An Epidemiological and Clinical Study of Ocular Manifestations of Congenital Rubella Syndrome in Omani Children

Rajiv Khandekar, MS (Ophth) PGDip Epi; Salah Al Awaidy, PGDip Epi; Anuradha Ganesh, MRCOphth; Shyam Bawikar, MD, MPH

Objective: To conduct a follow-up study in patients with congenital rubella syndrome (CRS) in Oman and analyze the prevalence of ophthalmic disorders and associated systemic problems.

Methods: This historical prospective cohort study included review of 32 surviving patients with CRS reported by the surveillance system in Oman from 1987 through 2002. All patients underwent a complete ophthalmic examination that included visual acuity estimation, refraction and anterior and posterior segment evaluation, and intraocular pressure measurement. Pediatric and otorhinolaryngologic consultations were also performed.

Results: The age-adjusted prevalence of CRS in Oman was 73.2 per million in the Omani population younger than 20 years, and the incidence was 0.6 per 1000 live births. Cataract, retinitis, microphthalmos, and glaucoma were observed in 11, 16, 6, and 4 patients, respectively. Keratoconus, corneal hydrops, and spontaneous resorption of lens were found in 1 patient each. Vision testing was possible in 16 children; 4 were bilaterally blind. Patients who had undergone eye surgery had significantly lower visual acuity, as compared with those who had not undergone surgery (relative risk 2.53; 95% confidence interval, 1.07-6.13). Among the 11 patients with CRS with cataract, we found hearing loss, cardiac anomalies, and neuropsychologic anomalies in 7, 4, and 6 children, respectively.

Conclusions: Congenital rubella syndrome has a wide variety of severe ophthalmic and systemic complications. High clinical vigilance for signs of CRS and regular observation of surviving patients with CRS is desirable. In patients with cataract, the functional results of surgery, despite state-of-the-art ophthalmic care, continue to be poor. Because of a high prevalence of visual, audiologic, and neurologic disabilities, surviving patients with CRS pose a burden on the medical and social communities. Emphasis in management ought to be prevention of CRS through effective immunization programs.

Arch Ophthalmol. 2004;122:541-545

CONGENITAL RUBELLA SYNDROME (CRS) was first described by an ophthalmologist who linked congenital cataract to German measles infection in mothers during pregnancy.1 Although rubella is a mild disease in adults, when a woman contracts rubella during pregnancy, there is a risk for transplacental transmission of the virus and development of serious complications in the fetus. The consequences of rubella infection in utero are the manifestations of CRS.2 Congenital cataract, glaucoma, and pigmentary retinopathy are considered cardinal features of the syndrome, and a diagnosis of CRS can be made in their presence despite lack of laboratory evidence.3

Patients with CRS exhibit progressive disease; patients without cataract or glaucoma in infancy might manifest them later, and patients with little or no hearing loss initially may later become deaf. Therefore, all reported and surviving patients with CRS need to be carefully observed for early detection and management of new disease manifestations.4

The World Health Organization encourages its member countries to strengthen their surveillance system for CRS to achieve global elimination of CRS by 2010.5 New cases of CRS have been rare since the development of an attenuated vaccine in 1969 and the effective implementation of immunization programs.6 However, epidemics of rubella continue to occur. De Owens et al7 reported the birth of 54 neonates with CRS in Panama in 1986. Lee et al8 reported a resurgence of CRS in the United States in the 1990s.

The Sultanate of Oman is a member country in the Eastern Mediterranean Region of the World Health Organization,
with a high-quality surveillance and disease control system for communicable diseases and aims to eliminate CRS by 2005. In Oman, there was an outbreak of rubella in 1992 and 1993, and many infants born in that year exhibited features of CRS. Since 1994, important milestones in the control of rubella in Oman have been achieved, notably mass vaccination of children, introduction of measles, mumps, and rubella vaccination in an immunization schedule, and rubella immunization for all mothers after childbirth. A high-quality surveillance and disease control system for communicable diseases has been established, and strategies have been reorganized to make surveillance of CRS more sensitive.

