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Birgit Lorenz
Josef Schroeder
Udo Reischl

First evidence of an endogenous *Spiroplasma* sp. infection in humans manifesting as unilateral cataract associated with anterior uveitis in a premature baby

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B. Lorenz (✉)
Department of Paediatric Ophthalmology and Ophthalmogenetics,
University of Regensburg,
93042 Regensburg, Germany
e-mail:
Birgit.Lorenz@klinik.uni-regensburg.de
Tel.: +49-941-9449219
Fax: +49-941-9449216

J. Schroeder
Institute of Pathology, Central EM-Lab, Germany

U. Reischl
Institute of Medical Microbiology and Hygiene Klinikum,
University of Regensburg,
93042 Regensburg, Germany

Abstract *Purpose:* To elucidate a previously unknown aetiology of rapidly progressive unilateral cataract in a premature baby associated with severe anterior uveitis. *Methods:* The lens and vitreous material were saved as part of a special protocol in a 4-month-old premature baby at the time of pars plana lensectomy with anterior vitrectomy. We performed (1) microbiological cultures to detect viable bacterial and fungal organisms; (2) PCR reaction to viral, bacterial and fungal agents; (3) transmission electron microscopy (TEM). In addition, serological examinations were performed for HSV-1 and -2, CMV, VZV and *Mycoplasma* infection. *Results:* PCR detected *Spiroplasma* sp.; TEM confirmed the presence of *Spiroplasma* within the lens fibres. Serological testing and microbiological cultures of the vitreous and lens were negative. *Conclusion:* Endogenous *Spiroplasma* infection in a premature baby may manifest as rapidly progressive acquired unilateral cataract with anterior uveitis. Beyond this, *Spiroplasma* infection has never been reported to occur naturally in vertebrates, although experimentally *Spiroplasma mirum* produces panophthalmitis associated with cataract in a wide range of rodents and in chicks. In acquired infantile cataract with inflammatory signs, PCR and TEM should be performed in the lensectomy/vitrectomy material to detect infectious agents not evident on routine laboratory and microbiological examinations.

Introduction

Congenital non-hereditary (mostly bilateral) cataract may be caused by intrauterine infections, usually viral in nature [14]. Cataract is then present at birth and typically associated with pathologies of various ocular structures such as cornea, retina and choroid. In premature babies acquired cataract occurring spontaneously has only rarely been seen [1, 15, 17]. These cases were usually transient in nature and occurred in infants with septicaemia and who were treated with kanamycin. Eighty percent of the infants also had an unexplained metabolic acidosis [1]. Acquired cataract associated with anterior uveitis in premature babies has been described in only a few cases [5, 19]. In those cases, cataract was related to endogenous intraocular *Candida* infection evident on histopathological examination of the lensectomy/vitrectomy material. In the two cases reported, cataract associated with severe inflammatory signs of both the anterior and posterior segment had developed 5 months and 6 weeks respectively after *Candida* septicaemia. The *Candida* septicaemia was treated by intravenous amphotericin. Subsequent repeat blood cultures had been negative for *Candida* [5, 19]. The incidence of concurrent *Candida* endophthalmitis in premature babies developing systemic candidiasis is not known. However, these babies are at considerable risk of developing systemic candidiasis. In one study, 4% of premature babies weighing less than 1500 g and 9.9% of babies weighing less than 1000 g developed systemic candidiasis [2].

We present, as part of a larger study, the case of a premature baby with unilateral acquired cataract associated

with anterior uveitis and not related to any infection detectable on routine laboratory and microbiological testing. In our institution, babies with cataract of unknown aetiology have been routinely tested with polymerase chain reaction (PCR) and transmission electron microscopy (TEM) since 1997. Bacterial "broad-range" 16S rDNA PCR has been carefully established and evaluated by one of the authors (U.R.) with about 350 ocular specimens (mainly vitrectomy material and aqueous humour from adult eyes with acute and subacute inflammation) and other clinical specimens from normally sterile sites. In the course of this ongoing prospective study, more than 80 specimens were found positive for bacterial organisms (U. Reischl, unpublished results) [16]. PCR and TEM in the present case disclosed an organism of the genus *Spiroplasma*, never reported to occur in human eyes. However, *Spiroplasma mirum*, also known as the suckling mouse cataract agent (SMCA), is known to produce a strikingly high incidence of cataract formation, usually bilateral, when injected intracerebrally into newborn CFM mice [4]. *Spiroplasma* as an agent of cataract formation in infants, particularly in premature babies, may have gone undetected in the past due to the lack of infectious signs on routine laboratory, microbiological and light microscopy examinations.

