complications, surgery, and vision examinations performed by ophthalmologists.

Materials and methods

A questionnaire was sent to the departments of ophthalmology in 1,151 major hospitals nationwide, all of which are authorized by the Japanese Ophthalmological Society as training institutions for physicians specializing in ophthalmology, to survey the number of patients with microphthalmia who visited their outpatient clinics between January 2008 and December 2009. Patients referred to other hospitals during this period were excluded.

The diagnostic criterion for pure microphthalmos is the presence of an eye with two-thirds the normal ocular volume, i.e., 0.87 below the normal axial length [1]. The Japanese criteria were established by Majima [8], based on the average axial length for each age group of Japanese patients. The clinical definition can be determined by a substantial size difference between the two eyes. Axial lengths of <21 mm in adults and <19 mm in 1-year-old children, i.e., two standard deviations below normal, are used. Corneal diameters of <10 mm in adults and <9 mm in infants are used for a simple diagnosis [9]. In our survey, either Majima's criteria for pure microphthalmos or the clinical definition for complicated microphthalmos was applied.

The questionnaire asked for either the numbers of patients or the number of eyes and was divided into two sheets. The first sheet comprised questions on the number of cases, the number of cases operated on, whether the condition was unilateral or bilateral, gender, age, family history; the second sheet consisted of questions about the number of associated ocular anomalies and complications, surgical treatment, associated systemic diseases, vision and management with glasses, low vision aid, and the use of a prosthetic shell.

A retrospective quantitative registry of microphthalmia was compiled from the responses from 454 hospitals (39.4%). The data from 1,254 microphthalmic eyes of 851 cases in total were collected from the first sheet, but as some hospitals did not complete the second sheet, only data from 1,069 eyes of 722 cases were collected from the second sheet. Of the data collected for these 1,069 eyes, data on the vision of 56 eyes (5.2%) were incomplete. Thus, data from 1,013 eyes were analyzed for vision.

We surveyed the number of patients managed in Japanese hospitals and analyzed the associated ocular anomalies and complications, surgical treatment, systemic diseases, vision and ophthalmic management.

Results

Of the 851 cases [396 (46.5%) male, 455 (53.5%) female] of microphthalmia reported on the first sheet, 444 (52%) were unilateral and 405 (48%) were bilateral (for two cases no information on unilateralism or bilateralism was reported). In terms of age distribution, 50% of the patients were 0–9 years and 16% were 10–19 years; between ages 20 and 79 years, the prevalence remained relatively constant, ranging between 4.3 and 6.8% (Fig. 1). Family histories were positive in 61 cases (7.2%), of which 25 cases (41%) of autosomal dominant inheritance, three cases of X-linked recessive inheritance, and one case of autosomal recessive inheritance were identified; the other 32 cases were undetermined.

The data from the 1,069 microphthalmic eyes of 722 cases retrieved from the second sheet were compiled and analyzed for associated ocular anomalies and complications, surgical treatment, associated systemic diseases, and management with glasses, low vision aids, and prosthetic shells. The ocular abnormalities and complications associated with microphthalmia are shown in Fig. 2. The identified ocular findings were nanophthalmos, coloboma (choroid, retina, lens, iris), vitreoretinal malformation (retinal dysplasia, retinal fold, persistent fetal vasculature, etc.), anophthalmos/extreme microphthalmos, anterior segment dysgenesis (Peters' anomaly, aniridia), and optic

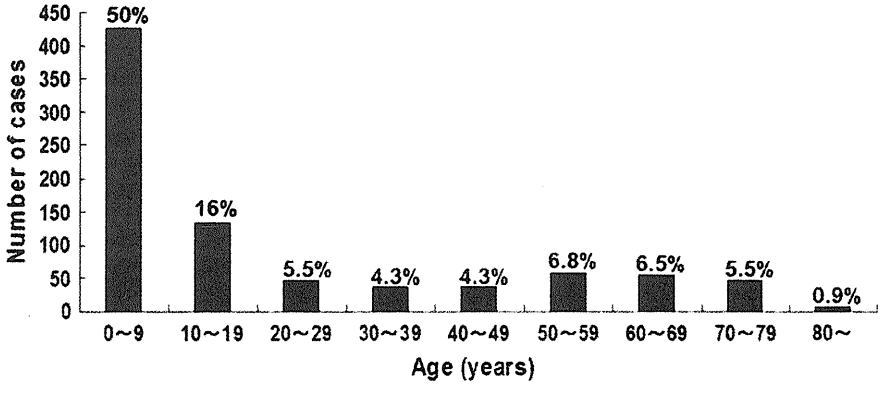

Fig. 1 Ages of patients with microphthalmia managed in the surveyed hospitals. The rate is given for each age group ($N = 851$ cases)