The ocular profile pertaining to congenital cataract during the 1992 epidemic of rubella in Oman has been reported. However, limited information is available about the entire spectrum of ocular manifestations of CRS in this cohort. We reviewed the magnitude of CRS and the ocular profile in children with CRS in Oman.

### METHODS

This was a historical prospective cohort study. All patients with CRS reported through the national surveillance system from January 1, 1987, through December 31, 2002, formed the study population. Patients had CRS diagnosed on the basis of criteria provided by the World Health Organization.12,13

At nearly 165 primary health institutions, physicians examine the newly born and children at the time of their vaccination visits to assess the presence of white pupil, nystagmus, and abnormal eyeball size. Clinically suspected CRS cases are referred to ophthalmologists for confirmation. A newborn with any congenital anomaly is screened by a pediatrician to rule out toxoplasmosis, other agents, rubella, cytomegalovirus, and herpes simplex infection in the mother and the possibility of CRS in the child. On the basis of the criteria set by the World Health Organization, all health institutions (governmental and private clinics) notify the Department of Disease Surveillance and Disease Control, Muscat, Oman, by fax of any child with CRS. This information includes the parents’ telephone number and health institution and the criteria observed for clinically suspected CRS. The child is immediately referred to a pediatrician for detailed examination and laboratory confirmation.

The patient is examined by a senior ophthalmologist, otolaryngologic surgeon, cardiologist, neurologist, and endocrinologist. All physicians and staff in the specialist clinic are aware of mandatory notification of a clinically suspected CRS case in Oman. The cases that fulfill the CRS definition are evaluated annually for the presence of newer manifestations. Patients with CRS who cannot be offered treatment at facilities available within Oman are sent abroad for treatment at the government’s expense. The tertiary child health care units maintain details of such cases. The information of all CRS cases reported through the surveillance system and case records at secondary and tertiary hospitals were reviewed to ensure complete listing of all CRS cases.

For the present study, so we could determine their present status, all children with CRS underwent a detailed ophthalmic examination that included evaluation of best-corrected visual acuity, slitlamp examination of the anterior segment, measurement of intraocular pressure, and examination of the posterior segment by means of indirect ophthalmoscopy through dilated pupils. B-scan ultrasonography was performed for posterior segment evaluation in cases of media opacities. Axial length was evaluated by means of A-scan ultrasonography. Presence of strabismus was established by performing the Hirschberg test. Children older than 6 years were tested by means of the Snellen chart. Younger children were evaluated by means of the Snellen chart and Kolt test. When formal visual acuity testing was not possible, counting fingers or identification of items used on a daily basis was tested at a distance of 1 m.

### QUALITY ENSURANCE PROCEDURES

A national seminar was conducted by the Department of Disease Surveillance and Disease Control to explain the revised surveillance and reporting system for CRS. Uniform pretested data collection forms were used. Multiple sources were used to ensure enrollment of all CRS cases.

### DATA MANAGEMENT SYSTEM

Data were collected from regional hospitals and computed using a pretested format (Epi Info 6.0; Centers for Disease Control and Prevention, Atlanta, Ga). Predetermined checks ensured a high standard of data entry. The frequencies, percentage, and proportion of different ocular manifestations were calculated (SPSS 9.0; SPSS Inc, Chicago, Ill), and a univariate method of analysis was adopted for the study. The prevalence of CRS in the Omani population younger than 20 years was adjusted by using an indirect standardization method, for which the proportion of the global population was used.14

### ETHICAL ISSUES

The permission of national and regional health administrators was obtained to conduct this study. Patient identity was kept confidential. The results of the study were shared with the regional health administrators, and recommendations to further improve the care of patients with CRS were discussed.

