Case Report

Transient severe non-proliferative retinopathy in an adolescent with type 1 diabetes and chronic myeloid leukemia


The onset of diabetic retinopathy correlates with the long-term quality of glycemic control. A 17-yr-old adolescent with type 1 diabetes presented unexpectedly with acute non-proliferative retinopathy despite good glycemic control. Two months later chronic myeloid leukemia (CML) was diagnosed. Chemotherapy was initiated and within a few weeks the patient was in full remission concerning leukemia. Retinopathy completely resolved within 8 months. The patient was in good metabolic control throughout the course. To our knowledge, this is the first report of CML-triggered retinopathy in a well-controlled diabetic adolescent. In case of unexpected retinopathy in patients with type 1 diabetes, other potential causes of retinopathy should be considered.

Retinopathy is a common microvascular complication in type 1 diabetes (1). Longstanding poor metabolic control with high levels of glycated hemoglobin A1c (HbA1c) has been identified as a critical risk factor for the development and progression of diabetic retinopathy (2). Other well-known risk factors are diabetes duration, smoking, hypertension, and dyslipoproteinemia (3). Age at onset of diabetes also significantly modifies the long-term risk of retinopathy (4, 5). Progression of diabetic retinopathy may also be influenced by hematological disorders (6, 7). We present an adolescent with well-controlled type 1 diabetes who developed retinopathy most probably triggered by chronic myeloid leukemia (CML).

Silvia Schmid⁎, Mariarosaria Lang-Muritano⁎, Urs Meier*, Riccardo De Peron⁎, Daniel Konrad⁎ and Eugen Schoenle⁎

⁎Department of Endocrinology and Diabetology, University Children’s Hospital, Zurich, Switzerland; Children’s Research Centre, University Children’s Hospital, Zurich, Switzerland; †Ophthalmological Private Practice, Lugano, Switzerland; and ‡Department of Ophthalmology and Ophthalmologic Surgery, Regional Hospital, Lugano, Switzerland

Key words: diabetic metabolic control – diabetic retinopathy – microvascular complications

Corresponding author:
Silvia Schmid, MD, Department of Endocrinology and Diabetology, University Children’s Hospital, Steinwiesstrasse 75, CH-8032 Zurich, Switzerland. Tel: +41-44-266 7309; fax: +41-44-266 7983; e-mail: silvia.schmid@kispi.uzh.ch

Submitted 8 March 2012. Accepted for publication 6 June 2012
Case report

Severe non-proliferative diabetic retinopathy was unexpectedly detected in a 17-yr-old adolescent with type 1 diabetes despite good glycemic control. His HbA1c at that time was 6.9% (normal value <6%; Bayer DCA 2000®, Bayer AG, Leverkusen, Germany). Visual acuity was slightly reduced (0.8 in both eyes) compared to previous examinations (1.0 in both eyes). However, he reported no subjective symptoms of sight impairment. The findings were confirmed by fluorescein angiography revealing severe non-proliferative ‘diabetic’ retinopathy with bilateral macular edema, retinal hemorrhages, and venous dilation (Fig. 1). Previous annual ophthalmologic assessments including retinal examination through dilated pupils had not revealed any sign of retinopathy. However, old chorioretinic scars were present in the left eye as a probable sequela of in utero exposure to toxoplasmosis. Renal failure (creatinine 84 μmol/L, normal value 65–120 μmol/L) including microalbuminuria (4.5 μg/mg creatinine, normal value <30 μg/mg creatinine) and possible causes of retinopathy such as hypertension, smoking, and coagulopathies were excluded. A white blood cell count was not determined at the time of retinopathy detection.

Type 1 diabetes had been diagnosed at the age of 9 yr. He was initially treated by a residential diabetologist for 4 yr. His average HbA1c level during that time was 8.9%. At the age of 13 yr he was referred to our specialized center for diabetic children and adolescents. Metabolic control improved as expressed by an average HbA1c value of 7.7% from age 13 to 17. During the year before the appearance of retinopathy his average HbA1c value was 7.3%.

