

HERBAL INTAKE: UNDIAGNOSED HYPOTHYROIDISM LEADING TO POSTOPERATIVE REFRACTORY CIRCULATORY COLLAPSE

- A Case Report -

JYOTSNA PUNJ* AND MK ARORA**

Abstract

There is a high probability of missing out on the preoperative diagnosis of hypothyroidism in elderly females, as most of the symptoms are attributed to old age. We report a patient with undiagnosed hypothyroidism, operated for excisional biopsy of carcinoma of tongue, who postoperatively developed septicemia refractory to maximum inotropic support and antibiotic coverage and succumbed within 40 hours. Her symptoms of constipation, sedentary life style, and joint pains were attributed to old age by the family and thus were not communicated to us in the preoperative assessment. Her long-standing hypothyroidism probably was associated with adrenocortical suppression exaggerated with intermittent and chronic ingestion of herbal powder, which generally contains steroids. We recommend that a more careful preoperative evaluation and history pertaining to hypothyroidism in obese female patients more than 45 years with joint pains should be sought for. Ingestion of herbal powders should alert us as these contain steroids. If there is a suspicion of hypothyroidism, then elective surgery should be deferred to rule out the same due to possibility of progression to myxedema coma under stress of anesthesia and surgery. We also recommend that in these

From Department of Anesthesiology, All India Institute of Medical Sciences, New Delhi, India.

* Assistant Professor.

** Professor.

Corresponding author: Dr Jyotsna Punj, Department of Anesthesiology and Critical Care, 5th Floor, Teaching Block, AIIMS, N Delhi, India, Tel: 9868397811.

E-mail: jyotsna_punj@yahoo.com.

cases preoperative blood cortisol level should be evaluated to rule out adrenocortical suppression and direct its management, if present.

Key words: Herbal medicines, hypothyroidism, myxedema, adrenocortical suppression, postoperative.

Introduction

Hypothyroidism is a chronic endocrine disorder that slows body metabolic functions as a result of impaired or absent production of thyroid hormone. After 60 years of age, the prevalence of hypothyroidism may be as high as 20% in women¹. Elderly patients with hypothyroidism often have atypical presentations, such as decreased mobility³ and some patients with compensated hypothyroidism are asymptomatic⁴.

We report of a patient with undiagnosed hypothyroidism who was operated for excisional biopsy of carcinoma tongue. Her history of constipation, sedentary life style, and joint pains with ingestion of herbal powder was not communicated to us in the preoperative assessment as the family attributed these to normal old age related problems.

Herbal medicines are commonly consumed by the people in India and are not considered out of the ordinary. It is a well-known fact that long-standing hypothyroid patients have associated hypothyroidism¹³ and reports of myxedema and coexisting adrenal crisis have been mentioned before^{14,15}. In our patient hypothyroidism was probably associated with adrenocortical suppression exaggerated with the ingestion of herbal powder, which generally contains steroids. She postoperatively developed septicemia refractory to maximum inotropic support and antibiotic coverage and succumbed within 40 hours. Even with optimum therapy, mortality rate as high as 30-60% has been reported in myxedema coma^{2,12}.

We recommend that an obese female more than 45 years of age with joint pains should be investigated for latent hypothyroidism and in these cases preoperative blood cortisol level should be evaluated to rule out adrenocortical suppression and direct its management, if present.

Case Report

A 80 kg, 75-year-old, ASA II female patient was admitted to our hospital with the diagnosis of carcinoma tongue and was scheduled for excisional biopsy. There was no significant history of any other illness. She underwent hysterectomy 20 years back under general anesthesia, which was uneventful. Her general and physical examination was unremarkable and airway examination showed adequate mouth opening of Malampatti-II with loose lower central incisors.

Preoperative laboratory investigations were within normal limits except total leucocyte count (TLC), of 3700/cumm. Preoperative ECG and X-ray were within normal limits. The patient was kept fasting overnight and was advised tablets ranitidine 150 mg and metoclopramide 10 mg in the night and morning. Injection glycopyrrolate 0.2 mg intramuscular and Xylometazoline nasal drops were given 1 hour prior to surgery.

Anesthesia was induced with fentanyl 120 µg and propofol 100 mg and tracheal intubation with cuffed nasotracheal tube of 7.5 mm ID was facilitated by vecuronium 6 mg. Anesthesia was maintained with O₂: N₂O (505:50) and isoflurane. Duration of surgery was 1 hour. After the conclusion of surgery, residual effect of neuromuscular blockade was reversed with neostigmine 3.5 mg and glycopyrrolate 0.6 mg. Normothermia was maintained.