### RESULTS

Thirty-two patients had clinical manifestations compatible with CRS; 28 (88%) had ocular manifestations. Their sex, age group, and regional distribution are shown in Table 1. The distribution of cases of CRS in Oman ac-

### Table 1. Profile of the 32 Patients With Congenital Rubella Syndrome in Oman

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>No. of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>22 (69)</td>
</tr>
<tr>
<td>Female</td>
<td>10 (31)</td>
</tr>
<tr>
<td>Age group, y</td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>2 (6)</td>
</tr>
<tr>
<td>5-9</td>
<td>4 (12)</td>
</tr>
<tr>
<td>10-14</td>
<td>20 (62)</td>
</tr>
<tr>
<td>15-19</td>
<td>6 (19)</td>
</tr>
<tr>
<td>Region</td>
<td></td>
</tr>
<tr>
<td>Muscat</td>
<td>5 (16)</td>
</tr>
<tr>
<td>Dhofar</td>
<td>9 (28)</td>
</tr>
<tr>
<td>Dhakhiliya</td>
<td>2 (6)</td>
</tr>
<tr>
<td>North Sharqiya</td>
<td>6 (19)</td>
</tr>
<tr>
<td>South Sharqiya</td>
<td>0 (0)</td>
</tr>
<tr>
<td>North Batinah</td>
<td>3 (9)</td>
</tr>
<tr>
<td>South Batinah</td>
<td>3 (9)</td>
</tr>
<tr>
<td>Dhaihir</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Musundam</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Al Wousta</td>
<td>2 (6)</td>
</tr>
</tbody>
</table>

©2004 American Medical Association. All rights reserved.
more than 50% of children with CRS were born during the epidemic of 1992 and 1993. The number of boys was greater than the number of girls, with 22 boys (69%) and 10 girls (31%) affected. The mean age of patients with CRS was 10.4 years (range, 3.2 to 16.4 years; SD, 3.3 years). More than one fourth of the patients resided in the mountainous southern region of Dhofar, Oman.

The prevalence of CRS was estimated to be 37.3 per million in the Omani population younger than 20 years, and the age-specific prevalence was 73.2 per million in this population. The incidence of CRS in 2002 was estimated to be 0.6 per 1000 live births.

Systemic manifestations of CRS in Omani children are shown in Table 2. Ocular complications (28 of 32), hearing loss (23 of 32), and neurologic deficits (24 of 32) were the chief manifestations. Of 30 children who could be tested, 12 (38%) had cardiac anomalies. All except 1 child had undergone cardiac surgery to treat the congenital anomalies.

The most common ocular finding was retinitis, seen in 16 patients (50%) and present in most patients in both eyes (14 of 16). Cataracts followed retinopathy in frequency (11 patients [34%]). Fifty-five percent of children with cataracts had bilateral involvement. Microphthalmos (axial length <17 mm) was noted in 6 patients (19%), and glaucoma was noted in 4 patients (12%). One case each of keratoconus, corneal hydrops, and spontaneous lens resorption (aphakia in the absence of surgery) were detected. No case of disciform maculopathy was found. Because of limited subgroup sample sizes, the statistical significance of each ocular manifestation in terms of sex and other variables was not calculated.

Systemic complications among patients with congenital cataract and retinitis are shown in Table 3. Sensory hearing loss was common among those with retinitis.

Of the 64 eyes in the 32 patients with CRS, 18 eyes (28.1%) had undergone surgery; their visual acuity was compared with that in the eyes that had not undergone surgery (Table 4). In 30 eyes, vision testing was not pos-
Acquired rubella is mild and self-limiting, and infection usually produces lifelong immunity. Mass vaccination of children induces immunity in 80% to 90% of the population. In countries with effective immunization programs, new cases of CRS are therefore rare. Unfortunately, outbreaks continue to occur, and investigation results suggest that failure to vaccinate susceptible individuals, rather than failure of the vaccine, is the major factor underlying resurgence. To eliminate CRS, it is crucial to monitor the magnitude of the disease and to observe surviving cases to manage newer complications and offer rehabilitative services. A study in Oman is crucial because of poor cooperation or the child being mentally challenged. Among those undergoing routine vision tests, visual acuity was normal in 10 eyes (16%). Five eyes (8%) had visual acuity less than 3/60, and 18 eyes (28%) had visual acuity less than 6/18 but greater than or equal to 3/60. The eyes that had undergone surgery had a significantly higher risk of visual impairment than those that had not (relative risk, 2.53; 95% confidence interval, 1.07-6.13). Observation of children who did not cooperate for vision testing revealed that 20 eyes had some residual vision: light perception, identification of familiar objects, counting fingers close to the face.

