Severe Sight-Threatening Orbitopathy Is a Very Rare Event in the Natural History of Graves’ Disease

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SUMMARY

Background
Graves orbitopathy (GO) is a worrisome condition with an unpredictable evolution. The results of currently available medical treatments (e.g., glucocorticoids and x-ray treatment) are rather disappointing, and immunotherapy is still experimental. Some endocrinologists have a dramatic experience with the occasional patient affected by the most severe form of GO, but few endocrinologists working in a primary care center have clear-cut information about the true incidence of this dreaded complication. Indeed, only a few studies have addressed this question. The present article is a valuable addition to the available data.

Methods
From 2002 to 2010, the study enrolled 346 newly diagnosed patients with Graves’ disease who presented to one clinic. At the time of diagnosis, 255 patients were free of GO, 70 had mild and inactive GO, 20 had moderate or severe eye disease, and 1 had sight-threatening GO. Of these 255 patients, 18 were lost to follow up and 237 were treated with methimazole alone. In 39 patients, the treatment could be stopped before 18 months, while it had to be continued for 18 months in 198. Ocular involvement was assessed according to the guidelines of the European Group on Graves’ Orbitopathy at 6, 12, and 18 months. At this time, some patients were already off methimazole.

Results
The patients were mainly women ages 18 to 84 years; 35% were smokers; 194 of the 237 patients treated with methimazole initially had no GO and 43 had mild GO. The majority of patients without initial GO remained disease-free (169 of 194 [87%]). In 20 patients (10%) mild disease developed, and only five (2.6%) presented with moderate to severe GO at the end of the study. This included soft-tissue changes and intermittent diplopia (clinical score 3 of 7) (1). One patient progressed to severe sight-threatening disease.

Among the 43 patients who initially had mild GO, 58% were free of GO after 18 months while 39% had still some mild but inactive form of GO.

Serum TSH receptor antibodies decreased in most cases but less so in those with active GO. Among the patients with initially mild GO, TSH receptor antibodies decreased more markedly in those who recovered from eye signs than in those with persistent GO. Yet the cohort was too small to identify significant differences. However, there was a significant association of the TSH-receptor antibodies between moderate to severe GO and smoking.

Conclusions
In a primary care environment, most patients presenting with Graves’ disease have no signs of orbitopathy initially. The present study indicates that continued on next page
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the overwhelming majority of these patients (i.e., 81%) will never have GO; in only one patient did the orbitopathy evolve into severe sight-threatening disease. In addition, in 58 patients with mild initial GO, all signs of eye disease disappeared during the 18 months of observation. Therefore, in Graves’ disease with minimal or no GO, the risk of evolution toward moderate to severe GO during methimazole therapy is minimal.

ANALYSIS AND COMMENTARY

These results are reassuring and corroborate the personal experience of most endocrinologists. The cohort of patients studied here initially included 70 individuals with mild GO. These patients need special follow-up since the eyes signs became worse during the treatment in 5 of them. These 5 patients represent, however, 25% of the 20 patients in whom mild GO was still present at the end of treatment. Since we lack reliable prognostic parameters for identifying cases of GO that may progress independently of hyperthyroidism, careful monitoring is indicated (2). Unfortunately, GO can appear many years after Graves’ hyperthyroidism has been cured. Also, there is ongoing debate concerning whether 131I treatment (with or without glucocorticoids) is associated with a worsening prognosis of GO. This problem is not discussed in the article.

References
