PROLIFERATIVE RETINOPATHY IN PATIENTS WITH TYPE 1 DIABETES OF LESS THAN 5 YEARS’ DURATION

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SUMMARY - The position statement about diabetic retinopathy postulates that at least 3-5 years of duration of diabetes are needed for the retinopathy to occur, and initial retinal examination should be performed within 3-5 years after the initial diagnosis. We report here the case of a 18 year-old type 1 diabetic woman with a proliferative retinopathy discovered 2 years after the onset of a clinical diabetes. The hypothesis of a Latent Autoimmun Diabetes in Adults (LADA) could not be excluded and we propose, particularly in this context, to detect a diabetic retinopathy at the onset of diabetes.

Key-words: diabetes, retinopathy, LADA.

RÉSUMÉ - Rétinopathie proliférative chez des patients diabétiques de type 1 dont le diabète a été découvert il y a moins de 5 ans : à propos d’un nouveau cas.
Les recommandations actuelles de prise en charge, de suivi et de surveillance des complications chez les diabétiques de type 1 soulignent qu’il est indispensable d’effectuer un fond d’œil dans les 3 à 5 ans qui suivent la découverte d’un diabète. Il est en effet classique de postuler qu’une rétinopathie ne survient pas avant ce délai. Nous rapportons ici le cas d’une jeune femme âgée de 18 ans au moment de la découverte d’un diabète de type 1, à l’occasion d’un syndrome polyuripolydipsique et d’infections cutanées récidivantes. Deux ans après sa découverte, le fond d’œil puis l’angiographie à la fluorescéine mettaient en évidence une rétinopathie proliférative pour laquelle des séances de laser ont été pratiquées. L’hypothèse d’un diabète de type 1 lent ne peut cependant être exclu compte tenu du mode de révélation de son diabète. Nous proposons, en particulier dans ce dernier contexte, de recommander d’effectuer un fond d’œil dès la découverte du diabète et non à partir des 3 à 5 premières années d’évolution.

Mots-clés : diabète, rétinopathie, diabète de type 1 lent.

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Retinopathy is a major complication of type 1 diabetes mellitus and a leading cause of visual impairment and blindness [1]. Approximately 25% of type 1 diabetic patients have retinopathy after 5 years, increasing to 60 and 80% after 10 and 15 years, respectively, and proliferative diabetic retinopathy is present in about 25% of type 1 patients with diabetes of 15 years’ duration [2]. Even if a slight reduction in the incidence of blindness has been recently observed, diabetic retinopathy remains a great public health problem [3].

A strong independent association between the glycemic control and the progression of retinopathy is reported, whereas intensive therapy to reduce hyperglycemia significantly slows its progression [4-6]. The French recommendations postulate that a retinopathy should be looked for at the onset of diabetes [7], but the 2000 American Diabetes Association position statement on diabetic retinopathy only indicates that an initial retinal examination should be performed within 3-5 years after the initial diagnosis [8]. They argue that the prevalence of retinopathy is directly related to the duration of diabetes and initial reports suggest that the prevalence of retinopathy is low during the first 5 years duration of type 1 diabetes [8, 9].

However, the WESDR study already revealed that 49% with type 1 diabetic patients of ≤4 years’ duration had retinopathy [10]. Recently, Malone et al. confirmed on a larger cohort that the beginning of the retinopathy could occur earlier than previously reported [11]. Among 1,613 patients from the DCCT cohort with type 1 diabetes of <5 years duration and undergoing retinal photographs, 1,083 (67.1%) had retinopathy. 874/1,613 (54.2%) had retinopathy at baseline: 716 (44.4%) were detected on stereoscopic colour photographs, DCCT follow-up identified 341 additional individuals in whom retinopathy was developing before 5 years, and 26 patients had retinopathy detected on fluorescein study alone. 158 cases were revealed only by fluorescein angiography, a more sensitive method to detect retinopathy. Retinopathy was observed in 19.4% and 48.4% of the patients with diabetes of 1 year and 4-5 years duration, respectively. Those with early retinopathy (<5 years duration) had progressed faster than those without retinopathy after 4 years duration of diabetes [11].

482/1,613 (29%) had only microaneurysms at entry and 6 patients had preproliferative or worse pathology. Unfortunately, neither the clinical characteristics nor the evolution of this last group were given [11].