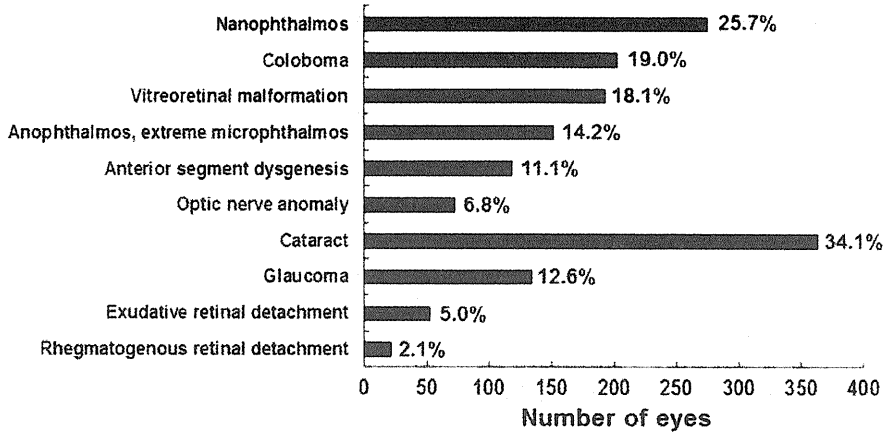

Fig. 2 Ocular abnormalities and complications associated with microphthalmia. The rate of each associated anomaly or complication is given ($N = 1{,}069$ eyes)

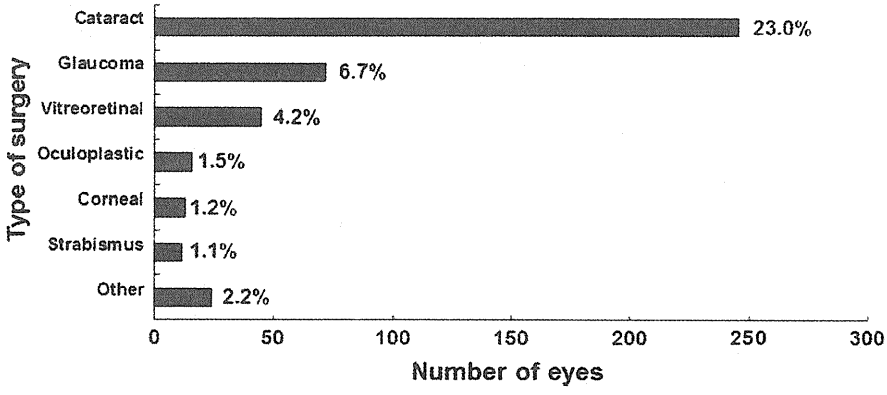

Fig. 3 Surgical treatments for ocular complications in microphthalmia. The rate of each surgical procedure is given ($N = 1{,}069$ eyes)

nerve anomaly (disc anomaly, optic nerve hypoplasia). The most frequent ocular complications were cataracts in 34.1%, followed by glaucoma and exudative or rhegmatogenous retinal detachment.

Surgery had been performed in 182 (21.4%) of the 851 cases; the surgical procedures for ocular complications are shown in Fig. 3. The procedures performed the most often were cataract extraction in 246 eyes (23.0%) of 1,069 eyes, followed by glaucoma surgery and vitreoretinal surgery.

Systemic diseases were present in 224 patients (31%) of 722 cases of microphthalmia, with 92 cases (12.7%) of developmental cerebral anomalies and mental deficiency, 68 cases (9.4%) of multiple anomalies and genetic syndromes, 26 cases (3.6%) of chromosomal disorders, and 38 cases (5.3%) of others.

The distribution of vision in microphthalmia is shown in Fig. 4. The data from 1,013 microphthalmic eyes were analyzed for vision. The visual acuity (VA) in microphthalmos was <0.02 in 348 eyes (34.4%), <0.1 but not <0.02 in 116 eyes (11.4%), <0.3 but not <0.1 in 93 eyes (9.2%), not <0.3 in 157 eyes (15.5%), unmeasurable with poor visual performance in 241 eyes (23.8%), and good visual performance in 58 eyes (5.7%).

