Bilateral cataracts as the first manifestation of type 1 diabetes mellitus
A case report

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Abstract

Rationale: Cataracts can occur in children and adolescents with Type 1 Diabetes Mellitus who have poorly controlled glycemia. Here, we report a case of a 16-year-old female, who was diagnosed with bilateral cataracts, and genetic screening identified a mutation in the PRRC2A gene which is rarely reported. After surgery, retinopathy was found in this patient, combined with the published literature, we encourage that postoperative monitoring for retinal lesions during the follow-up visits should be conducted.

Patient concerns: In this article, we present an adolescent diagnosed with bilateral cataracts, and developed retinopathy during the follow-up visits. Genetic screening identified a mutation in the PRRC2A gene.

Diagnoses: The diagnoses of Diabetic cataracts, Type 1 diabetes and Diabetic retinopathy was made.

Interventions: The patient underwent surgery in both eyes, and hypoglycemic treatment was provided.

Outcomes: The surgery achieved satisfactory results, during the follow-up visits, the visual acuity was reported as 0.8 in the right eye and 1.0 in the left eye. Besides, her blood glucose was well controlled, and her glycated hemoglobin was reduced to 6.9% after three months of continuous treatment.

Lessons: This case highlights the importance of genetic screening for detecting mutations in diabetes-related genes, and postoperative monitoring for retinal lesions during the follow-up visits.

Abbreviations: ATP = adenosine triphosphate, GAD = glutamic acid decarboxylase, HbA1c = hemoglobin A1c, ICA = islet cell antibodies, SNP = single nucleotide polymorphism. TGAb = thyroglobulin, TPOAb = thyroid autoantibodies, VA = visual acuity.

Keywords: cataracts, diabetes mellitus, diabetic cataract, PRRC2A, type 1 diabetes

1. Introduction

Type 1 diabetes mellitus commonly occurs in children and adolescents and is associated with chronic medical complications gravely affecting vision and kidney function, such as retinopathy and nephropathy, respectively.[1] However, these complications rarely occur at an early age. Cataracts have been linked to several factors, including aging, genetics, local nutritional disorders, immune and metabolic abnormalities, trauma, poisoning, and radiation exposure.[2] For diabetic patients, cataracts can be a result of long-term uncontrolled hyperglycemia and large fluctuations in blood glucose levels, both symptoms leading to an osmotic pressure imbalance inside and outside the lens.[3] For this reason, cataracts can occur in patients with type 1 diabetes who have poorly controlled glycemia long term. Anterior and posterior subcapsular subcortical opacities represent the typical structural features of cataracts in diabetic patients.[4,5] While, surgical treatment for cataracts are often successful, many cases of diabetic cataracts are misdiagnosed in young patients due to the low incidence rate.[6–8]

This case study investigates a 16-year-old female patient who presented with blurry vision and was ultimately diagnosed with type 1 diabetic ketosis and bilateral diabetic cataracts. The patient had a mutation in a rarely reported gene. We further summarize the characteristics of patients with diabetic cataracts in the literature, highlighting the importance of early genetic screening for these patients.

2. Case report

A 16-year-old female, who was admitted to the Department of Ophthalmology in the Second Affiliated Hospital of Nanchang University on October 31, 2017, presented with blurred vision in both eyes for more than 3 months. In August 2017, the patient showed decreased bilateral vision with a more pronounced reduction in visual acuity (VA: commonly refers to the clarity of vision and is dependent on optical and neural factors) in her right eye and 1.0 in the left eye. Besides, her blood glucose was well controlled, and her glycated hemoglobin was reduced to 6.9% after three months of continuous treatment.
eye without apparent cause. She also presented with fluctuations in visual acuity in both eyes. In September 2017, the patient was diagnosed with bilateral cataracts. She was treated symptomatically to unsatisfactory results. The visual acuity in the right eye further deteriorated over the course of treatment from counting fingers to hand motion on the visual acuity scale. While the patient had a year-long history of polydipsia and polyuria, without weight loss or other discomforts, these symptoms went unnoticed and untreated. She had no family history of diabetes or other clinically significant familial diseases.

During the initial examination, her visual acuity was reported via the hand motion test in the right eye and the counting figures test in the left eye. An ophthalmological examination revealed an opacity in the subcortical and posterior capsules. The patient was conscious with no headache, abdominal pain, or other symptoms.