Case report

General history

A female child born on 8 November 1996 was referred at age 4 months because of a rapidly developing unilateral cataract. She had been born prematurely at 27 weeks' gestational age (birthweight 945 g) by caesarean section because of acute maternal bleeding due to placental separation and premature rupture of membranes. The mother was known to be a heavy smoker (100 cigarettes/day). The pregnancy had been complicated by recurring infections, premature labour, and oligohydramnios noted at 23 weeks' gestation prior to the premature rupture of membranes. Because of mycoplasma infection diagnosed in vaginal smears during pregnancy (*Ureaplasma urealyticum*), systemic antibiotic treatment (erythromycin) had been initiated in the 29-year-old mother (7th pregnancy, 5th birth) 3 days prior to the child's delivery. In addition to the antibiotic treatment corticosteroids had been given.

At birth the baby had multiple contractions of the extremities with bilateral clubfoot and left hip dislocation. She was immediately intubated and artificially ventilated. On auscultation the lungs were well ventilated with some fine rales. At day 1, surfactant was given. The Guthrie test and TSH were normal. Blood cell count showed a left shift. CRP was negative, as were smears from the ear and nose. Blood cultures were sterile. A tracheal smear showed some streptococci from the D group. Cranial and cardiac ultrasonography were unremarkable. Ultrasonography of the kidneys showed increased echogenicity. X-rays of the chests were initially grossly normal but showed at day 8 some turbid changes of the lungs interpreted as early bronchopulmonary dysplasia. A short course of systemic steroids was therefore given. The pulmonary changes cleared, and artificial ventilation could be stopped and the child extubated at day 13. At 3 months, atelectasia of the right superior pulmonary lobe was noted compatible with pneumonia.

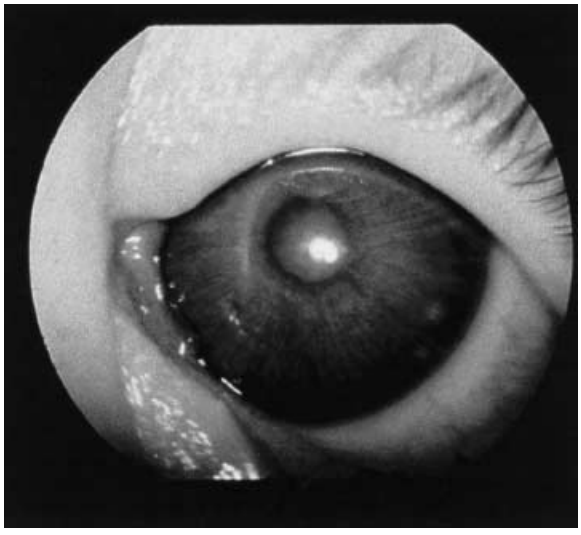

Fig. 1 Preoperative photograph of the anterior segment of the left eye at 4.5 months (Kowa hand-held fundus camera). Diffuse cataract associated with posterior synechiae. Only mild inflammatory signs seen because of successful topical treatment with antibiotics and steroids. Because of the young age of the patient, no slit-lamp photography was performed

Ophthalmological history

Because of prematurity, ophthalmological screening for retinopathy of prematurity (ROP) took place at 6 weeks' postnatal age (35 weeks' postmenstrual age). The local ophthalmologist, experienced with ROP screening, confirmed ROP stage 1, zone II in both eyes. At 8 weeks' postnatal age, ROP stage 1 zone III was confirmed in the right eye. Because the left pupil was miotic, the left fundus could not be seen. At 4 months a complicated complete cataract with posterior synechiae was noticed in the left eye. At that time, the baby was referred to the Department of Paediatric Ophthalmology and Ophthalmogenetics, University of Regensburg. Simultaneously, i.v. antibiotic treatment was initiated with ampicillin (over 10 days), tobramycin sulfate (over 8 days) and erythromycin (over 7 days).