Two months after the diagnosis of assumed diabetic retinopathy CML was detected when the patient presented with acute onset of myalgia. Hematological parameters were as follows: hemoglobin 13.2 g/L, hematocrite 39.5%, platelet count 222 g/L, and white blood cell count 116 g/L; 89% blasts present in the bone marrow were Philadelphia chromosome positive. Chemotherapy with hydroxycarbamide (Litalir®) and imatinib (Gleevec®) was initiated and the patient was in remission concerning CML within a few weeks. During treatment, metabolic control remained good (average HbA1c value of 7.4% for the 9 months of follow-up). Retinopathy resolved completely within 8 months after the diagnosis of leukemia, as was apparent in fundoscopy and proven by fluorescein angiography (Fig. 1).

Discussion

The overall prevalence of diabetic retinopathy among children and adolescents with type 1 diabetes ranges from 10 to 42% (8–11). Its risk may be calculated according to the Berlin Retinopathy Study. The latter revealed an individual median expectation of retinopathy after more than 25 yr of diabetes for patients with an average HbA1c <8% and after more than 16.2 yr for patients with an average HbA1c 8–9% (12). According to this model, the 9 yr duration of diabetes in our patient with an overall average HbA1c value of 8.3% in the absence of other risk factors such as smoking, hypertension, and dyslipoproteinemia can hardly explain a retinopathy of such severity.

Furthermore, the occurrence of retinopathy in our patient was unexpected because of excellent metabolic control during the preceding 3 yr (mean value of HbA1c 7.4%) and all previous annual ophthalmologic examinations had revealed no sign of retinal alteration, except the known congenital chorioretinic scars. Because HbA1c values were determined every 3 months, missed short-time deterioration of metabolic control was unlikely.

Although leukemia was shown to be responsible for rapid progression of a pre-existing diabetic retinopathy, there has been no evidence in the literature that leukemia per se can cause onset of diabetic retinopathy.

Fig. 1. Macular edema and retinal hemorrhages at the time of diagnosis. Photographs of fundus and fluorescein angiographies are shown before (A) and eight months after start (B) of CML-therapy. Macular edema (asterisk) involving the fovea, bleedings throughout the retina (small arrows) and venous dilation (dotted arrows) were observed in both eyes at the time of diagnosis (A). Eight months later these changes have completely resolved. Persistent old chorioretinic scars are depicted in the left eye (large arrow).
in a well-controlled type 1 diabetic patient. Given the temporal coincidence of onset as well as resolution of the retinopathy with the diagnosis and the clinical course of CML, it appears likely that retinopathy was triggered only by the latter in our patient. A ‘fundus leukemicus’ consisting of unspecific ocular manifestations similar to those of non-proliferative diabetic retinopathy can appear as the first sign of CML in the absence of severe symptoms of systemic hematologic disease and was reported in 50% of patients with acute and CML (13, 14). Since leukemic retinopathy is rarely associated with ocular symptoms and since it is observed more commonly in adults than in children and in acute than in chronic forms of leukemia, little is known about its prevalence in adolescents with CML (15, 16).

The prompt resolution of the retinopathy supports the concept that the CML played a major role in the onset of the eye problem. A direct influence on endothelial cells of the antiproliferative drug imatinib (Gleevec®) via the inhibition of vascular endothelial growth factor secretion is possible (17). Besides diabetes and leukemia the differential diagnosis of retinopathy with retinal hemorrhages and venous dilation includes central retinal vein occlusion and hypertension. However, our patient did not suffer from hypertension and fluorescein angiography showed no evidence for venous occlusion.

In conclusion, in children and adolescents with well-controlled type 1 diabetes and unexpected retinopathy, diabetes should not be considered as the only possible cause of the eye disease and the presence of other causes such as hematono-logical disorders should be sought.

References