

Dismetabolic Cataracts: Clinicopathologic Overview and Surgical Management with B-MICS Technique

Cavallini GM¹, Forlini M¹, Masini C¹, Campi L¹, Chiesi C¹, Rejdak R² and Forlini C^{3*}

¹Institute of Ophthalmology, University of Modena, Modena, Italy

²Department of Ophthalmology, Medical University of Lublin, Lublin, Poland

³Department of Ophthalmology, "Santa Maria Delle Croci" Hospital, Ravenna, Italy

Abstract

Background: Dismetabolic cataract is a loss of lens transparency due to an insult to the nuclear or lenticular fibers, caused by a metabolic disorder. The lens opacification may occur early or later in life, and may be isolated or associated to particular syndromes.

We describe some of these metabolic conditions associated with cataract formation, and in particular we report our experience with a patient affected by lathosterolosis that presented bilateral cataracts.

Methods: Our patient was a 7-years-old little girl diagnosed with lathosterolosis at age 2 years, through gas chromatography/mass spectrometry method for plasma sterol profile that revealed a peak corresponding to cholest-7-en-3 β -ol (lathosterol).

Results: The lens samples obtained during surgical removal with B-MICS technique were sent to the Department of Pathology and routinely processed and stained with haematoxylin-eosin and PAS; then, they were examined under a light microscope. Histological examination revealed lens fragments with the presence of fibers disposed in a honeycomb way, samples characterized by the presence of homogeneous eosinophilic lens fibers, and other fragments characterized by bulgy elements referable to cortical fibers with degenerative characteristics. These findings were compatible with cortical dismetabolic cataract.

Conclusion: We conclude that lathosterolosis is a complex malformative syndrome that can lead to dismetabolic cataract development. This unique case of cataract in such a patient, has been successfully managed with cataract extraction and IOL implant.

Keywords: Dismetabolic cataract; Lathosterolosis; B-MICS; Bimanual microincisions cataract surgery; Phacoemulsification

Introduction

Dismetabolic cataract is a loss of lens transparency due to an insult to the nuclear or lenticular fibers, caused by a metabolic disorder. The lens opacification may occur early or later in life, and may be isolated or associated to particular syndromes. The exact incidence of this kind of cataract is not known, as it is often numbered in the group of congenital cataracts. Actually, metabolic and systemic disease are found in as many as 60% of bilateral congenital cataracts. Screening for metabolic disorders in all children with bilateral cataracts is essential, as in some inherited metabolic disorders progressive and severe symptoms can be avoided with timely initiation of treatment [1].

Galactosemia
Mucopolipidosis tipe I
Mucopolipidosis tipe II
Fabry disease
Galactokinase deficiency
Glucose-6-phosphate dehydrogenase deficiency
Mannosidosis
Refsum disease
Lowe syndrome
Alport syndrome
Familiar hypoparathyroidism
Cholesterol biosynthesis defects (Smith-Lemli-Opitz syndrome, lathosterolosis...)
Metabolic syndrome
Diabete

Table 1: The metabolic disorders those are more frequently associated to cataract formation.

The metabolic disorders that are more frequently associated to cataract formation are reported in Table 1.

We describe some of these metabolic conditions associated with cataract formation, and in particular we report our experience with a patient affected by lathosterolosis that presented bilateral cataracts.

Cataract in galactosemia

Classical galactosemia is an autosomal recessive disorder caused by a severe compromission of galactose utilization due to deficiency of the enzyme galactose-1-phosphate uridyltransferase (GALT). The GALT enzyme is responsible for the conversion of galactose-1-phosphate with UDP glucose to glucose-1-phosphate and UDP galactose. The gene encoding for GALT is located on chromosome 9p13. Patients present with hepatomegaly, liver failure, food intolerance, hypoglycaemia, muscle hypotonia, sepsis and cataract. The typical appearance of galactosemic cataract is an "oil-drop" central opacity (Figure 1), caused by the accumulation of galactitol in the lens. This causes an increase

***Corresponding author:** Cesare Forlini, Chief of Department of Ophthalmology, "Santa Maria delle Croci" Hospital Viale V. Randi n. 5, (48121) Ravenna, Italy, Tel.: +39 0544 270385; Fax: +39 0544 280049; E-mail: forlinic@forlinic.it

Received July 25, 2013; **Accepted** August 05, 2013; **Published** August 07, 2013

Citation: Cavallini GM, Forlini M, Masini C, Campi L, Chiesi C, et al. (2013) Dismetabolic Cataracts: Clinicopathologic Overview and Surgical Management with B-MICS Technique. J Genet Syndr Gene Ther 4: 165. doi:10.4172/2157-7412.1000165

Copyright: © 2013 Cavallini GM, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.