Ophthalmological findings at presentation (at age 4 months)

The right eye was normal for age and the retina was completely vascularised. The left eye showed signs of anterior uveitis with iris hyperaemia, corneal endothelial mutton fat precipitates, large whitish aggregates concentrated in the central anterior chamber and an extremely miotic pupil. After medical mydriasis, extensive posterior synechiae became visible. The lens was covered with fibrin and appeared partially opaque. Ultrasonography (A- and B-scan) documented a clean vitreous.

Treatment and diagnostic work-up

Anti-inflammatory topical therapy with Isoptomax eye drops (dexamethasone 1 mg, neomycin sulfate 5 mg, polymyxin-B-sulfate 6000 IU) every 2 h, Dexasine SE (dexamethasone-21-dihydrogenphosphate 1 mg) every 2 h and atropine 0.1% twice daily was initiated to reduce the inflammatory signs prior to surgery. A complete laboratory work-up, including urine analysis and serology (in-

corporating mycoplasma*)*, was initiated as well as an MRI of the brain. All examinations were normal. In particular, blood serology (complement binding reaction, IgM and IgG for mycoplasma, HSV-1 and -2, CMV and VZV) was unremarkable. Rubella as an aetiology was excluded, based on the maternal antibody titre during pregnancy (IgG 1:128). With local treatment the inflammatory signs decreased within 2 weeks. By then, the partial cataract had progressed to complete (Fig. 1) and a pars plana lensectomy, combined with anterior vitrectomy, was performed at age 4.5 months. The posterior synechiae and a cyclitic membrane were removed. The posterior synechiae were only partially removed to avoid bleeding, as iridal vessels invaded the anterior surface of the lens. The vitreous appeared clear. Surgery was otherwise uncomplicated and the eye remained quiet under topical antibiotics and corticosteroids (Isoptomax) combined with i.v. acyclovir (3×40 mg daily) and i.v. decortin H 4×2 mg daily). On funduscopy the retina appeared normal for age with no signs of inflammation. Once *Spiroplasma* sp. was diagnosed with PCR and TEM (12 days after surgery), the acyclovir was stopped and another course of systemic erythromycin was given (3×80 mg orally daily over 3 weeks).

Methods

At the time of surgery (standard vitrectomy machine in the cutting/aspiration mode) the lensectomy/vitrectomy material was collected in balanced saline solution (BSS) for (1) microbiological cultures to detect bacteria and fungi, (2) PCR reaction to viral, bacterial and fungal agents, and (3) transmission electron microscopy (TEM). At least 95% was lens material, no more than 5% vitreous. With respect to the high sensitivity of subsequent PCR analysis, special care was taken to avoid contamination of the specimen with extrageneous bacterial or fungal DNA.

Bacterial and fungal cultures

Specimens were processed within 30 min after collection for microscopy and culture of aerobic and anaerobic bacteria and fungi according to standard methods [7]. Slides for Gram and Giemsa staining were prepared, and blood agar (5% CO_2), Columbia agar (5% CO_2), MacConkey agar, Sabouraud glucose agar and brain–heart infusion medium were inoculated. Cultures for bacteria were incubated up to 10 days and for fungi up to 30 days before they were discarded as negative.

Molecular genetic analysis

Total DNA was prepared according to previously published protocols [11], including a 30-min incubation step with zymolase to ensure proper lysis of the fungal cell walls. The DNA preparation was divided into three aliquots. One aliquot was subjected to PCR with primer oligonucleotides DG 74, RW 01 and RDR080, specific for a conserved sequence within bacterial 16S rRNA genes (primer sequences and amplification conditions are described in [10]). In the case of a positive PCR result, a second fragment of the bacterial 16S rRNA gene (V3 loop) was amplified with PCR primers BF (5′-ACTCCTACGGGAGGCAGCAGT-3′) and CR (5′-ACGTCATCCCCACCTTCCTC-3′). The second aliquot was subjected to PCR with primer oligonucleotides KWC348 (5′-ATGCATGTCTAAGTATAA-3′) and KWC 352 (5′-ACGGTATCTGATCATCTT-3′) specific for the 18S ribosomal RNA gene of fungal organisms. The third aliquot was subjected to PCR for *Toxoplasma gondii*, HSV and VZV according to previously published protocols [8, 20].

