. The patient had been treated for bacterial conjunctivitis. The patient’s symptoms had not responded to topical ofloxacin treatment started by her pediatrician a week before. Patient history was negative except for an MMR vaccine (Priorix, strain Wistar RA 27/3; GlaxoSmithKline, Brentford, Middlesex, UK) 3 months before, when the patient was 9 months old. The vaccine was administered because of an outbreak of rubella in Switzerland between December 2010 and August 2011. The second injection of the MMR vaccine was administered 7 days before our examination. Systemic and neurologic examinations were normal. Family history was negative except for occasional arthralgia and oral aphthous ulcerations described by the mother. Two days after our first examination we performed an examination under general anesthesia that revealed a conjunctival redness, a flare, an iris heterochromia and ruberosis, a secluded pupil by posterior synechiae, and a total dense nuclear and cortical white cataract in the left eye (Fig 1A). The right eye was normal (Fig 1B). Intraocular pressure and ultrasonography were within normal limits. Ultrasonography, magnetic resonance imaging, and computed tomography ruled out the presence of any orbital or ocular foreign body, vitreous inflammation, or retinal thickening. Extended blood infectious and inflammatory workup revealed anemia (81 g/L) and an elevated erythrocyte sedimentation rate (50 mm/h). Human leukocyte antigen restriction element (HLA-B51) was positive. The serology was negative for toxoplasmosis, toxocariasis, cytomegalovirus, treponematosis, bartonellosis, borreliosis, HSV-1 and -2, and VZV and positive for rubella immunoglobulin G (IgG 37 UI/L, immunoglobulin M negative), compatible with the vaccine administration at 9 and 12 months old. The Mantoux test was negative, and a chest x-ray was normal. Her mother’s blood workup showed a positive HLA-B51 and an old immunization for rubella, with a vaccination done 8 and 15 years ago. Aqueous humor workup by polymerase chain reaction for *Candida* and *Tropheryma* was negative. Aqueous humor was extracted from both eyes to perform a Goldman–Witmer coefficient analysis for rubella IgG. The amount of IgG was 4.31 g/L in the serum and 0.10 g/L in the aqueous humor of the affected eye, whereas no IgG could be measured in the aqueous humor of the unaffected eye. Values for rubella-specific IgG, although lower than the normal reference range (10 000 UI/L) calculated for the serum, were higher in the affected eye (4980 UI/L) than in the healthy eye (321

**FIGURE 1**

A, Photograph of left eye showing iris heterochromia and ruberosis, a secluded pupil by posterior synechiae, and a total white cataract. B, Normal right eye.
UI/L. Thus we obtained a Goldmann–Witmer coefficient of 1.69 for the affected eye. This value could not be related to an intraocular rubella-specific antibody synthesis because a Goldmann–Witmer coefficient is considered significantly positive if greater than 3.22 The patient was treated with systemic prednisolone 1 mg/kg, topical steroids 3 times a day, and a 0.05-mL injection of anti–vascular endothelial growth factor (ranibizumab) in the vitreous and 0.05 mL in the anterior chamber. Uncomplicated cataract extraction was performed 1 month later with a 0.05-mL injection of ranibizumab in the vitreous. The fundus examination after cataract extraction was normal (Fig 2). A contact lens was adapted, and amblyopia was treated with daily patching (1 hour per day). Three months after surgery an examination under general anesthesia showed isochromicity of both irises and an inflammatory eye. The patient had no strabismus, visual performances were noted with proper fixation and tracking of human faces, and the patient was able to keep the affected eye open and was no longer falling down.

DISCUSSION

The patient developed unilateral anterior uveitis with iris heterochromia and cataract 3 months after MMR vaccination performed at 9 months of age, with a second injection during the development of eye symptoms. Laboratory examinations excluded the major infectious agents and revealed a positive HLA-B51. Although the patient was positive for HLA-B51, which is associated with Behçet disease in 60% of cases, she showed no systemic sign for this disease, including genital ulcers, oral aphthous lesions, or joint involvement. The mean age at onset of Behçet uveitis is 14.6 years, and rubeosis iridis, posterior synechiae, and cataracts are found in <2% of cases. A diagnostic aid in identifying a causative agent is the paired aqueous humor and serum sampling to assess intraocular production of antibodies. Antibodies synthesized in the eye and detected in aqueous humor can have 2 different sources: a polyclonal concomitant immune response or a persisting antigen. Rubella-specific IgG was higher in the affected eye than in the unaffected eye.

One potential mechanism for development of uveitis could be related to a delayed hypersensitivity reaction with deposition of immune complexes, with subsequent complement activation. Quentin and Reiber demonstrated that FHUS is a rubella virus–driven disease with persistence of the virus and synthesis of intraocular rubella antibody. Since the introduction of the rubella vaccination program, the number of FHUS cases has dramatically decreased. FHUS is unilateral in >90% of cases, and common clinical findings include lack of synechiae, early cataract, low-grade iridocyclitis with keratic precipitates, and anterior stromal iris atrophy. Iris heterochromia is often present. Because our patient shared significant similarities with previously reported cases and differed only in the presence of rubeosis and posterior synechiae, we believe that MMR vaccine–associated FHUS is the most probable cause of uveitis. To our knowledge, this is the second report of an association between MMR vaccination and anterior uveitis and the first supported by the presence of intraocular rubella antibodies, emphasizing the potentially causative effect of the MMR vaccine. The reason why rubella virus has a predilection for the eye or triggers AU is unknown. Such reports are of major importance to help us understand and study the potential effects on the eye of this widely administrated vaccine.

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