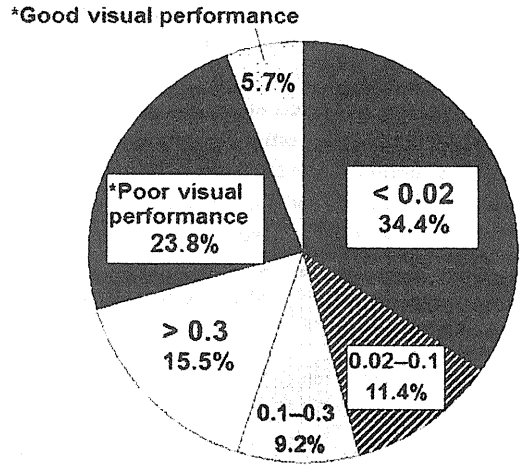

Fig. 4 Visual acuity (VA) in microphthalmos. *Asterisk* VA not measured due to young age or mental retardation. The rate of each VA group is given ($N = 1{,}013$ eyes)

Glasses and low vision aids were used in 156 cases (21.6%) of 722 cases, while prosthetic shells were applied in 211 eyes (19.7%) of 1,069 eyes.

Discussion

This is the first national survey that reports the epidemiologic aspects and current status of patients with microphthalmia in Japan. It is also the largest survey conducted by ophthalmologists of patients with microphthalmia who present at a hospital. The results based on cross-sectional surveys of patients' hospital visits may be considerably biased and may not be comparable with those of previous epidemiologic studies in other countries. However, the results of this survey showing the precise ocular associations, complications, types of surgeries, and vision, may be useful for future ocular management and investigation.

Approximately one-half of the patients in this survey who presented to a hospital were children under the age of 10 years, indicating that diagnosis and treatment of microphthalmia during the period of visual development are both needed and common practice in Japan. In addition, continuous management of low vision and ocular complications is required in order to maintain proper vision throughout life. Among the responders in this study, the distribution of microphthalmia was evenly divided between men and women and between unilateral cases and bilateral cases. Previous studies also report no biased association between microphthalmia and gender; however, those on laterality are mixed, with bilateral being more common in some studies and unilateral cases being more common in others [10]. Kallen et al. [11] reported that among their patient population, >70% of microphthalmia cases were bilateral and associated with chromosomal disorders, 53–60% were either associated or not associated with other malformations, but only 27% were cases of isolated microphthalmia. Microphthalmos associated with systemic diseases, nanophthalmos, colobomatous microphthalmos, and some cases of complicated microphthalmos often develop bilaterally and need more medical management for low vision and periodic follow-up. However, the current survey indicated that unilateral cases also require ophthalmic treatment and management.

The family histories were positive in 7.2% of cases; however, most cases have not been investigated for genetic etiology. To clarify the pathogenesis of various microphthalmia and develop useful treatments, effective genetic screening should be performed.

The current patient population had varying kinds and degrees of ocular-associated anomalies; among these, posterior segment dysgenesis, including coloboma and vitreoretinal malformations, was seen frequently. Thus, early morphologic and electrophysiologic evaluation of the posterior segment may be required to assess the visual potential and indications for surgical, optical, and amblyopia treatment or for a cosmetic shell.

The rates of developing cataracts, glaucoma, and retinal detachments were extremely high among the young patients. These ocular complications were major indications for surgical intervention, although the prognoses were generally poor [12]. Patients with microphthalmia require lifelong management for early prevention and detection of these complications. A less invasive surgical procedure for microphthalmia should be developed [13–19].

Various systemic anomalies are frequently associated with microphthalmia, indicating that initial assessment and continuous management by pediatricians are essential. Although 31% of the cases in our survey were microphthalmia associated with systemic disease, analysis of a population-based birth defects registry in Hawaii from 1986 to 2001 revealed that only 5% of the 96 cases had either isolated anophthalmia or microphthalmia, whereas 25% had confirmed chromosomal abnormalities, such as trisomy 18 and 13, and others had malformation syndromes, limb and musculoskeletal system defects, and cardiac and circulatory system defects [10]. Our survey included more unilaterally isolated cases, probably because ophthalmologists conducted the survey and provided detailed descriptions of the ocular status of the patients who presented to the hospitals.

Overall useful vision and good visual performance >0.1 were obtained in about 30% of microphthalmia cases, whereas about 34% of microphthalmia patients were blind (VA <0.02). However, glasses and low vision aids were used in around 22% of the cases, while prosthetic shells were used in about 20% of eyes. The visual prognosis of microphthalmos depends largely on the difference between the two eyes. The chances of obtaining good VA are limited in cases of severe unilateral microphthalmos, where orbital growth may be retarded and facial deformity may develop. Early socket expansion and wearing of a prosthetic shell are important for cosmetic treatment in anophthalmos and extreme microphthalmos [20]. However, microphthalmos with visual potential should be assessed early and glasses prescribed to maximize the VA.

In summary, our analysis of the survey data revealed that patients with microphthalmia have various ocular and systemic anomalies and that the rates of ocular complications are high in young patients. Early assessment, preservation of vision, and long-term management of complications are needed for these patients.

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