Endocrinology Sample Case

Hyperthyroidism and Graves disease (thyrotoxicosis) causing exophthalmos (bulging eyes), and treatment.

Before I discuss the specific facts of this case, let me discuss the function of the thyroid gland and its hormones. The thyroid gland, sitting at the uppermost part of the trachea (windpipe), produces two hormones: T3 and T4. T3 is very active in regulating the body's burning of calories and the normal function of all the cells of the body. T4 also serves in that same manner, but is less active. However, it is converted into T3 in the cells, to meet the demands of the body.

The pituitary (master) gland in the brain measures the blood level of those hormones. When their level decreases, it produces thyroid-stimulating hormone (TSH), to increase the hormone output of the thyroid gland. Likewise, when the blood thyroid hormone (T3 and T4) levels rise too high, there is very little TSH produced. TSH is a very sensitive measure of thyroid gland hormone blood levels.

When the thyroid gland is overactive and does not respond to a reduction of TSH, it is called hyperthyroidism. When it is symptomatic, it is called thyrotoxicosis (Graves' disease). One of its consequences can be a bulging of the eyes, even beyond the point where the normal closure of the eyelids during sleep do not meet, and the cornea (clear outer "lens," or window into the eye), can dry out and develop an ulcer.

When the patient is symptomatic, the usual initial therapy is with a drug such as Tapazole, to decrease the thyroid hormone production. This sometimes results in a permanent remission (cure) of their Graves' disease. Also, a "beta blocker" drug such as Inderal (propranolol) can be used to control the symptoms (physiological effects) of the excess thyroid hormone in their body.
Often this is not successful and definitive therapy is required, which can either be from surgery, to remove 75-85 percent of the gland, or radioactive iodine. Surgery, which has immediate results, may or may not remove enough of the gland, and has risks of permanent hoarseness from damage to one of the two small nerves (recurrent laryngeal nerves) that sit adjacent to the thyroid gland. It can also cause permanent tetany (painful diffuse muscle spasms) from damage to the three to five tiny parathyroid glands that lie on or within the thyroid gland's surface layer.

Radioactive iodine, which takes months to have its full effects, is selectively absorbed by the thyroid gland and destroys those functioning cells that make the T3 and T4 hormone. However, it will turn an overactive gland into an underactive (hypothyroid) gland in almost all cases. Therefore, it is critical to monitor the thyroid function tests (T3, T4, and TSH levels) and to add thyroid in pill form. This is either dried out (desiccated) animal thyroid, or synthetic thyroid (Synthroid or Levoxyl).

In most cases, those patients who develop bulging of their eyes (exophthalmos), eye muscle spasm and pain secondary to their Graves' disease, will have either some improvement or no further progression once their disease has been successfully treated. But a small percentage of patients may actually develop the condition during or shortly after their Graves' disease has been resolved (based on thyroid function tests). Graves' disease is an auto-immune condition, where the body will react against its own flesh, just like rheumatoid arthritis is an auto-immune disease against its own joints, and fibromyalgia is the body's reaction against its connective tissue and muscles. Sometimes x-ray therapy directed at their eyes may be needed to treat that bulging eye and eye muscle spasm condition.

In the case of this patient, she had a very strong family history of rheumatoid arthritis (mother and two siblings) and she had a positive blood test for this disease. She responded to therapy for rheumatoid arthritis.

She also had a mass in her chest, found on a chest x-ray and CT scan, which required surgery. She also had findings of fibromyalgia (connective tissue disease causing fatigue and muscle pain), consistent with her chest mass (thymoma: a benign thymus gland tumor) and her Graves' disease.

I will outline the facts in her case as they evolved sequentially, and make comments as appropriate:

On 12/31/96 she had normal thyroid blood tests. The normal (reference) range will be in T3 27 (22-35), T4 6.8 (4.5-12.5), TSH 2.3 (0.4-5.5). They vary slightly from laboratory
to laboratory, and I will not repeat these ranges unless they used a different type of test with a major difference in "normal."