Postoperatively patient was drowsy but responding to verbal commands and maintained a respiratory rate of 20/min, pulse rate of 94/min, BP of 160/86 mmHg and oxygen saturation of 98%. She was shifted to high dependency unit with tube in situ to check for any bleeding from surgical site. After 2^{1/2} hours, her oxygen saturation decreased to 86%. ABG revealed respiratory acidosis. She was shifted to the ICU for ventilatory support. The left radial artery and internal jugular vein were cannulated. In the next 2 hours, blood pressure decreased for which infusion of dopamine was started. Subsequently her temperature increased to 40° C along with fall in urine output. Chest auscultation revealed bilateral crepts. On the basis of above symptoms, latent sepsis was suspected as the most probable cause of her symptoms for which antibiotic coverage with injections of piperacillin,

tazobactam, levofloxacin, metronidazole along with hydrocortisone was prescribed.

On close inspection her coarse, dry skin and truncal obesity was noticed, which probably was missed during preanesthetic check up. On taking a detailed history from the patient's family, it was revealed that she had consumed herbal medications for joint pains, off and on, for last 10 years. She also suffered from constipation, and lead a sedentary life for last many years. Blood samples were sent for thyroid profile to rule out hypothyroidism. In the next 24 hours, she continued to be hypotensive despite maximum inotropic support of dopamine, noradrenaline, adrenaline and vasopressin. After about 40 hours post surgery, patient suffered a cardio-respiratory arrest and could not be revived. The investigations received a day after the patient's demise revealed hypothyroidism. T3-0.29 uIU/ml (0.79-1.49 uIU/ml T4-2.73 uIU/ml (4.5-12.5 uIU/ml), TSH-21.84 uIU/ml (0.4-4.67 uIU/ml), total leucocyte count of 11,200 and a negative blood culture for bacteremia.

Discussion

Hypothyroidism is a chronic endocrine disorder that slows body metabolic functions as a result of impaired or absent production of thyroid hormone. The disease typically progresses over months or years. Primary hypothyroidism most often occurs in adults aged 40-60 years. Incidence is greater in females than males (5-10:1). After 60 years of age; the prevalence of hypothyroidism may be as high as 20% in women¹. The classical symptoms of hypothyroidism include fatigue, constipation, weight gain, cold intolerance, a deep voice, coarse hair, and dry pale cool skin². However, elderly patients with hypothyroidism often have atypical presentations, such as decreased mobility³ and some patients with compensated hypothyroidism are asymptomatic⁴. According to American Association of Physicians, evidence is insufficient to recommend for or against routine screening for thyroid disease in adults⁵. But American Academy of Family Medicine says that obese female above 45 yrs with a history of joint pains should be

screened for hypothyroidism⁶. Hypothyroidism is frequently accompanied by musculoskeletal manifestations ranging from myalgias and arthralgias to true myopathy and arthritis⁷.

Our patient lead sedentary life, suffered joint pains and constipation. These were thought to be normal old age problems by the family⁸ and not given much importance and thus were not communicated to us during preanesthetic check up. We got a suspicion of hypothyroidism when patient did not recover well from anesthesia and was drowsy in the immediate post operative period. On close examination of her physical appearance and a detailed history from her family, possibility of hypothyroidism was considered and blood samples were sent for the same.

Myxedema coma occurs almost exclusively in age group of 60 years and above, with 80% preponderance in females^{8,9}. They usually have longstanding hypothyroidism, although it may not have been previously diagnosed. More than 90% of cases occur during the winter months⁸, probably due to age-related loss of the ability to sense temperature and lower production secondary to hypothyroidism¹⁰. Myxedema coma causes drastic decrease in metabolic rate, hypoventilation leading to respiratory arrest, hypotension, hypothermia, decreased mental state progressing to coma, decreased cardiac output due to profound bradycardia and cardiomegaly¹¹. It occasionally follows surgery, anesthesia or severe infection. Mortality in untreated or unrecognized myxedema coma reaches nearly 100%. Even with optimum therapy, mortality rate as high as 30-60% has been reported^{2,12}.

It is a well-known fact that long-standing hypothyroid patients have associated hypopituitarism¹³ and reports of myxedema and coexisting adrenal crisis have been mentioned before^{14,15}. Thus hydrocortisone should be administered until adrenal insufficiency has been ruled out; failure to do so may result in the precipitation of adrenal crisis. Preoperative cortisol levels should be evaluated to rule out any adrenocortical suppression and guide us regarding initiating and dosage of corticosteroids perioperatively. An adrenocorticotrophic hormone stimulation test could also be administered if clinically warranted. Though we did not evaluate cortisol levels,

corticosteroids in low dose of 25 mg QID were supplemented early in the course of events but with no hemodynamic improvement. In hindsight, this was a lacuna on our part. Had we evaluated cortisol levels, the absolute value would have directed our therapy.

