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CASE STUDY

A CASE REPORT OF GRAVES' DISEASE IN LIBERIA AND SURGICAL INDICATION

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ABSTRACT

Graves' disease is an autoimmune disease that may consist of hyperthyroidism, goiter, eye disease (orbitopathy), and pretibial or localized myxedema. The presence of thyrotropin-receptor antibodies (TRAb) in serum and orbitopathy on clinical examination distinguishes the disorder from other causes of hyperthyroidism. However, the diagnosis may be obvious on presentation; a patient with new-onset ophthalmopathy, a large non-nodular thyroid, and moderate to severe hyperthyroidism has Graves' disease. Because there is no consensus as to the "best" treatment, the American Thyroid Association (ATA) guidelines emphasize the importance of fully discussing the options with patients and considering their values and preferences before deciding on a treatment plan. Patients who are intolerant of antithyroid drug therapy and radioiodine ablation or who have active Graves orbitopathy are surgical candidates. Most experts now agree that total or near-total thyroidectomy is considered the optimal procedure. To date, there is no published data available on Graves' disease in Liberia and the management options remain limited. Thereof, we present a 34-year-old Liberian female who underwent a near total thyroidectomy for Graves' disease at the Eternal Love Winning Africa (ELWA) Hospital Monrovia, Liberia.

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INTRODUCTION

Graves' disease is an autoimmune disease that may consist of hyperthyroidism, goiter, eye disease (orbitopathy), and occasionally a dermopathy referred to as pretibial or localized myxedema (Ross *et al*., 2016). Of the autoimmune diseases of the thyroid, Graves' disease is the predominantly documented in Africa (Ogbera *et al*., 2007). The overall incidence of autoimmune diseases of the thyroid in Tunisia is 9.9% and this was noted to have occurred in conjunction with 6.3% of other autoimmune diseases (Chabchoub *et al*., 2006). In Ethiopia, the prevalence of autoimmune thyroid disease is reported to be 1.2% (Mengistu, 1993) and reports from Libya indicate a prevalence rate of disease 3.7% (Elhamel *et al*., 1988). Approximately 3% of women and 0.5% of men develop Graves' disease during their lifetime (Nyström *et al*., 2013). The peak incidence of Graves' disease occurs among patients aged 30 to 60 years, but all ages are affected. Recent data suggest a possible increased incidence among young African Americans (McLeod *et al*., 2014). Like other parts of the world, Graves' disease is the most common cause of thyrotoxicosis in Nigeria (Ogbera *et al*., 2007). Hyperthyroidism is the most common feature of Graves' disease, affecting nearly all patients, and is caused by thyroid-stimulating hormone (TSH) thyrotropin-receptor antibodies (TRAb) that activate the receptor, thereby stimulating thyroid hormone synthesis and secretion as well as thyroid growth (causing a diffuse goiter) (Ross *et al*., 2016). The presence of thyrotropin-receptor antibodies in serum and orbitopathy on clinical examination distinguish the disorder from other causes of hyperthyroidism (Ross *et al*., 2016). Surgery was the first definitive treatment for Graves' disease, but with the development of antithyroid drugs and radioiodine ablation therapy in the 1940s and 1950s, surgery is now recommended by fewer than 1% of experts for the initial management of Graves' disease (Burch *et al*., 2012). However, recent data indicate that surgery has become the main definitive therapy

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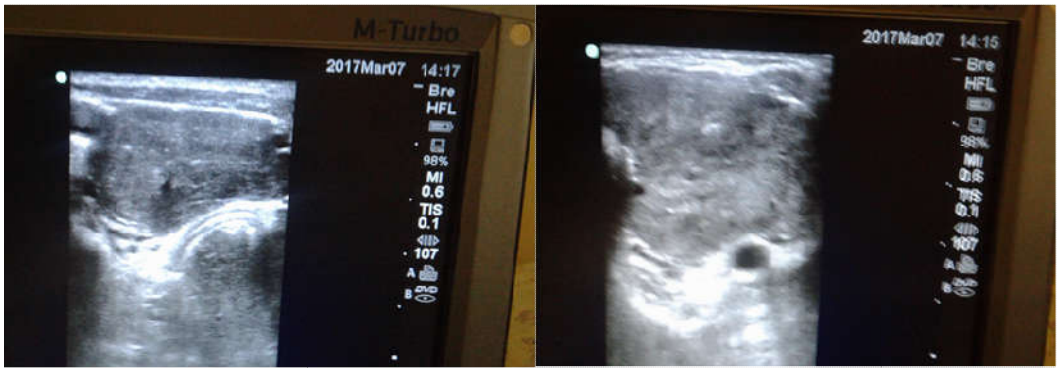
versus radioiodine therapy in some US centers, particularly among patients with low socioeconomic status (Elfenbein *et al*., 2015). To date, there is no published data available on Graves' disease in Liberia and the management options remain limited. Thereof, we present a 34-year-old Liberian female who underwent a near total thyroidectomy for Graves' disease at the Eternal Love Winning Africa (ELWA) Hospital Monrovia, Liberia.