PCR reaction mixtures were electrophoretically separated and analysed for the presence of specific amplification products. Nucleotide sequences of the amplicons were determined for differentiation of bacterial and fungal pathogens down to species level. Gel-purified amplification products were subjected to direct sequencing of both strands with the dye-terminator strategy using an automated ABI 377A DNA sequencer (Applied Biosystems, Weiterstadt, Germany). Sequencing reactions were performed with the original PCR primer oligonucleotides. Computer-assisted comparison of the determined ribosomal sequence with all GenBank sequence entries deposited so far revealed a list of candidate species.

Transmission electron microscopy (TEM)

After short centrifugation (approximately 1000 rcf for 10 min) the resulting pellet was routinely fixed in 0.13 M cacodylate-buffered 5% glutaraldehyde (overnight, +4°C) and postfixed in 1% osmium tetroxide (2 h) at pH 7.3, dehydrated in graded ethanols, and embedded in the EmBed-812 epoxy resin (all reagents from Science Services, Munich, Germany). After 48 h heat polymerisation at 60°C, semithin (0.8 µm) sections were cut, stained with toluidine blue, and after selection of appropriate areas of interest the Epon block was trimmed for ultrathin sectioning. Serial ultrathin (80 nm) sections were cut with a diamond knife on a Reichert Ultracut-S ultramicrotome and double contrasted with aqueous 1% uranyl acetate and lead citrate solutions for 10 min each. The sections were examined in a Zeiss EM902/A electron microscope operated at 80 kV.

Results

Bacterial and fungal cultures

Microscopic examination of the Gram- and Giemsa-stained lensectomy/vitrectomy material was negative. Diagnostic cultures for aerobic and anaerobic bacteria, as well as for fungal organisms, were negative.

Molecular genetic analysis

As illustrated in Fig. 2, the clinical specimen was clearly positive for bacterial DNA (lane 3), while the DNA preparation did not contain any *Taq* DNA polymerase inhibitors (positive control in lane 1). No amplification products were obtained with the primer pair KWC384/KWC352 specific for fungal DNA. PCR reactions for *Toxoplasma gondii*, HSV and VZV DNA also remained negative (data not shown).

The respective DNA sequences of the amplification products were determined for unambiguous genotypic identification of the underlying bacterial pathogen. A computer-assisted comparison with all GenBank entries revealed the highest level of overall homology with the 16S rDNA sequence of *Spiroplasma taiwanense*, *Spiroplasma* group VI (see Figs. 3 and 4). Due to the limited number of nucleotide sequences from different *Spiroplasma* species deposited at the GenBank, a more precise species determination than "*Spiroplasma* sp." was not possible or plausible in this case.

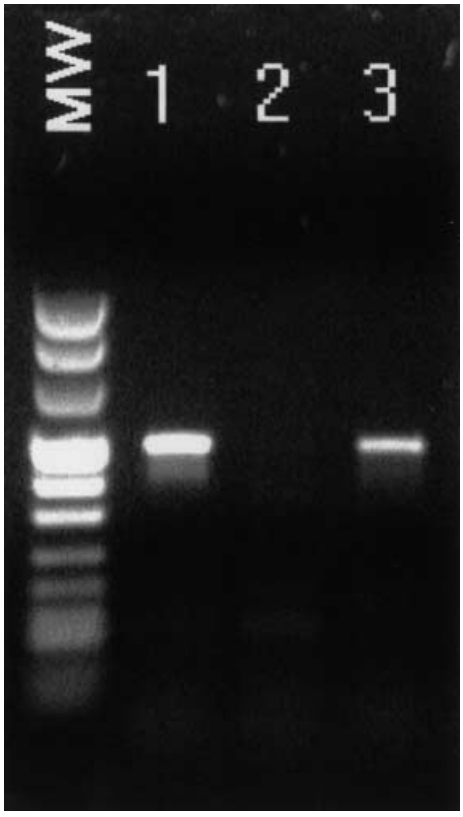

Fig. 2 Analysis of PCR products on an ethidium bromide-stained agarose gel. *Lane MW* contains DNA molecular weight marker VIII (Roche Molecular Biochemicals, Mannheim, Germany). *Lane 1* contains the amplification mixture of the positive control. The negative control was applied to *Lane 2*. *Lane 3* contains the amplification products obtained on the DNA preparation of the patient specimen