Figure 1: Galactosemic dismetabolic cataract.



Figure 2: Cataract in microphakia in a patient with Lowe syndrome.

in the osmotic pressure within the lens, with a subsequent osmotic water inflow and lens opacification. The ophthalmologist may play an important role in this disease, since early recognition of cataract development followed by the initiation of a galactose-free diet may lead to clearing of lenticular opacities [2]. Treatment involving the total restriction of lactose-containing foods is also life-saving but many patients develop late complications such as problems of mental development, disorders of motor function, disorders of speech and hypergonadotrophic hypogonadism [3].

Cataract in galactokinase deficiency

Galactokinase (GALK1) deficiency is an autosomal recessive disorder, which involves the first enzyme of galactose metabolic chain. Galactokinase deficiency results from mutation in the GALK1 gene mapped on 17q24. Cataract and, rarely, pseudotumor cerebri caused by galactitol accumulation seem to be the only consistently reported abnormalities in this disorder [4]. Cataracts may develop during infancy or may be presenile in the adult population. The lens opacity has typically a lamellar shape.

As cataract and pseudotumor cerebri appear to be the only complications of galactokinase deficiency, the outcome for patients with galactokinase deficiency is much better than for patients with classical galactosemia.

Cataract in lowe syndrome

The oculo-cerebro-renal syndrome of Lowe (OCRL) is a rare X-chromosomal disorder characterised by the triad of congenital cataracts, renal tubular dysfunction, and mental retardation. The mutation of the gene OCRL1 localized at Xq26.1, coding for the enzyme phosphatidylinositol [4,5] biphosphate 5 phosphatase, PtdIns [4,5]

P2, in the trans-Golgi network is responsible for the disease. Bilateral cataract and severe hypotonia are present at birth. In the subsequent weeks or months the ocular picture may be complicated by glaucoma and cheloids. Psychomotor retardation is evident in childhood, while behavioural problems prevail and renal complications arise in adolescence [5].

Typically complete opacification and discoid deformation of the lenses (microphakia) are seen, indicating a developmental defect in early embryogenesis (Figure 2). Patients with mild Lowe syndrome phenotype may show incomplete lenticular opacities without visual impairment [6].

Cataract in mannosidosis

Mannosidosis is a rare disorder of glycoprotein metabolism. The primary metabolic defect in mannosidosis is the deficiency of the acidic alpha-mannosidase A and B activities which results in the lysosomal accumulation of mannose-rich substrates. People with mannosidosis appear normal at birth and that their typical phenotype develops by two years of age. This is characterized by a distinctive coarse facies and dysostosis multiplex. Although recurrent infections, hearing loss and mental retardation occur, the course in this storage disorder generally is stable and is compatible with adult life [7]. Alpha-mannosidosis in the human has been associated with cataract development in infancy [8]. The lens opacities do not have typical appearance, but may be nuclear or capsular, or total.

Cataract in hypoparatiroidism

Cataract is a well-known complication of hypoparathyroidism, albeit the mechanism is obscure. The typical appearance is characterized by cuneate radial opacities (Figure 3). The progression of cataract is typically slow in patients with idiopathic hypoparathyroidism. Anyway, there are also cases in which the typical hypocalcemic cataracts have an extremely rapid evolution, in particular when hepatic and renal failure occurs, with alteration in the serum calcium and phosphorus levels [9]. Physicians and ophthalmologists must be aware of cataracts developing rapidly in the setting of such metabolic derangements.

Cataract in lathosterolosis

Lathosterolosis is a singular defect of cholesterol biosynthesis due to the lack of lathosterol-5-desaturase (SC5D), the enzyme that catalyzes the conversion of lathosterol to 7-dehydrocholesterol in the cholesterol synthetic pathway. Cholesterol is an abundant lipid in eukaryotic membranes, implicated in different structural and functional capacities, and its partial or complete lack as well as the accumulation



Figure 3: Cataract in hypoparathyroidism.

of precursors, may lead to a group of malformative syndromes of recent identification [10]. Lathosterolosis is a rare disorder that leads to developmental abnormalities, including mental retardation, and to date has only been identified in two patients [11,12] one of which died at 18 weeks of age with diffuse intracellular storage.