Case Report

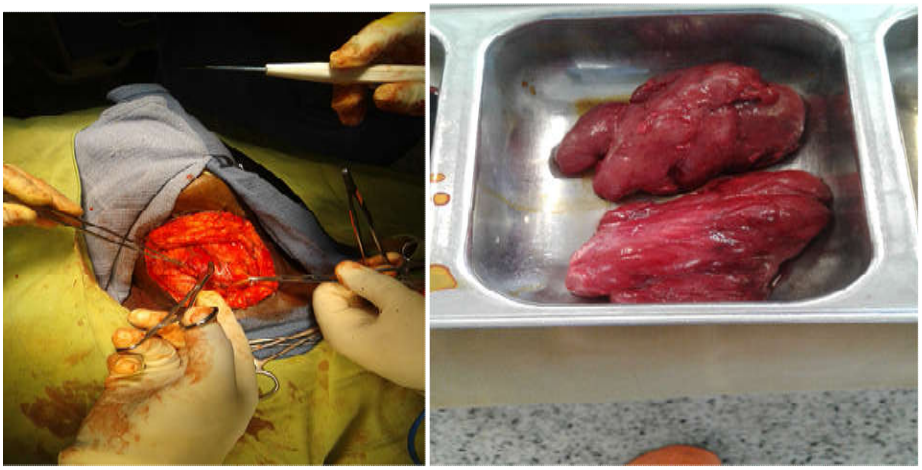
A 34-year-old Liberian female came through outpatient department of the Eternal Love Winning Africa (ELWA) Hospital in Monrovia March 6, 2017 with complaint of a gradual progression of a painless anterior neck swelling for a 2-year duration. Two months following the onset of the swelling, she experienced excessive sweating even at sedentary

Figure 1. (EKG –Borderline Left Ventricular Hypertrophy AVL, Lead I, III (tall R waves > 13mm)



A **B**

Figure 2. Sonogram of the Thyroid Gland Panel A is a sonogram of the right lobe measuring (10.5cm/8.1cm) with a homogenous echotexture. Panel B is asonogram of left lobe measuring (9.9cm/8.2cm)



A **B**

Figure 3. Intraoperative photos of a Near Total Thyroidectomy

Table 1. Hormonal Profile of Thyroid hormone at presentation and 8 week followup

Hormones	At presentation	At8-weekfollow-up	Reference range
T3	1.5ng/dl	1.1ng/dl	(0.79-1.58)
T4	<4.9ng/dl	5.5ng/dl	(4.9-11.0)
TSH	15.6uU/ml	4.1 uU/dl	(0.5-5)

Abbreviations- T3: Tri-iodothyronine, T4: Thyroxine, TSH: Thyroid Stimulating Hormone

