Pre-diagnosis hemoglobin decline is an unbiased signal for hyperprolactinemia onset in male patients with prolactinoma

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Introduction

Men harboring prolactinoma frequently suffer from central hypogonadism and secondary anemia. We hypothesized that a decrease in hemoglobin (HB) levels prior to prolactinoma diagnosis, in otherwise healthy male patients with prolactinoma, may signal the appearance of hyperprolactinemia and estimate disease duration.

Methods

- Single-center retrospective cohort study.
- We evaluated the pre-diagnosis HB curves (HB measurements over time) of 70 male patients with prolactinoma.
- The HB curve was regarded "informative" if the patient had 2 previous normal ("baseline") HB measurements that were at least 1.0 g/dL above the HB measured later, at diagnosis.
- Patient's demographic, clinical and biochemical parameters, sellar MRI and visual fields were obtained.

Results (1)

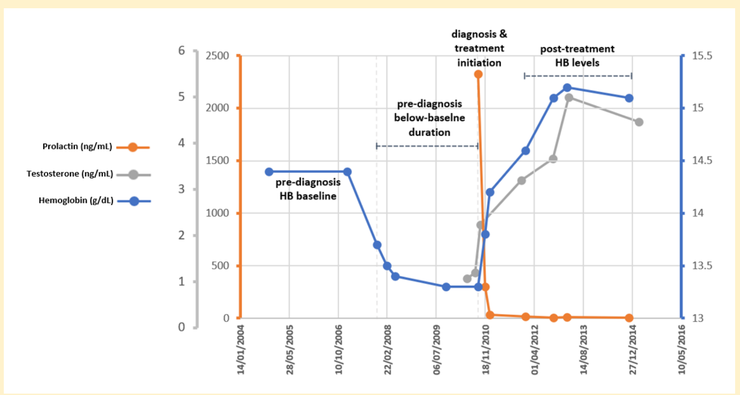
Out of 70 patients, 61 men (87%) presented with hypogonadism, and 40 men (57%) had HB levels lower than 13.5 g/dL at diagnosis.

We identified 25 male patients with "informative" HB curves (median follow-up of 14.0 years). These 25 men (age, 46.1±14.9 years) presented with median prolactin of 952 ng/ml (IQR, 374-2612 ng/mL), mean total testosterone levels of 1.3±0.8 ng/mL, and adenoma diameter of 23.8±10.3 mm.

Table 1. Patients' characteristics at prolactinoma diagnosis.

Variable	Cohort
N	25
Age at diagnosis (years), mean (SD)	46.1 (14.9)
Prolactin (ng/ml), median (IQR)	952 (374-2612)
Adenoma maximal diameter (mm), mean (SD)	23.8 (10.3)
Testosterone (ng/ml), mean (SD)	1.3 (0.8)
Luteinizing hormone (mIU/ml), mean (SD)[a]	1.9 (1.8)
Follicle-stimulating hormone (mIU/ml), mean (SD)[a]	3.4 (3.7)
Hemoglobin (g/dL), mean (SD)	12.9 (0.5)
Sexual dysfunction, n (%)	17 (68%)
Headaches, n (%)	8 (32%)

Figure 1. Example of an "informative" hemoglobin curve.



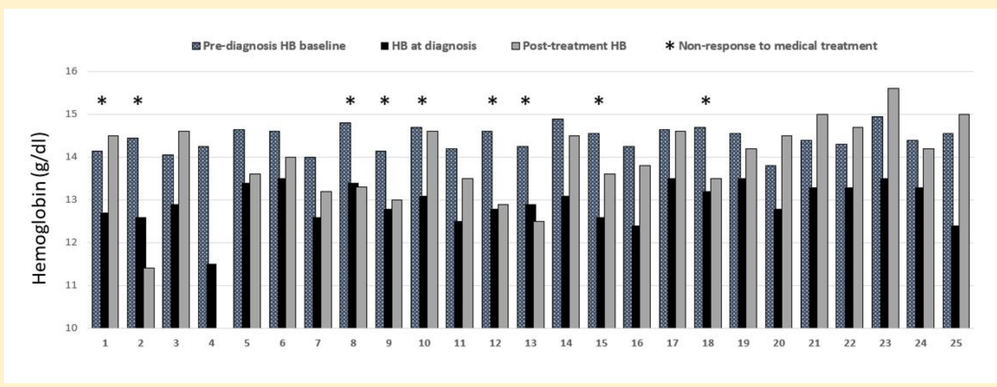
Results (2)

The median "below HB baseline" duration (from the first below-baseline HB measurement to hyperprolactinemia diagnosis) was 6.3±3.9 years.

The mean HB decrement from pre-diagnosis baseline (14.4±0.3 g/dL) to diagnosis nadir (12.9±0.5 g/dL) was 1.5±0.5 g/dL.

We discovered a correlation between "below HB baseline" duration and patient-reported sexual dysfunction duration (n=17, Pearson's R=0.502, p=0.04, Figure 5). "Below-baseline" duration was significantly longer than sexual dysfunction duration (7.0±4.5 vs 2.9±2.5 years, p=0.01), with a mean difference of 4.1 years.

Figure 2. Pre-diagnosis, at diagnosis, and post-treatment HB levels in all 25 men.



Conclusions

- Over 50% of male patients with macroprolactinoma exhibit anemia at diagnosis.
- In our cohort of otherwise healthy men with prolactinoma and hypogonadism, we found a marked decrease in HB levels that preceded prolactinoma diagnosis by a median of 6.3 years.
- We found that pre-diagnosis low HB duration correlated well with patient-reported sexual dysfunction duration, and yet, a mean delay of 4.1 years between HB decrease and symptoms appearance was demonstrated.
- These results support our hypothesis that pre-diagnosis low HB duration may serve as a more accurate marker for disease duration in a subset of hypogonadal men harboring prolactinoma.

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