We report here the case of an 18 years old patient whose diabetes was discovered in August 1998 because of recurrent cutaneous furuncles in spite of adequate antibiotherapy. Two fasting glycemias were 17.6 and 16.5 mM. Retrospective analysis suggested that a polyuria had occurred for 10 months but without weight loss. No ketoacidosis was noted at the onset and she had neither other illness nor medication or contraceptive pills. Puberty began when she was 11 years old. She smoked about 2 cigarettes a day. Clinical examination revealed a BMI of 21.1 kg/m², a normal blood pressure: 110/60 mmHg and nothing else. Probably because she was young, 4 injections of insulin a day were immediately prescribed and preferred to other drugs. Since the beginning of this treatment, weight was unchanged but insulin doses were still high, about 0.84 U/kg-day⁻¹, suggesting that she really needed insulin treatment. In 2001, serum C-peptide concentration was 0.7 ng/ml in the fasting state and 3.3 ng/ml after a standard meal (Clinutren Iso: 6 ml/kg, maximum 360 ml; Nestle Clinical Nutrition, Brussels, Belgium) (normal fasting values: 1.5-3.5 ng/ml by RIA). The HbA1c measured at the onset of the diabetes was 15.2%, decreased 6 months later and remained stable thereafter, around 7.7% (normal values < 5.6). In April 1999, she complained for the first time of visual impairment and the first fundus ophthalmoscopy performed revealed a proliferative retinopathy, which was confirmed by a fluorescein angiography (Fig. 1). Laser treatment was required and led to the stabilisation of the lesions assessed by fluorescein angiographies, without a worsening progression after 2 years of follow-up. No other complication related to diabetes was found, and urinary albumin excretion remained normal.

The diagnosis of a slowly progressive autoimmune diabetes, also referred to as latent autoimmune diabetes in adults (LADA) could not be excluded. The prevalence of LADA varied widely, depending on the markers chosen to define the characteristics of the patients: from 10% in non-insulin requiring diabetes to 20% in all new diabetes, with ICA and GAD antibodies [12]. In the reported case, polyuria occurred about 1 year before the biological diagnosis, no ketoadipososis occurred at the onset, suggesting a progressive disease. Unfortunately, neither urinary nor blood analysis was performed earlier than 1997 at school. However, both Antibodies to Islet Cell cytoplasmic antigens (ICAs) and to Glutamic Acid Decarboxylase (GADA) were negative, and HLA type was DR13[6]-DR7. No other stigma of autoimmunity was found, e.g. clinical hypothyroidism and thyroperoxidase antibodies were negative. Maternally inherited diabetes associated to 3243A>G transition in the mitochondrial rRNA (U12) was excluded by genetic characterization. As her grandfather probably had type 2 diabetes and because of the early onset of diabetes in this patient, genes encoding glucokinase and hepatocyte nuclear factor-1α associated with the most prevalent forms of maturity-onset diabetes of the young (MODY) were studied. No mutation was identified into these two MODY genes.

This case report indicates again that a severe form of diabetic retinopathy can occur at the onset of type 1 diabetes. Mechanisms underlying the occurrence of
proliferative retinopathy are unknown, but plausible hypothesis such a possible deleterious effect of the puberty and of a growth hormone secretion [13], or an incapacity to evaluate the real duration of diabetes in patients with LADA could be suggested. A rapid lowering of blood glucose may also contribute to progression of retinopathy, but generally, it was commonly accounted for by the appearance of soft exudates, microvascular abnormalities or both [14, 15]. In the Kroc Collaborative study group, the group whose retinopathy worsened received continuous subcutaneous insulin infusion, and standardized glycated hemoglobin levels fell by two months from 10.3 ± 0.4% to 8.2 ± 0.2%. In this study, 1/11 cases with moderate non proliferative retinopathy progressed to a proliferative one and 0/4 cases with severe non proliferative and proliferative retinopathies worsened during 8 months of follow-up [16].

Anyway, the diabetic retinopathy is rarely at a proliferative stage at the onset of diabetes and generally remained mild [11]. We reported in a prospective follow-up study in 40 patients with type 1 diabetes of childhood onset that no retinopathy appeared before 5 years duration of diabetes, except in 1 patient with 4 years of duration of diabetes who had microaneurysms only. No retinopathy appeared before the age of 15 years [17].

Complications related to diabetes in patients with LADA are not well known, but a lower prevalence of retinopathy in patients with LADA after about 12 years of duration is reported, when compared with that in type 1 diabetic subjects (respectively 51% versus 76%, included 9% versus 21% with severe retinopathy) [18].

This case report suggests that a dilated eye examination should be performed at the onset of type 1 diabetes, and especially in patients with LADA, whose duration of diabetes is unknown. This study also pointed out the necessity to screen for diabetic retinopathy before each optimization of glycemic control.

REFERENCES