The random peripheral blood glucose level was beyond the test range in the patient, and her random serum blood glucose level was 42.18 mmol/L with 16.8% glycosylated hemoglobin. A routine urine test revealed that the urinary glucose level was ++++, while the urinary ketone level was ++. Patient’s blood gas analysis revealed compensatory metabolic acidosis with low blood sodium concentrations. The patient was then transferred to the Department of Endocrinology and Metabolism at the Second Affiliated Hospital of Nanchang University. The C-peptide release test and blood glucose concentrations were measured (Table 1). All other clinical findings were normal, including islet cell antibodies (ICA), glutamic acid decarboxylase (GAD) thyroid function, thyroid autoantibodies (TPOAb), thyroglobulin (TGAb), and other autoimmune antibodies.

Genetic testing was performed to screen for potential mutations and identified the rs1046089 single nucleotide polymorphism (SNP) site of the PRRC2A gene in the patient. The patient was given rehydration and hypoglycemic treatment for ketone bodies and blood sugar control after admission at the Department of Endocrinology and Metabolism. When the ketone bodies were completely removed and the blood glucose concentration was stabilized, she was transferred back to the Department of Ophthalmology for phacoemulsification/phaaco aspiration and intraocular lens implantation. The surgery achieved satisfactory results with a full recovery of vision in the right eye. The patient was discharged on November 13, 2017, and provided hypoglycemic treatment, which included insulin glargine once daily at a dose of 24 IU taken at night, insulin aspart 3 times daily with 10 IU before breakfast and 6 IU each before lunch and dinner, and acarbose (30 mg) 3 times daily.

After discharge (on November 30, 2017), the patient was tested again for C-peptide release, which confirmed poor function of her pancreatic islets (Table 1). In January 2018, the patient underwent cataract surgery for the left eye. After surgery, her visual acuity was reported as 0.8 in the right eye and 1.0 in the left eye, however, retinopathy was discovered in the patient’s right eye. The patient used a subcutaneously implanted device for self-glucose monitoring, and adjusted the dose of insulin as per her glucose monitoring results throughout the day, particularly after meals. As such, the patient’s blood glucose was well controlled, and her glycate hemoglobin was reduced to 6.9% after 3 months of continuous treatment. Except for hypoglycemic events, no other adverse events occurred during the treatment.

### Table 1

| Hospitalization period (November 3, 2017) and after discharge (November 30, 2017). | November 3, 2017 (during hospitalization) | November 30, 2017 (follow-up after discharge) |
|---|---|---|
| Item name | C-peptide, ng/mL | Serum glucose, mmol/L | C-peptide, ng/mL | Serum glucose mmol/L |
| Fasting (normal) | 0.05 (1.1–4.4 ng/mL) | 6.62 (3.9–6.1 mmol/L) | <0.01 (1.1–4.4 ng/mL) | 5.33 (3.9–6.1 mmol/L) |
| 1 hour postprandial | 0.50 | 14.24 (3.9–10.5 mmol/L) | 1.71 | 10.91 (3.9–10.5 mmol/L) |
| 2 hours postprandial | 0.81 | 12.9 (4.4–7.8 mmol/L) | 3.22 | 13.24 (4.4–7.8 mmol/L) |

#### 3. Discussion

Cataracts pose a serious medical complication for children and adolescents with type 1 diabetes mellitus, as it is associated with decreased visual acuity, resulting in an impaired quality of life. Diabetic cataracts are more prevalent in female adolescents whereby they develop rapidly often in both eyes.[4,5] The lens can become completely cloudy in days, weeks, or months.[4,5] Patients with diabetic cataracts often present initially with anterior and posterior subcapsular white spots or snowflake-like opacity. The most common lesion occurs in the posterior subcapsular pole.[4,9]

This 16-year-old female patient presented with typical diabetes-induced polydipsia and polyuria for more than a year. The high glycosylated hemoglobin level detected during admission (16.8%) suggests that she had hyperglycemia for an extended period of time before the diagnosis. She had blurred vision and visual acuity inconsistencies, which were likely caused by the large fluctuations in blood glucose levels and subsequent changes in the lens osmotic pressures and refractive errors. The patient was officially diagnosed with bilateral cataracts. Since the patient’s islet failure (according abnormal C-peptide release test results showed in Table 1) and onset of diabetic ketosis, she was further diagnosed with type 1 diabetes mellitus.