Transmission electron microscopy (TEM)

Focal aggregates of *Spiroplasma* organisms were found within the severely damaged lens fibre cells. Multiple filamentous, round, curved and helical profiles of the *Spiroplasma* cells admixed with lens cells debris could be demonstrated (Fig. 5a, b). The width of the cell profiles ranged from 80 nm to 120 nm. The short helices of two to three turns were 0.7 µm long at maximum. The filamentous forms had diverse lengths – the longest observed expanded filamentous *Spiroplasma* cell measured 1.5 µm. As well as the regularly-shaped organisms, some spherical or irregularly blebbed and pleomorphic bodies were noted. The *Spiroplasma* cells showed a fine granular cytoplasm with irregularly distributed dark ribosomes of about 15 nm diameter enclosed in a uniform cell membrane. In one of the filamentous elongated *Spiroplasma* organisms a transverse barred periodicity of approximately 13 nm was visible (Fig. 5c).

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   1 TTATGACCTGGGCTACACACGTGCTACAATGGCTGATACAAAGAGTCGCT 50
     ||||||||||||||||||||||||||||||||||||||||||||||||||
1194 TTATGACCTGGGCTACACACGTGCTACAATGGCTGATACAAAGAGTCGCT 1243
            .         .         .         .         .
  51 AAACCGCGAGGTCAAGCAAATCTCAAAAAGTCAGTCTCAGTCCGGATTGA 100
     ||||||||||||||||||||||||||||||||||||||||||||||||||
1244 AAACCGCGAGGTCAAGCAAATCTCAAAAAGTCAGTCTCAGTCCGGATTGA 1293
            .         .         .         .         .
 101 AGTCTGCAACTCGACTTCATGAAGTCGGAATCGCTAGTAATCGCGAATCA 150
     ||||||||||||||||||||||||||||||||||||||||||||||||||
1294 AGTCTGCAACTCGACTTCATGAAGTCGGAATCGCTAGTAATCGCGAATCA 1343
            .         .         .         .         .
 151 GCAATGTCGCGGTGAATACGTTCTCGGGTCTTGTACACACCGCCCGTCAA 200
     ||||||||||||||||||||||||||||||||||||||||||||||||||
1344 GCAATGTCGCGGTGAATACGTTCTCGGGTCTTGTACACACCGCCCGTCAA 1393
            .         .         .         .         .
 201 ACCACGAGAGTTGGCAATGCCAGAAGTCGGTGTCCTAACCGTAAGGAGGG 250
     ||||||||||||||||||||||||||||||||||||::|||||||
1394 ACCACGAGAGTTGGCAATGCCAGAAGTCGGTGTCCTAACCGNNAGGAGGG 1443
            .         .         .         .         .
 251 AGCTGCCAAAGGCAGGGTTGATGATTGGGG 280
     |: : :|||||||||||||| ||||||||||
1444 ANGNCNCAAAGGCAGGGTTAATGATTGGGG 1473 (positions according
                                          to GenBank M24477)
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Fig. 3 Partial alignment of the nucleotide sequences obtained from the patient specimen with primers DG 74, RW 01 and RDR080 (*upper sequence*) and GenBank sequence M24477 (*Spiroplasma taiwanense*; *lower sequence*). Homologies are indicated by *vertical lines*