moments. Her appetite had been consistently good but she had lost 3 Kilograms over 6 months. Her bowel habit increased from 1 to 3 motions of stool daily with normal intervals. She denied history of tremors or palpitations but she had some discomfort and redness of her eye from which her husband became nervous. She had 1 live birth, 1 still birth, last pregnancy 3 years before presentation with oligomenorrhea. She is a College graduate, unemployed with frequent dispute with her spouse over his alleged infidelity for the past 3 years before presentation. She was diagnosed a year earlier of Graves's Disease in Ghana and placed on Carbimazole 30mg daily and 40mg propanol daily but complained of malaise and fatigue despite medications. She had undergone a Fine Needle Aspiration Biopsy at the Jackson F.Doe Hospital in Tapeta, Liberia before visiting the ELWA Hospital with findings consistent with a Toxic Nodular Goiter. Physical examination revealed 58-kilogram female, not diaphoretic on presentation with bilateral exophthalmos and scleral injection. Her blood pressure was 140/80mmHganda pulse of 86 beats per minute, full volume and regular. She had a grade II soft non-radiating systolic murmur at the pulmonary area. She had a 10cm/8cm diffusely enlarged smooth goiter that was non-tender, soft with regular borders. It was non-pulsatile and without bruit. A provisional diagnosis of Diffuse Toxic Goiter, Graves' Disease was made. Investigation revealed that the patient was biochemically hypothyroid with elevated thyroid stimulating hormone and suppressed thyroxine hormone probably due to the Carbamizole. A thyrotropin-receptor antibodies (TRAb) was not available. The complete blood count, calcium, creatinine and liver function test were normal. The electrocardiogram (EKG) revealed left ventricular hypertrophy (Figure 1). Sonography of the neck showed a (10.5cm/8.1cm right lobe), (9.9cm/8.2 left lobe) and grade II Doppler flow (Figure 2).

Preoperatively, the Carbimazole was stopped and was assessed by the anesthetic team. She was classified as ASA- Class II based on the American Society of Anesthesiologists (ASA) Physical Status Classification System. An informed consent form for Surgery and Anesthesia was signed and the operating theater was prepared for complications of thyroid storm. Under general anesthesia endotracheal intubation, a Near Total Thyroidectomy was done with no intraoperative complication (Figure 3). She was extubated following close cardiopulmonary monitoring and kept in the recovery room until she recovered fully from anesthesia. Day 1 Postoperatively, there was no voice change nor hematoma but she developed transient hypocalcemia that resolved within 12 hours without medication. The patient was discharged home within 5 days on Levothyroxine at 1.6mcg/kg/day. She was subsequently followed through the outpatient department and her thyroid function test was normal after 8 weeks. Panel A on the right shows a near total thyroidectomy with separation of the strap muscles. Panel B shows the thyroid specimen that was removed.

DISCUSSION

The presence of thyrotropin-receptor antibodies (TRAb) in serum and orbitopathy on clinical examination distinguishes the disorder from other causes of hyperthyroidism (Ross *et al*., 2016). However, the diagnosis may be obvious on presentation; a patient with new-onset ophthalmopathy, a large non-nodular thyroid, and moderate to severe hyperthyroidism has Graves' disease (Barbesino and Tomer, 2013). Even though our patient could not get a thyrotropin-receptor antibodies (TRAb) assay due to financial reason, she presented with opthalmopathy, a large diffuse goiter and a history of hyperthyroidism which is clinically diagnostic of Graves' disease. She was biochemically hypothyroid on presentation which could have been most likely caused by the antithyroid medication (Carbimazole). There are three treatment options for Graves' disease: antithyroid drugs (thionamides), radioiodine, or surgery. All three options are effective, but all three options have significant side effects (http:// www.uptodate.com/contents/surgical-management-of-hyperthyroidism). Because there is no consensus as to the "best" treatment, the American Thyroid Association (ATA) guidelines emphasize the importance of fully discussing the options with patients and considering their values and preferences before deciding on a treatment plan (Ross *et al*., 2016; Ross, 2011). Liberia is a resource limited country with limited options available to manage Graves' Disease. The most effective approach in thesetting of a large goiter and orbitopathy will be surgery. Furthermore, recent data indicate that surgery has become the main definitive therapy versus radioiodine therapy in some US centers, particularly among patients with low socioeconomic status (Elfenbein *et al*., 2015). A prospective study in Ghana recommended bilateral sub-total thyroidectomy for Grave's disease (thyrotoxicosis) in patients managed with carbimazole and esmolol combination (Kuubiere *et al*., 2015). Hyperthyroidism in Graves' disease results from immunoglobulin that stimulate the TSHreceptoronthyrocytes (Bahn, 2012). Levels of these thyrotropin-receptor antibodies (TRAbs) correlate with disease activity and likely cause Graves orbitopathy by binding to TSH receptors in retro-orbital tissues (Bahn, 2012). Factorscontributing to the development of thyrotropin-receptor antibodies (TRAb) include Human Leukocyte Antigen (HLA type), the postpartum state, tobacco smoking, physical or emotional stress, and antigen release following thyroid injury such as radiation exposure (Burch *et al*., 2012).

