Vomiting as harbinger for Graves' disease

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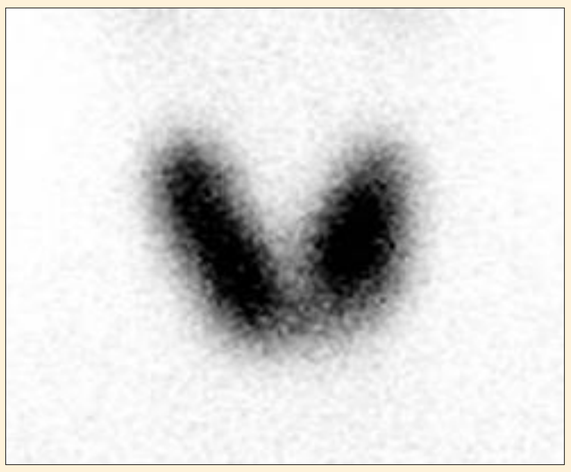
Introduction: Isolated vomiting is a rare often forgotten presentation of Graves's disease[1] and can lead to delayed diagnosis. Multiple case reports quote vomiting in thyrotoxicosis co-presenting with Addisonian crisis[2], diabetic ketoacidosis[3,4] or with abnormal liver function and jaundice[5,6]. Another common association is hyperemesis gravidarum. Vomiting in paraneoplastic hyperthyroidism occurs through a similar mechanism of beta-HCG secretion, mainly related to germ-line tumours[7]. We present a case of severe prolonged vomiting caused by Graves' disease.

Case presentation: A 46 years old postmenopausal woman of Afro-Caribbean origin presented with unremitting vomiting and dramatic 38 Kilograms weight loss over 2-3 months. She reported tiredness, headaches and anxiety. Her heart rate was 91/min sinus rhythm, BP 115/80, temperature 37.2^{O}C. She had no palpable thyroid nor thyroid eye signs. Thyroid function tests showed suppressed TSH<0.01 mU/L and elevated fT4 86.9 pmol/L. The **Burch and Wartofsky's score** was 20 (temperature 37.2, heart rate 91 in sinus rhythm, absent agitation or CNS symptoms), indicating this was not a thyroid storm presentation.

Further investigations: Thyroid uptake scan and anti-thyroid antibodies confirmed Graves's disease. Liver function tests were normal. Thyrotoxicosis related hypercalcaemia was noted (corrected calcium 2.75 mmol/l with low parathyroid hormone 1.3 pmol/l). Coeliac, autoimmune screen and beta-HCG were negative. Gastroscopy with duodenal biopsy and CT body imaging were normal.

	Normal range	15.03.16	21.03.16	22.03.16	04.05.16	11.07.16	29.09.16
TSH (mU/l)	0.27-4.20	<0.01	<0.01	<0.01	0.02	<0.01	<0.01
FT4 (pmol/l)	11.0-22.0	85.9	50.5	35.2	18.8	25.6	37.3
FT3 (pmol/l)	3.7-6.8				9.0	13.2	
PTU dose (24 hours)		300mg	300mg	300mg	200mg	300mg	400mg
TRAB (U/l)	<1.4					1.4	
TPO (U/ml)	<34		234		186		
cCa (mmol/l)		2.75		2.47	2.51	2.68	
PTH (pmol/l)	1.6-6.9	1.3			5.3		

Progress: The patient required a prolonged two weeks admission for managing her unremitting vomiting during which Propylthiouracil and Propranolol were administered via nasogastric tube. Vomiting was refractory to antiemetics but improved alongside amelioration of hyperthyroidism with antithyroid medication.



Follow up: There was recurrence of isolated vomiting with weight loss 6 months following presentation during Propylthiouracil titration. Her Propylthiouracil dose has currently been titrated back to 400mg daily.

Burch and Wartofsky's Diagnostic criteria for thyroid storm[19]
***A score >45 is highly suggestive; 25-45 is suggestive and <25 is improbable**

Temperature		**Central nervous system**		**GI system**	
37.2-37.7	5	Mild agitation	10	Moderate (diarrhoea, nausea/vomiting, abdominal pain)	10
37.8-38.2	10	Moderate (delirium, psychosis, extreme lethargy)	10	Severe (unexplained jaundice)	20
38.3-38.8	15	Severe (seizures, coma)	30		
38.9-39.4	20				
39.4-39.9	25				
>40.0	30				
Triggering factors		**Cardiovascular system**			
Negative	0	Heart rate		Atrial fibrillation	10
		99-109	5	Heart Failure	
Positive	10	110-119	10	Mild(peripheral oedema)	5
		120-129	15	Moderate (bibasilar rales)	10
		130-139	20	Severe (pulmonary oedema)	15
		>=140	25		

Conclusion: Vomiting is commonly associated with endocrine disorders. Literature review reports female predominance of thyrotoxic vomiting. Previous case reports of isolated vomiting have no Graves's thyroid eye signs making early diagnosis challenging. Typically, they were associated with significant weight loss in the context of a delayed diagnosis, and persistent tachycardia as diagnostic clues. Characteristically such vomiting fails to respond to usual antiemetics, but responds to antithyroid medications. Glucocorticoids are also useful adjuncts in bringing symptoms under control[11].

Mechanisms of thyrotoxic vomiting

Increased beta-adrenergic activity	Increases the number of beta-adrenergic receptors[8,9]
Increased thyroid hormones	Stimulates the chemical trigger zone[12]
	Decreases gastric emptying and causes pyloric sphincter malfunction[13,14]
	Increases magnesium urinary excretion. Hypomagnesaemia inhibits gastric smooth muscle[15,16]
Increased oestrogen level in patients of both sexes[10,12]	Raised oestrogen level may induce nausea and vomiting only in susceptible patients[17]
Functional duodenal obstruction	Hypermotility induced volvulus of duodenal third portion has been described[18]

Recommendations: Increased awareness of vomiting as presentation of thyrotoxicosis is necessary in order to avoid a delayed diagnosis and over-investigations. There is a potential risk of precipitating a thyroid storm while exposing patients unnecessarily to invasive investigations such as endoscopy or exploratory laparoscopy.

Ruling out alternative aetiologies is also important. Rare paraneoplastic thyrotoxic conditions may present as such.

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BES2016 99--EP
Thyroid
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DOI: 10.3252/pso.eu.BES2016.2016
Poster presented at: SfE BES 2016