Our patient was ingesting herbal medicines for joint pains for the last 10 years. History of ingestion of herbal preparations is common in India and is not considered out of the ordinary by the people and thus was not communicated to us. Though formal analysis of the herbal formulation consumed by the patient could not be carried out, many studies have confirmed the presence of steroids in these preparations^{16,17,18}. Because of long-term ingestion of steroids, our patient was probably immunosuppressed. A low TLC could have been a feature of immunosuppression or hypothyroidism per se (low TLC frequently features in hypothyroidism). Associated hypopituitarism in our patient seemed more severe probably due to chronic herbal medications.

Bacteremia is associated with various oral and maxillofacial surgical procedures¹⁹. Our patient developed septic shock following oral surgery manifested by hyperthermia and an increase in total leucocyte count from 3,700 to 11,200. Though blood culture was negative for bacteremia, only 30% of patients with presumed septic shock have positive blood cultures and 25% of presumed septic shock patients remain culture negative from all sites²⁰.

Various cases of previously undiagnosed hypothyroidism manifesting intraoperatively have been reported. Mizono et al in 2000 encountered delayed awakening in a 55-year-old male patient after laparoscopic cholecystectomy²¹. The patient suffered from elevated creatinine phosphokinase and cartinoembryonic antigen (CEA) of unknown origin and developed hypotension, low arterial oxygen saturation, hypothermia and metabolic acidosis. Awakening was delayed for about 2 hours. Hypothyroidism was suspected, diagnosed and treated.

Regaller et al 1993 encountered a series of complications in an undiagnosed hypothyroidism in a 46-year-old woman scheduled for hip replacement²². She developed intraoperative hypotension and tachycardia.

Catecholamines and intravenous fluids administered for low cardiac output resulted in no hemodynamic improvement. Patient subsequently developed pneumonia, ARDS, acute renal failure and remained in coma for the next 5 days. Patient evaluation revealed hypothyroidism and myxedema coma was diagnosed and treated with intravenous L thyroxine. The patient regained consciousness after 36 hours of initiating treatment and was discharged 6 weeks later. Vretzakis G et al 2002 encountered a 49-year-old male suffering from hypertension and diabetes, with undiagnosed hypothyroidism, dramatically developed severe myxedema intraoperatively during cardiac surgery impairing cardiac output²³. There was a marked increase in airway pressure and a fall in oxygen saturation along with tense, distended abdomen with massively edematous face and head with a swollen and protruding tongue. A peritoneum incision, bronchoscopy and bilateral chest tube insertion revealed no positive findings. Hypotension developed and epinephrine infusion was started. Review by endocrinologist suspected myxedema and was confirmed with a TSH of 79 uIU/ml (normal, 0.38-6.5 uIU/ml). After intravenous levothyroxine was administered, his hemodynamic status improved and trachea was extubated on 3rd postoperative day. The authors speculate whether a more careful preoperative evaluation would have suggested possibility of underlying thyroid dysfunction.

These case studies clearly indicate a high probability of missing out on preoperative diagnosis of hypothyroidism in unsuspecting patients. The complications ensuing due to this can be multiple and grave.

Complications in our patient developed postoperatively, whereas the reported patients suffered the aforesaid problems intraoperatively. The drastic development of clinical events in our patient is in contrast to the other reported patients who in spite of manifesting severe features did not have a protracted course like ours. None of the mentioned patients developed sepsis and ionotropes were able to maintain vital parameters in all of them except in the second mentioned case. Whereas in our patient, sepsis was unresponsive to full antibiotic coverage and maximum inotropic support developed within a short time of 40 hours.

The most important elements in treatment of myxedema coma are early recognition, presumptive thyroid hormone replacement, hydrocortisone and appropriate supportive care. However, the accelerated course of events did not give us much time to diagnose and treat hypothyroidism and we watched helplessly as maximum support to all ionotropes had no favorable outcome.

To summarize, stress of anesthesia and surgery in the cold weather decompensated our old female patient with long standing undiagnosed hypothyroidism. Hypopituitarism frequently co-exists with long standing hypothyroidism and in our patient, adrenal suppression was probably exacerbated by ingestion of herbal medicines and she developed myxedema coma along with adrenal crisis. Oral surgery can lead to sepsis and our patient's immunosuppressed state lead to fulminant sepsis refractory to maximum ionotropic support and full antibiotic coverage and she succumbed within 40 hours. In retrospect, whether a more careful preoperative evaluation would have suggested the possibility of underlying thyroid dysfunction and prevented mortality is unknown, as treatment of diagnosed myxedema coma is associated with a high mortality of 30-60%.