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   1 TTTTCACAATGGGCGAAAGCCTGATGGAGCAATGCCGCGTGACTGATGAA 50
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 360 TTTTCACAATGGGCGAAAGCCTGATGGAGCAATGCCGCGTGACTGATGAA 409
            .         .         .         .         .
  51 GGTCTTCGGATTGTAAAGGTCTGTTGTAAGGGAAGAAGTGCTAGAATAGG 100
     ||||||||||||||||||||||||||:||||||||||||||||||||||
 410 GGTCTTCGGATTGTAAAGGTCTGTTGTNAGGGAAGAAGTGCTAGAATAGG 459
            .         .         .         .         .
 101 AAATGATTTTAGTATCGACCATACCTTACCAGAAAGCCACGGCTAACTAC 150
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 460 AAATGATTTTAGTATCGACCATACCTTACCAGAAAGCCACGGCTAACTAT 509
            .         .         .         .         .
 151 GTGCCAGCAGCCGCGGTAATACATAGGTGGCAAGCGTTATCCGGATTTAT 200
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 510 GTGCCAGCAGCCGCGGTAATACATAGGTGGCAAGCGTTATCCGGATTTAT 559
            .         .         .         .         .
 201 TGGG 204
     ||||
 560 TGGG 563  (positions according to GenBank M24477)
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Fig. 4 Partial alignment of the nucleotide sequences obtained from the patient specimen with primers BF and CR (*upper sequence*) and GenBank sequence M24477 (*Spiroplasma taiwanense*; *lower sequence*). Homologies are indicated by *vertical lines*