The patient tested negative for islet cell-related antibodies, thyroid-related antibodies, and autoimmune antibodies, which excluded the possibility of autoimmune diseases. As there was no family history of diabetes, hereditary diabetes was not a consideration in her diagnosis. The patient had the rs1046089 single nucleotide polymorphism (SNP) site of the PRRC2A gene, which is a missense mutation associated with type 1 diabetes.[10]

As other studies suggest, identification of a genetic mutation may play a key role in the development and progression of cataracts, particularly in children and adolescents with type 1 diabetes mellitus. The clinical characteristics of the patient, including age, gender, long-term diabetic symptoms, high glycosylated hemoglobin levels, and diabetic ketosis, support the diagnosis of diabetic cataracts.[4,9,11]

To date, only a few studies have reported on the role of genetic mutations in diabetic cataracts. An animal study by Renner et al[12] demonstrated that cataracts appeared earlier in pigs with an insulin gene mutation (C94Y), and progressed with age. In addition, Wasserman et al[13] described a case of insulin gene mutations similar to our case, in that the patient suffered from bilateral cataracts. Lenfant et al[14] reported that a 6-year-old girl had a heterozygous p.R825Q ABCC8 mutation that was responsible for her diabetes and a homozygous p.G71S mutation.
in CRYBB1 that was responsible for her congenital cataract, suggesting that double-gene mutations may contribute to the clinical manifestation of diabetic cataracts as well. While further studies into the effects of genetic mutations on cataract development are necessary, these results along with those presented in our case, demonstrate the potential complications in vision that could arise in these patients.

The pathogenesis of diabetic cataracts is unclear at this time. In animal models, the aldose reductase pathway is widely recognized to contribute to the pathogenesis of diabetic cataracts. Aldose reductase, an enzyme involved in the alternative glucose metabolic pathway, converts glucose into sorbitol, which is then transformed into fructose via the action of sorbitol dehydrogenase. Aldose reductase primarily resides in the lens epithelium and converts excess glucose to sorbitol when blood glucose levels are elevated. Sorbitol accumulation increases the osmotic pressure of lens cells, leading to vacuolization in the lens, lamellar separation, broken crystalline fibers, and eventually the development of cataracts. Glycosylation due to high carbohydrate and oxidative stress may contribute to the opacification of the lens. Aldose reductase inhibitors have been reported to induce a protective effect on cataract formation. In addition, increased levels of aldose reductase in female adolescents may result in the prevalence of diabetic cataracts in female patients. Recently, Su et al. reported that acute diabetic cataracts are caused by the loss of glutathione and decreased levels of adenosine triphosphate (ATP). Furthermore, Papadimitriou et al. suggested that acute bilateral cataracts in type 1 diabetic patients may be caused by autoimmune factors.

Regarding the relationship between glycemic control and cataracts in adolescents with diabetes, the results from different studies vary greatly. Further complicating the issue, cataract development may be unrelated to blood glucose levels, as cataracts have also been seen in some diabetic patients with strictly controlled blood glucose levels. Despite those reports, several studies have shown that cataracts can dissipate after the blood glucose levels are stabilized in some patients, suggesting that blood glucose fluctuations may contribute to cataract formation. Further investigations demonstrate that patients suffering from diabetic cataracts may also have retinopathy. In this study, the patient developed retinal lesions 3 months post-surgery. The presented case encourages proper patient monitoring after surgery to identify retinal lesions in a prompt manner. Appropriate therapeutic interventions should be actively performed to prevent further deterioration of vision if retinal lesions occur.

4. Conclusion

In summary, we recommend routine examination of the lens and retina for diabetic adolescents and children who have diabetic ketosis or high levels of HbA1c. For those patients with cataracts, postoperative retinoscopy should be routinely performed, and regular follow-up visits are advised. If abnormalities are identified, it is encouraged that patients are immediately referred to an ophthalmologist for further evaluation. In addition, diabetes-related genetic screening is highly recommended for patients who can afford the test.

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