We recommend that a more careful preoperative evaluation and history pertaining to hypothyroidism in obese female patients more than 45 years with joint pains should be sought for. If there is a suspicion of hypothyroidism, then elective surgery should be deferred to rule out the same due to possibility of progression to myxedema coma under stress of anesthesia and surgery. A history of consuming herbal or any local medications should be asked for and should alert us of adreno-cortical suppression. We also recommend that in these cases preoperative blood cortisol level should be evaluated to rule out adrenocortical suppression and direct its management, if present.

References

1. WILSON GR, CURRY RW JR: Subclinical thyroid disease. *Am Fam Physician*; 72(8):1517-24, 2005.
2. WERNER SC, INGBAR SH, BRAVERMAN LE, UTIGER RD: Werner & Ingbar. *The thyroid: a fundamental and clinical text*. 8th ed. Philadelphia: Lipincott Williams & Wilkins, 2000.
3. MINTZER MJ: Hypothyroidism and hyperthyroidism in the elderly. *J Fla Med Assoc*; 79:231-5, 1992.
4. ROBUSHI G, SAFRAN M, BRAVERMAN LE, GNUDI A, ROTI E: Hypothyroidism in the elderly. *Endocr Rev*; 8:142-53, 1987.
5. US Preventive Services Task Force. Screening for thyroid disease: recommendation statement. *Ann Intern Med*; 140(2):125-7, 2004.
6. American College of Physicians. Clinical guideline, part 1. Screening for thyroid disease. *Ann Intern Med*; 129(2):141-3, 1998.
7. McLEAN RM, PODELL DN: Bone and joint manifestations of hypothyroidism. *Semin Arthritis Rheum*; 24(4):282-90, 1995.
8. ABILES BK: Hypothyroidism in elderly patients. *AORN J*; 69:1026-30, 1999.
9. DAVID PJ, DAVIS FB: Hypothyroidism in the elderly. *Compr Ther* 4; 10:17-23, 1984.
10. BALLESTER JM, HARCHELROAD FP: Hypothermia: an easy-to-miss, dangerous disorder in winter weather. *Geriatrics*; 54(2):51-2, 55-7, 1999.
11. WARTOFSKY L: Myxedema coma. *Endocrinol Metab Clin North Am*; 35(4):687-98, vii-viii, Dec. 2006.
12. ARLOT S, DEBUSSCHE X, LALAU JD, MESMACQUE A, TOLANI M, QUICHARD J: Myxedema coma: response of thyroid hormones with oral and intravenous high-dose L-thyroxine treatment. *Intensive Care Med*; 17:17-8, 1991.
13. CHRISTEN RHODES WALL: *American Family Physician*; 62(11), Dec. 2000.
14. KASPERLIK-ZALUSKA AA, CZARNOCKA B, CZECH W, WALECKI J, MAKOWSKA AM, BRZEZINSKI J, ANISZEWSKI J: Secondary adrenal insufficiency associated with autoimmune disorders: a report of twenty-five cases. *Clin Endocrinol (Oxf)*; 49(6):779-83, 1998.
15. ROOSSENS B, MAES E, VAN STEIRTEGHEM A, VANHAELST L: Primary hypothyroidism associated with secondary adrenocortical insufficiency. *J Endocrinol Invest*; 5(4):251-4, 1982.
16. LIU H, HUANG Y, WANG Q, ZHANG T, SONG Y: Detection of saponins in extracts from the rhizomes of Paris species and prepared Chinese medicines by high performance liquid chromatography-electrospray ionization mass spectrometry. *Planta Med*; 72(9):835-41, Epub 2006.
17. RAMSAY HM, GODDARD W, GILL S, MOSS C: Herbal creams used for atopic eczema in Birmingham, UK illegally contain potent corticosteroids. *Arch Dis Child*; 88(12):1056-7, 2003.
18. COURDIER-FRUH I, BARMAN L, WETTSTEIN P, MEIER T: Detection of glucocorticoid-like activity in traditional Chinese medicine used for the treatment of Duchenne muscular dystrophy. *Neuromuscul Disord*; 13(9):699-704, 2003.
19. TAKAI S, KURIYAMA T, YANAGISAWA M, NAKAGAWA K, KARASAWA T: Incidence and bacteriology of bacteremia associated with various oral and maxillofacial surgical procedures. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*; 99(3):292-8, Mar. 2005.
20. SAT SHRMA: Septic Shock. 2007 E medicine from web md.
21. MIZUNO J, NAKAYAMA Y, DOHI T, TOKIOKA H: A case of hypothyroidism found by delayed awakening after the operation. *Masui*; 49(3):205-8, 2000.
22. REGALLER M, QUINTEL M, BENDER HJ, ALBRECHT DM: Myxedema coma as a rare postoperative complication. *Anaesthesist*; 42(3):179-83, 1993.
23. VRETZAKIS G, FERDI E, PAPAIOGAS B: Insidious hypothyroidism unmasked after operation. *Eur J Anaesthesiol*; 19(7):532-4, 2002.