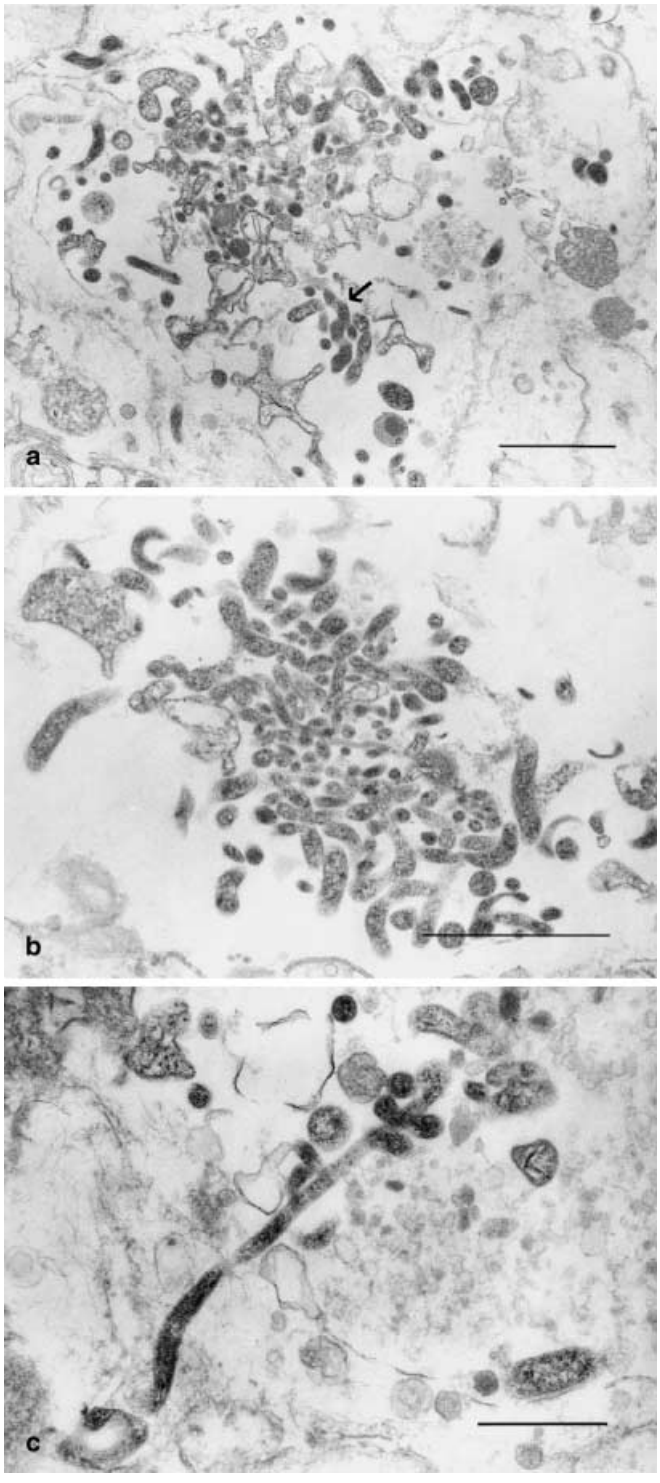

Fig. 5a–c Transmission electron microscopy of the material. **a** Accumulation of multiple filamentous, curved, round, and helical (*arrow*) profiles of *Spiroplasma* organisms within a damaged lens fibre cell. Note also the irregular and pleomorphic forms. Original magnification ×13,500; *bar* 1 µm. **b** Another focal aggregation of *Spiroplasma* organisms with differently cut profiles. The small round profiles are probably transversely sectioned cells. Original magnification ×21,000; *bar* 1 µm. **c** Higher magnification with an example of a filamentous, probably expanded, *Spiroplasma* cell. Note the transverse barred periodicity of approximately 13 nm in one third of the organism. Original magnification ×30,000; *bar* 0.5 µm

Discussion

To the best of our knowledge, this is the first report of a *Spiroplasma* sp. in humans demonstrated on TEM and confirmed by molecular genetic analysis. PCR amplification and sequence analysis of the 16S rDNA amplicons revealed the highest level of homology with *Spiroplasma* group VI (ixodid tic host).

The genus *Spiroplasma* is a subgroup of the class Mollicutes, which are the smallest free-living micro-organisms, contained only by a cell membrane and characterised by motility and helical morphology in their exponential growth phase [6, 21]. *Spiroplasma mirum*, known as suckling mouse cataract agent, was isolated in 1976 from rabbit tics and induces cataracts, posterior uveitis, encephalitis and death in newborn mice, rats, hamsters, rabbits and chicks [4, 9].

Spiroplasma mirum was also studied in a rabbit lens cell culture (AG-4676 [18]). The organism grew rapidly in this cell line, but did not grow in Dulbecco minimal essential medium–10% fetal bovine serum, the medium for AG-4676, indicating the need for cells or a cellular product. This is in agreement with the intracellular location of *Spiroplasma* organisms in lens fibres in the infant, and also in all experimental animals. These data explain the inability to demonstrate growth of the infectious agent in standard fungal or bacterial culture media. As the result of *Spiroplasma* sp. was completely unexpected in the present case, no portion of the lens material had been preserved for inoculating any special culture media.

In experimental animals, *Spiroplasma mirum* produces not only cataract but severe inflammation of all ocular compartments, including the retina [4, 9, 12, 13]. Microphthalmia also forms. At higher doses, the infection is lethal due to multiorgan involvement. In the case presented, the inflammatory signs were limited to the anterior segment of the eye. This may be due to several facts: (1) The *Spiroplasma* organisms in the present case suggested an ixodid tic (group VI) host. It has been reported that different *Spiroplasma* species have different pathogenic effects, and also that the pathogenicity of a given species may be dependent upon the host organism [3, 9]. (2) In the present case the infection most likely occurred transplacentally as a *Mycoplasma* infection had been diagnosed serologically in the mother during pregnancy. Since the diagnostic specificity of *Mycoplasma* serology is not exceptionally high, a cross-reaction with the phenotypically related group of *Spiroplasma* organisms could be assumed. (3) The clinical picture of naturally-

occurring *Spiroplasma* infection during pregnancy is not known. Also, the mother had been treated with antibiotics during pregnancy, which may have altered the course of the disease in the infant.

Due to the need for sophisticated cell culture procedures or culture media supplemented with specific cell products, naturally occurring *Spiroplasma* infections may have gone undetected in the past or been misdiagnosed as mycoplasma infections by means of serology. With the growing availability of PCR-based technology for examination of the tissues involved clinically, *Spiroplasma*, among other organisms, can be directly detected and identified on a genomic level. Combining PCR results with TEM further allows identification of specific infectious agents and their precise localisation on a cellular level. Since 1997, we have performed routine PCR and TEM analysis on seven infants with cataract of unknown aetiology. The case presented was the only one with a positive result, and also the only one associated with anterior uveitis. We recommend routine PCR and TEM analysis in all cases of acquired infantile cataract, particularly when associated with inflammatory signs, as specific infections may manifest as complicated cataract only in infancy.