COMMENT

The prevalence of CRS in our study is much lower than that reported in the past in Oman and in other developing countries. During the rubella epidemic of 1992 and 1993, the incidence of clinical CRS was 0.7 per 1000 live births. The serologically confirmed CRS rate in Saudi Arabia was 2.2% among children aged 1 to 14 years. The rate of CRS was 1.7 per 1000 births in Jamaica and Israel, 0.9 in Sri Lanka, and 1.5 in Singapore. The absence of new CRS cases in Oman in the past 3 years and the deaths of some patients with CRS during the epidemic in 1992 could be responsible for this observation. A high rate of immunization of children aged 15 months, the mass vaccination campaign in 1994 for children aged 15 months to 18 years, and the vaccination of mothers postpartum has resulted in a marked decrease in CRS cases in Oman.

Ocular disease accounts for much of the effect that CRS has on the medical and social communities, a finding also observed in our cohort. Among the Omani population with CRS, retinitis was the most common ocular complication; however, congenital cataract and glaucoma accounted for the most cases of visual disability. Inability to obtain fundus details in a number of patients may have resulted in underestimation of this complication. Congenital cataract and glaucoma were also the main reported ocular manifestations in the past in Omani children. In comparison with the high prevalence (85%-95%) of cataract due to CRS reported in other studies, only 11 cases (34%) were detected in our cohort, which is difficult to explain. Isolation of virus from lens material might enable us to determine the strain of virus and its affinity for retinal tissue rather than lens tissue. We detected 1 case each of spontaneous lens resorption, keratoconus, and corneal hydrops. These changes are reported as rare and delayed ones. Long-term follow-up of CRS cases is thus justified.

The 8% (5 of 64 eyes) bilateral blindness in patients with CRS in our study is much higher than the childhood blindness rate of 0.07% reported in 1997. This finding supports the need for special care and periodic evaluation in this high-risk population.

Visual impairment was significantly greater in eyes that had undergone ocular surgery, mainly for cataract, as compared with those that had not undergone surgery. Poor outcomes after cataract surgery in patients with rubella are documented in the literature. Inflammation and incidence of pupillary membrane, posterior synechiae, and secondary glaucoma are increased in patients with CRS. These findings have been attributed to release of virus from the lens at the time of surgery and initiation of an immune reaction after cataract surgery. The level of visual impairment in our patients, despite quality care free of cost, favors the argument that even though surgical and medical treatment of complications of CRS are available, the emphasis ought to be on prevention.

Most patients with CRS with congenital cataract had additional nonocular disabilities, such as hearing loss and...
cardiac and mental or behavioral anomalies, that compounded visual disability. Many patients with retinitis had associated sensorineural hearing loss. Further studies are needed to confirm this association.

Few patients with CRS died during follow-up, which could be because of prompt management of cardiac anomalies in our cohort. Late ocular manifestations of CRS thus can be observed, provided cardiac complication in a CRS case is managed effectively to increase the patient’s chances of survival.

In conclusion, the prevalence of CRS is lower in Oman since 1994. Although ocular complications were a major complication of CRS, congenital cataract was less common than that observed in other studies. A high proportion of visual disability in eyes that underwent surgery, as compared with those that did not, needs further investigation. Effective immunization programs can prevent CRS and childhood blindness from its ocular manifestations.

Submitted for publication June 19, 2003; final revision received January 6, 2004; accepted January 15, 2004.

We thank the staff of the Department of Disease Surveillance and Disease Control, Muscat, Oman, for providing CRS case data. We also appreciate the efforts of the pediatricians, ophthalmologists, and otolaryngologists who helped in evaluating these cases. We thank the authorities in the Ministry of Health, Muscat, Oman, for their support of this study. A. Raju’s assistance in data entry and Mohammed Hosammudin’s sincere efforts to trace these cases were crucial.

Corresponding author: Rajiv Khandekar, MS (Ophth), PGDip Epi, Eye and Ear Health Care Programme, Noncommunicable Disease Control Department, Directorate General of Health Affairs, Ministry of Health, PO Box 393, Pin 113, Muscat, Oman (e-mail: rajshpp@omanTel.net.om).

REFERENCES