Original Article

Diabetic retinopathy in acromegaly

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ABSTRACT

Introduction: Although growth hormone (GH) has been implicated in the pathogenesis of diabetic retinopathy (DR), DR is deemed to be rare in patients with GH excess. Our aim was to study its prevalence in subjects with acromegaly suffering from diabetes mellitus (DM), to analyze its characteristics, and to look for predictive factors such as age at diagnosis, GH concentration and duration, DM duration, DM control, and family background. **Materials and Methods:** Forty patients with acromegaly and DM (21 males, 19 females), median age = 50 years, underwent a systematic ophthalmological examination with dilated funduscopy to seek diabetic retinopathy. **Results:** Among this population, 05 (12.5%) had DR. It was at an early stage or background retinopathy in 3 cases and at a more advanced stage or proliferative retinopathy in 2 cases. We did not find any correlation with age at diagnosis, GH levels and duration, DM duration and family history of DM, but poor glycemic control seems to play a role although statistical analysis showed borderline significance. **Conclusion:** From this study, we conclude that prevalence of DR in patients with acromegaly is 12.5%, and it is slight or moderate. Among studied factors, only poor glycemic control seems to be implicated in its development.

Key words: Acromegaly, diabetic retinopathy, growth hormone excess, growth factors, predictive factors

Introduction

Growth hormone (GH) and insulin-like growth factor I (IGF I) have long been incriminated in the development of diabetic retinopathy.[1-3] In acromegaly, diabetes mellitus (DM) is the most frequent metabolic complication after high blood pressure.[4-6] But, as acromegaly is a relatively rare affection, the frequency and severity of diabetic retinopathy (DR) in patients with acromegaly are diversely appreciated. The aim of our study was to analyze DR frequency in subjects with growth hormone excess suffering from DM, to assess its severity, and to look for predictive factors such as: Age at diagnosis, DM duration, glycemic control, acromegaly duration, family history of DM, and growth hormone concentrations.

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Materials and Methods

In this work, we have retrospectively studied 40 patients with acromegaly and diabetes mellitus. Twenty-one were males, and 19 were females. Their median age was 50.73 ± 13.3 years. Their growth hormone excess was secondary to somatotroph adenomas in all cases. Diabetes mellitus diagnosis was based on WHO criteria [two or more fasting glycemias ≥1.26 g/l and or glycemia 2 hours after glucose intake (75 g) ≥2 g/l, or people already treated for DM]. Acromegaly median duration was 8.62 years, and diabetes mellitus was diagnosed 6.61 years before acromegaly diagnosis. All patients underwent dilated funduscopy by an experienced ophthalmologist. Glycemic control was assessed by self-monitoring blood glucose and glycated hemoglobin.

To analyze predictive factors, we have separated our population in two groups: Group 1 with diabetic retinopathy (n = 5) and group 2 without DR (n = 35). Then we compared family background, age at diagnosis, DM duration, glycemic control, acromegaly duration, and growth hormone levels.

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For statistical analysis, we used Fisher, Student, and Chi 2 tests. The difference was considered as significant if $P < 0.05$

Results

Among this population, we observed 5 patients with DR (12.5%). Diabetic retinopathy was at an early stage (background retinopathy) in 3 cases and at a more advanced stage (proliferative retinopathy) in 2 cases. We did not find any diabetic cataract.

On statistical analysis, there were no correlations between prevalence of retinopathy and familial background of diabetes mellitus or age at diagnosis (44.6 ± 15.1 years in patients with retinopathy versus 51.3 ± 13.1 years in patients without retinopathy). We did not find any difference in GH concentrations between patients with retinopathy (56.8 ± 42.9 ng/ml) and those without retinopathy (65.2 ± 70.5). Glycemic control was worse in patients with acromegaly who exhibit DR than in patients without DR. Poor control was observed in all patients with DR (100%) vs. 50% for those without DR, but the difference is of the borderline significance ($P = 0.051$).

Discussion

Diabetic retinopathy is a classical micro vascular complication in primary diabetes mellitus. Its mechanism is still debated, but genetic predisposition, local action of numerous growth factors, and hypoxic phenomenon seem to play an important role in the development of diabetic retinopathy in general.

For secondary diabetes mellitus, due to some endocrinopathies such as hyperthyroidism, pheochromocytoma, Cushing's syndrome, and acromegaly, little is known about eye vascular damage.

For acromegaly, GH excess has been implicated in diabetic eye and kidney damage for a long time. The role of GH/IGF I excess on the eye damage was first reported by Poulsen in 1953. This author demonstrated that hypophysectomy leads to a decrease in severity of retinopathy.[7] Consequently, the GH/IGF I axis was extensively studied. Although reports were contradictory,[8,9] most authors think diabetic retinopathy is rare and discrete in acromegaly, and it is due to an increase in local growth factors such as insulin growth hormone (IGF1) and vascular endothelial growth factor (VEGF) that act via autocrine and paracrine actions.[10] This theory is supported by the fact that DR is not correlated to GH and IGF1 plasma concentrations.

In acromegaly, DR frequency varies from 2.9%[11] to 30%.[12] Our frequency is higher than Ballentin's who analyzed diabetic and non-diabetic populations[13] and lower than Amameya's[12] who studied only 10 diabetic subjects with growth hormone excess.

As we observed it, DR in acromegaly is described as slight or moderate,[12] but severe ones, although uncommon, are also reported in anecdotic cases.[14-16] According to some authors, severe forms are rather due to a very long standing of diabetes disease, advanced age, eye refractive errors, or to genetic disorders as in primary diabetes mellitus.[12]

For predictive factors**,** as Amemya,[12] we didn't find any correlation between DR, family history of diabetes mellitus, GH levels, and acromegaly duration. But, poor glycemic control seems to play a role, although statistical analysis pleads for a borderline significance. However, some authors who did not demonstrate poor glycemic control think retinopathy in acromegaly is rather related to genetic predisposition as DR is more frequent in patients with a family history of diabetes mellitus. One can also think that micro-angiopathy in acromegaly maybe a result of repetitive vascular thrombosis that looks like diabetic retinopathy at early stage. This theory is supported by the fact that in acromegaly, DM is mostly due to insulin resistance.

The inconsistency in studies linking diabetic retinopathy to GH/IGF I axis may be due to the fact that in uncontrolled primary or secondary diabetes mellitus, local production of IGF I and other growth factors in ocular tissues may be responsible of diabetic retinopathy.[17,18] So, many authors insist on the pivotal role of local growth factors rather than systemic factors induced by sustained hyper glycemia to explain the lack of diabetic cataract and the rarity of diabetic retinopathy in patients with GH excess.

Conclusion

In this study that analyzes 40 diabetic patients with acromegaly, the prevalence of diabetic retinopathy is 12.5%. DR in acromegaly is mild or discrete, and is not associated to diabetic cataract. Our results agree with previous reports based on small series, but some severe or very severe retinopathies have been reported in anecdotic cases. Among predictive factors, only a poor glycemic control seems to play a role in its development, although statistical analysis pleads for a borderline significance.

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