Pretreatment Evaluation

Prior to initiating thionamides, obtaina baseline blood tests, including a complete blood count (white count with differential) and a liver profile (bilirubin and transaminases) (Ross *et al*., 2016). A beta blocker should be started (assuming there are no contraindications to its use) in most patients as soon as the diagnosis of hyperthyroidism is made, even before confirming that the cause of hyperthyroidism is Graves' disease (Tagami *et al*., 2012). Beta blockers ameliorate the symptoms of hyperthyroidism that are caused by increased beta-adrenergic tone (Geffner and Hershman, 1992). For patients with significant symptoms of hyperthyroidism, it is recommended to start a thionamide (in addition to beta blockers) to achieve euthyroidism relatively quickly, prior to more definitive therapy with radioiodine or surgery (http://www.uptodate.com/contents/surgical-management-of-hyperthyroidism). The goal of thionamide therapy in Graves' hyperthyroidism is to attain a euthyroid state within three to eight weeks. This can be followed by ablative therapy with radioiodine or surgery (http://www.uptodate.com/contents/ surgical-management-of-hyperthyroidism). Methimazole is the primary drug used to treat Graves' hyperthyroidism.In countries where methimazole is unavailable, carbimazole can be used (Geffner and Hershman, 1992; http://www.uptodate.com/ contents/surgical-management-of-hyperthyroidism).Treatment with iodine pre-operatively has been shown to reduce thyroid blood flow and blood loss during surgery.

Surgical Management

Surgery is an unpopular therapy for Graves' hyperthyroidism, being selected by only 1 percent of thyroid specialists (Burch *et al*., 2012), but is being used more frequently in patients with active orbitopathy (Elfenbein *et al*., 2015). Indications for surgery include very large goiters with compressive symptoms, concomitant suspicious thyroid nodules, concurrent hyperparathyroidism requiring surgery, and patient preference (Bahn Chair *et al*., 2011). Women with Graves' disease who plan to become pregnant within the next 6 months sometimes select thyroidectomy rather thanradioiodine ablation because of theoreticalconcerns related to radiation exposure prior to pregnancy and the known sustained increases in TRAb titers after radioiodineablation, which could increase the risk of neonatal thyroid dysfunction. Patients who are intolerant of antithyroid drug therapy and do not wish to be treated with RAI or who have active Graves orbitopathy are surgical candidates (http://www.uptodate.com/contents/surgical-management-of-hyperthyroidism). Most experts now agree that total or near-total thyroidectomy is considered the optimal procedure (Ross *et al*., 2016). For patients with Graves' disease who undergo near-total or total thyroidectomy, thyroid hormone should be initiated prior to discharge in a euthyroid patient, and serum TSH should be measured six to eight weeks later to adjust the dose to maintain the TSH in the normal reference range (http://www.uptodate.com/contents/surgical-management-of-hyperthyroidism). In a randomized trial of subtotal versus total thyroidectomy for Graves' disease involving 191 patients followed over five years, recurrent hyperthyroidism occurred in 4.7 percent of patients after subtotal versus none after total thyroidectomy, while transient hypoparathyroidism was seen in 6.8 and 12.6 percent, respectively, and permanent hypoparathyroidism in none and 0.5 percent, respectively (Barczyński *et al*., 2012). The complications of surgery in children are like those in adults, and mortality is very rare. Transient hypocalcemia occurs in approximately 10 percent of patients and permanent hypoparathyroidism in 2 percent. Injury to the recurrent laryngeal nerve occurs in approximately 1 percent, and postoperative hemorrhage in 0.7 percent (Zimmerman and Gan-Gaisano, 1990). Hypothyroidism occurs in approximately one-half of patients within the first year after surgery, and in about 1 to 2 percent per year thereafter (http://www.uptodate.com/contents/surgical-management-of-hyperthyroidism).

Conclusion

Graves' disease is a complex pathology that can affect most body systems. The presence of thyrotropin-receptor antibodies (TRAb) in serum and orbitopathy on clinical examination distinguishes the disorder from other causes of hyperthyroidism. However, the disease is most often diagnosed clinically. Because all available treatments have serious drawbacks, extensive discussion with the patient about therapeutic options is key to disease control and persistent long-term health. In low resource countries, medical management is often more expensive. Therefore, in these settings surgery remains a viable option. Nevertheless, it may necessitate a livelong levothyroxine replacement.

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Conflict of Interest

The authors admit no conflict of interest.

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