Acknowledgments The paediatric data of the infant and the clinical data of the mother were kindly provided by the Paediatric and Obstetric Departments, Klinikum Passau, Germany.

References

1. Alden ER, Kalina RE, Hodson WA (1973) Transient cataracts in low-birthweight infants. J Pediatr 82:314–318
2. Bayley S, Robinson PS, Eykyn SJ (1981) Successful treatment of systemic nocardiosis with co-trimoxazole. J Infect 3:230–233
3. Bove JM (1997) Spiroplasmas: infectious agents of plants, arthropods and vertebrates. Wien Klin Wochenschr 109:604–612
4. Clark HF (1964) Suckling mouse cataract gene. J Infect Dis 114:476–487
5. Clinch TE, Duker JS, Eagle RC, Jr, Calhoun JH, Augsburger JJ, Fischer DH (1989) Infantile endogenous *Candida* endophthalmitis presenting as a cataract. Surv Ophthalmol 34:107–112
6. Cole RM, Tully JG, Popkin TJ, Bove JM (1973) Morphology, ultrastructure, and bacteriophage infection of the helical mycoplasma-like organism (*Spiroplasma citri* gen. nov. sp. nov.) cultured from “stubborn” disease of citrus. J Bacteriol 115:367–384
7. Coulter Mackie MB (1994) Molecular characterization of both alleles in an unusual Tay–Sachs disease B1 variant. Am J Hum Genet 54:1126–1127
8. Fox GM, Crouse CA, Chuang EL, et al (1991) Detection of herpesvirus DNA in vitreous and aqueous specimens by the polymerase chain reaction. Arch Ophthalmol 109:266–271
9. Friedlaender RP, Barile MF, Kuwabara T, Clark HF (1976) Ocular pathology induced by the suckling mouse cataract agent. Invest Ophthalmol 15:640–647
10. Greisen K, Loeffelholz M, Purohit A, Leong D (1994) PCR primers and probes for the 16S rRNA gene of most species of pathogenic bacteria, including bacteria found in cerebrospinal fluid. J Clin Microbiol 32:335–351
11. Hykin PG, Tobal K, McIntyre G, Matheson MM, Towler HM, Lightman SL (1994) The diagnosis of delayed post-operative endophthalmitis by polymerase chain reaction of bacterial DNA in vitreous samples. J Med Microbiol 40:408–415
12. Kirchhoff H, Heitmann J, Trautwein G (1981) Pathogenicity of *Spiroplasma* sp. strain SMCA in rabbits: clinical, microbiological, and histological aspects. Infect Immun 33:292–296
13. Kirchhoff H, Kuwabara T, Barile MF (1981) Pathogenicity of *Spiroplasma* sp. strain SMCA in Syrian hamsters: clinical, microbiological, and histological aspects. Infect Immun 31:445–452
14. Lambert SR, Drack AV (1996) Infantile cataracts. Surv Ophthalmol 40:427–458
15. Liebmann SD (1955) Postnatal development of lamellar cataract in premature infants. Arch Ophthalmol 54:257
16. Lohmann CP, Linde HJ, Reischl U (2000) Improved detection of microorganisms by polymerase chain reaction in delayed endophthalmitis after cataract surgery. Ophthalmology 107:1047–1051
17. McCormick AQ (1968) Transient cataracts in premature infants. A new clinical entity. Can J Ophthalmol 3:202–206
18. Megraud F, Gamon LB, McGarrity GJ (1983) Characterization of *Spiroplasma mirum* (suckling mouse cataract agent) in a rabbit lens cell culture. Infect Immun 42:1168–1175
19. Shah GK, Vander J, Eagle RC (2000) Intralenticular *Candida* species abscess in a premature infant. Am J Ophthalmol 129(3):390–391
20. Short GA, Margolis TP, Kuppermann BD, Irvine AR, Martin DF, Chandler D (1997) A polymerase chain reaction-based assay for diagnosing varicella-zoster virus retinitis in patients with acquired immunodeficiency syndrome. Am J Ophthalmol 123:157–164
21. Williamson RF, Tully JG, Whitcomb RF (1989) The genus *Spiroplasma*. In: Whitcomb RF, Tully JG (eds) The mycoplasmas. Academic Press, New York, pp 71–111