We describe a unique case of cataract in a lathosterolosis patient who underwent cataract surgery. Our patient was a 7-years-old little girl diagnosed with lathosterolosis at age 2 years, through gas chromatography/mass spectrometry method for plasma sterol profile that revealed a peak corresponding to cholest-7-en-3 β -ol (lathosterol). The biosynthesis of cholesterol in her fibroblasts was defective, showing a block in the conversion of lathosterol into 7-dehydrocholesterol. Physical examination revealed dismorphic features, including severe microcephaly, receding forehead, anteverted nares, micrognathia, prominent upper lip, high arched palate, haxadactyly and syndactyly of the left foot. Severe psychomotor delay became increasingly evident with age; conductive deafness was found at the auditory evoked potentials. She also had liver disease with signs of cholestasis [11]. At the first ophthalmic evaluation, carried out in June 2005, the little patient presented with bilateral posterior subcapsular cataracts at byomicroscopy and bilateral pale optic nerve head at fundus examination. In November 2005, after a severe gastroenteric Rotavirus infection with subsequent metabolic decompensation, a marked worsening in the lens opacity of the left eye occurred. There was no history of ocular trauma reported by parents, and Eco-B scan examination revealed normal vitreous-retinal structures. Marked subconjunctival jaundice was evident at biomicroscopy, due to a severe intrahepatic cholestasis. After metabolic improvement, the little patient was encouraged to surgery for left cataract extraction. Surgery was performed on February 2006, under general anaesthesia. We performed a bimanual microphacoemulsification mainly working in aspiration mode; an acrylic hydrophobic flexible IOL was inserted (Acri.Smart 48S- Acri.Tec, Co. Berlin, Germany) and manual posterior continuous curvilinear capsulorhexis (PCCC) and optic entrapment of the IOL were performed [13]. No intraoperative or postoperative complications occurred. After surgery, refraction was +0.75 sph with an astigmatism of +0.50 (90°) diopter, remaining stable during the whole follow-up; biomicroscopic evaluation revealed absence of significant inflammation and good IOL centration; no posterior capsule opacification occurred 2 years after surgery. Visual acuity was not assessable due to complete lack of patient's collaboration; anyway, we noted a better orientation of the proband during the subsequent control visits, and parents referred a greater confidence and autonomy in her daily life attitudes.

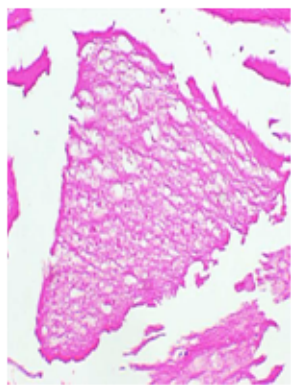


Figure 4: Fragments of lens characterized by the presence of fibers disposed in a honeycomb way.

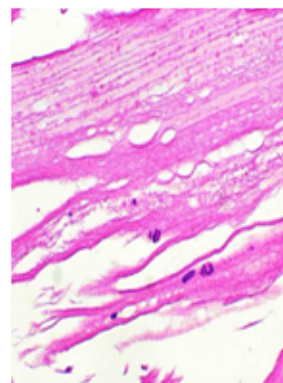


Figure 5: Fragments characterized by bulgy elements referable to cortical fibers with degenerative characteristics.

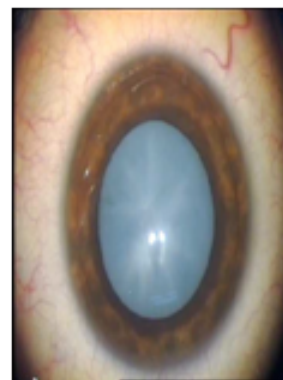


Figure 6: Dismetabolic cataract in lathosterolosis.

The lens samples obtained during surgical removal were sent to the Department of Pathology and routinely processed and stained with haematoxylin-eosin and PAS; then, they were examined under a light microscope. Histological examination revealed lens fragments with the presence of fibers disposed in a honeycomb way, samples characterized by the presence of homogeneous eosinophilic lens fibers, and other fragments characterized by bulgy elements referable to cortical fibers with degenerative characteristics (Figures 4 and 5). These findings were compatible with cortical dismetabolic cataract (Figure 6).