On 1/3/97 the cardiologist Dr. #1 evaluated her with a stress treadmill test and echocardiogram (sound-like study of her heart), and concluded that her fatigue was secondary to "deconditioning and depression."

On 10/16/97 a CT scan of her chest confirmed the presence of the thymus gland tumor (thymoma).

On 10/24/97 neurologist Dr. #2 diagnosed her as having "myopathy (muscle disease and pain) symptoms in presence of rheumatoid arthritis and thymoma."

10/27/97: T3 37 (high), T4 13.2 (high). 11/3/97: TSH less than 0.1 (very low). Also, the thyroglobulin antibody test level was high at 10.6 (normal less than 1.0). All of these are consistent with Graves' disease. On 11/3/97 she had a thyroid radioactive uptake scan (not therapy), and this was also high at 53% in 24 hours (5-35%). All this confirmed her overactive thyroid gland (hyperthyroidism) condition.

On 11/14/97 she came under the care of Dr. #3, an Endocrinologist. Her pulse was very elevated to 130 and she had "no sign of exophthalmos." Dr. #3 ordered laboratory tests: The thyroid autoantibodies were high at 9.9 (less than 1.0), T3 314 (60-181), T4 2.7 (high), and TSH less than 0.005 (very low). All this confirmed the diagnosis he made of Graves' disease. On 12/5/97 her pulse was moderately elevated to 96 and he started her on the antithyroid drug Tapazole and the beta blocker Inderal (propranolol) to help control her symptoms. All this is good, standard care.

On 12/15/97 her T4 was normal at 2.3. On 12/17 and 12/31 her pulse was normal at 80. On 1/8/98 her T4 was again normal at 1.5. He concluded it was safe for her to go ahead with her chest surgery for the thymoma tumor.

Her chest surgery took place on 1/29/98. The tumor was large (weighed 66 grams), and because it partially surrounded the left phrenic nerve (that controls the left half of the diaphragm, or breathing muscle), it had to be cut in order to remove the whole tumor without cutting into it. If it had been malignant (cancer), cutting into this tumor would have decreased her chance for a cure. Fortunately, after it was removed, the pathologist noted that it was benign (not cancer), and had an unusual pattern of cells: "Follicular B-cell hyperplasia associated with Graves' disease and auto-immune connective tissue disorders," (fibromyalgia and rheumatoid arthritis, both of which she also had). Because the left phrenic nerve had to be cut, she may experience some increased shortness of breath, with part of that "bellows" (muscle) non-functional.
On 3/2/98 the T4 0.8 and TSH 4.3 tests were normal. On 4/7/98: T4 1.01 (normal), and TSH - 0.13 (low). On 4/15 her pulse was 88.

On 5/5/98: T4 0.39 (low) and TSH 31.5 (high), caused by the Tapazole blocking thyroid hormone production. However, she developed a severe rash and Dr. #3 properly discontinued both the Tapazole and Inderal drugs, and she received 12 mCi of radioactive iodine. This would destroy her thyroid gland.

Because she would no longer have a functioning thyroid gland, she was begun on Synthroid (synthetic T4) on 5/13/98 at 0.1 mg (milligrams) = 100 mcg (micrograms). On 5/27/98 her pulse was normal at 80 and she was receiving 0.1 mg of Synthroid.

On 6/9/98: T4 0.8, TSH 21 (high). The thyroid gland was not yet fully suppressed, because her pituitary gland did not sense enough thyroid hormone in her blood (from the Synthroid and any residual from her thyroid gland) to stop making its thyroid-stimulating hormone (TSH).

On 6/24/98 she complained that her eyes were bulging, she had fatigue, had arm and leg pains and muscle weakness.

On 7/21/98 her TSH was 0.519 (low normal).

On 7/31/98 her TSH was noted to be 0.519 and her pulse was 88 (high normal). She also had "very mild exophthalmos" and was taking 0.15 of Synthroid per day. This is proper therapy. She was referred to an ophthalmologist specializing in this problem. This is also good care.