The relationship between abnormal cholesterol metabolism and disturbed morphogenesis have been extensively studied in recent years [14,15], and it has been questioned whether cholesterol deficiency or increased levels of intermediate sterols are responsible for the abnormal functioning of the pathway in these syndromes. The prototypical example is the Smith-Lemli-Opitz syndrome (SLOS), a complex malformation syndrome including the presence of congenital cataracts [14]. Our proband presented with bilateral subcapsular posterior cataracts, with rapid worsening in the left eye after a severe metabolic decompensation. Hystopathologic examination confirmed the presence of a dismetabolic cortical cataract. We don't really know the exact pathologic mechanism involved; in two cases of dismetabolic cataracts in patients with SLO syndrome, it has been advocated a dysfunction or rupture of the lens capsule leading to acute osmotic shifts [16]. We can hypothesize the same pathogenetic mechanism for our case. We conclude that lathosterolosis is a complex malformative syndrome that can lead to dismetabolic cataract development. This unique case of

cataract in such a patient, has been successfully managed with cataract extraction and IOL implant.

Conflict of Interest

The authors do not have any financial interest or conflicts of interest related to this submission.

References

1. Wijburg MT, Wenniger-Prick LJ, Bosch AM, Visser G, Bams-Mengerink A (2008) [Bilateral cataract in childhood years: always an indication for screening on a metabolic disorder]. *Ned Tijdschr Geneesk* 152: 632-636.
2. Stambolian D (1988) Galactose and cataract. *Surv Ophthalmol* 32: 333-349.
3. Bosch AM, Waterham HR, Bakker HD (2004) [From gene to disease; galactosemia and galactose-1-phosphate uridylyltransferase deficiency]. *Ned Tijdschr Geneesk* 148: 80-81.
4. Bosch AM, Bakker HD, van Gennip AH, van Kempen JV, Wanders RJ, et al. (2002) Clinical features of galactokinase deficiency: a review of the literature. *J Inher Metab Dis* 25: 629-634.
5. Loi M (2006) Lowe syndrome. *Orphanet J Rare Dis* 1: 16.
6. Keilhauer CN, Gal A, Sold JE, Zimmermann J, Netzer KO, et al. (2007) [Clinical findings in a patient with Lowe syndrome and a splice site mutation in the OCRL1 gene]. *Klin Monbl Augenheilkd* 224: 207-209.
7. Yunis JJ, Lewandowski RC Jr, Sanfilippo SJ, Tsai MY, Foni I, et al. (1976) Clinical manifestations of mannosidosis--a longitudinal study. *Am J Med* 61: 841-848.
8. Arbisser AI, Murphree AL, Garcia CA, Howell RR (1976) Ocular findings in mannosidosis. *Am J Ophthalmol* 82: 465-471.
9. Haviv YS, Safadi R, Zamir E (1999) A rapidly progressive cataract in a patient with autoimmune hypoparathyroidism and acute liver and renal failure. *Am J Nephrol* 19: 523-526.
10. Gondré-Lewis MC, Petrache HI, Wassif CA, Harries D, Parsegian A, et al. (2006) Abnormal sterols in cholesterol-deficiency diseases cause secretory granule malformation and decreased membrane curvature. *J Cell Sci* 119: 1876-1885.
11. Brunetti-Pierri N, Corso G, Rossi M, Ferrari P, Balli F, et al. (2002) Lathosterolosis, a novel multiple-malformation/mental retardation syndrome due to deficiency of 3beta-hydroxysteroid-delta5-desaturase. *Am J Hum Genet* 71: 952-958.
12. Krakowiak PA, Wassif CA, Kratz L, Cozma D, Kovárová M, et al. (2003) Lathosterolosis: an inborn error of human and murine cholesterol synthesis due to lathosterol 5-desaturase deficiency. *Hum Mol Genet* 12: 1631-1641.
13. Grieshaber MC, Pienaar A, Stegmann R (2005) Posterior vertical capsulotomy with optic entrapment of the intraocular lens in congenital cataracts--prevention of capsule opacification. *J Cataract Refract Surg* 31: 886-894.
14. Kelley RI, Hennekam RC (2000) The Smith-Lemli-Opitz syndrome. *J Med Genet* 37: 321-335.
15. Villavicencio EH, Walterhouse DO, Iannaccone PM (2000) The sonic hedgehog-patched-gli pathway in human development and disease. *Am J Hum Genet* 67: 1047-1054.
16. Goodwin H, Brooks BP, Porter FD (2008) Acute postnatal cataract formation in Smith-Lemli-Opitz syndrome. *Am J Med Genet A* 146A: 208-211.

This article was originally published in a special issue, [Genetic Disorders](#) handled by Editor(s), Dr. Xiaobo Li, Yeshiva University, USA