Dr. #4 first saw her on 8/20/98. He noted she had thyroid eye disease and dry eye syndrome (also seen in some connective tissue diseases), and exposure keratopathy (from drying of her cornea). He prescribed proper medical therapy and she improved, but developed a progression of her thyroid eye disease. He recommended radiation (x-ray) therapy to her eyes to try to control that condition. Dr. #5, a radiation therapist at the Hospital #1, administered 2000 rads over 10 days, which was completed on 2/24/99. She had some improvement in her symptoms, according to his letter.

Referring back to her thyroid tests and therapy on 8/31/98: TSH 0.45 (0.4-4.0). This is ideal, based on her disease.

On 9/3/98 she was "feeling strange," had severe fatigue and was taking 0.15 mg of Synthroid.
On 9/10/98 Dr. #6, her primary care physician, noted, "On Synthroid 0.45 mg apparently and endocrinologist reports her level is doing well." I found no other records supporting that three-times-the-daily-dosage value. Are there any prescriptions for that 0.45 mg total per day dose? If so, by whom? Was she taking it on her own?

On 9/28/98 Dr. #6's record says, "rapid (heart) rate with regular rhythm." However, the nurse recorded a heart rate of only 68 on the office "Vital Signs Flow Sheet." She was wheezing and he treated her with an Albuterol nebulizer for "asthmatic bronchitis." That was proper care and it relieved her wheezing caused by spasm of the bronchial tubes in her lungs. It can also temporarily speed up her heart rate. On that day the laboratory T3 was normal at 32, the T4 was slightly high at 11.2 (4-11), and the TSH was low at 0.1.

On 10/2/98 an office note of Dr. #6's said that she finished her last refill of Synthroid 0.15 mg daily per Dr. #3, and she was not happy with Dr. #3, "who told patient current thyroid dosage too high; prescribed (Rx) Synthroid 0.10 but when at this lower dose in the past felt like it did her no good." Dr. #6 told her to decrease it to 0.125 mg.

On 10/1/98 Dr. #6 wanted to decrease the Synthroid to 0.1 (the TSH was 0.4), but Dr. #3 said to keep it at 0.15.

On 10/21/98 her Synthroid dosage was decreased to 0.1 mg (100 micrograms).

On 11/2/98 she had fatigue, probably secondary to fibromyalgia.

On 12/14/98 the TSH was 0.876 (0.35-5.5).

On 3/18/99: T3 = 34, T4 = 10.2, and TSH = 0.86 (all normal).

On 4/6/99 she twisted her body and developed a limp, probably from a pinched nerve.

On 6/15/99 her TSH was 0.77, and on 8/30/99 her TSH was 3.06 (all in the normal range).

It is generally recommended that the TSH level should be suppressed to below normal levels, to assure no failure of thyroid suppression, which could stimulate any residual thyroid tissues (flesh = cells), and cause the eye disease to worsen.

Based on the voluminous records I reviewed, mostly summarized above, it appears that she received very good care by her first Endocrinologist. After her radioactive iodine therapy, Dr. #3 attempted to suppress her TSH levels to the lower limit of normal, or just below normal, as he should have done. When her eye disease was symptomatic, he
referred her to an ophthalmology specialist in that condition. That physician gave her good eye care, and had to recommend the radiation therapy to her eyes to try to control her exophthalmos (bulging eyes) and the symptoms of pain and light sensitivity (photophobia) she was experiencing.

Unfortunately, she developed exophthalmos, which persisted, as noted in the enclosed photographs. Perhaps she would be recommended to see a physician specializing in plastic surgery of the eyes for his opinion on any potential operative therapy.

Her physical symptoms of incapacity (fatigue) are not related to her thyroid disease care, but as her doctors noted, probably related to fibromyalgia, deconditioning, and depression.

Based on all of the above, it appears that she wanted to have a higher dose of Synthroid than Dr. #3 prescribed. His dose was reasonable, based on the TSH blood levels and her diagnosis, as I noted. I do not find an "overdose" of Synthroid prescribed by her treating Physicians as the cause of her exophthalmos (bulging eyes).