CASE REPORT

Graves' disease and coeliac disease: screening and treatment dilemmas

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Accepted 6 October 2014

SUMMARY

The association between autoimmune thyroid disorders (AITD) and coeliac disease (CD) is well known, however, most of the literature concentrates on hypothyroidism and CD. We report a case of a 37-year-old woman with Graves' disease (GD) who presented with thyrotoxicosis that was not responsive to medical management. The screening for coeliac autoimmunity (CA) was positive. After initiation of a gluten-free diet the patient's thyrotoxicosis responded to medical management. She was given radioiodine therapy and is currently hypothyroid on a stable dose of thyroxine.

BACKGROUND

Most of the literature on autoimmune thyroid disorders (AITD) and coeliac disease (CD) concentrates on hypothyroidism and its association with CD.^{1 2} The impact of coeliac autoimmunity (CA) on Graves' disease (GD) is less well described. GD and CD both have gastrointestinal symptoms such as weight loss and hyperdefaecation in common (which point to CD in other autoimmune disorders as well) and there are no guidelines on screening for CD in cases of GD.² Coexistence of CD with GD may complicate the management of GD, and initiation and adherence to a gluten-free diet (GFD) may be helpful, as seen in the management of our case.

CASE PRESENTATION

A 37-year-old woman presented with a history of weight loss, tremulousness, palpitations and increased sweating for the past 3 years. There was a history suggestive of hyperdefaecation. There was no history suggestive of any eye or skin symptoms. The patient had been having irregular menstrual cycles for the past 8 months. She had two children, 10-year-old and 6-year-old. Initial investigations were suggestive of hyperthyroidism with positive antithyroid peroxidase antibodies and thyroid-stimulating hormone (TSH) receptor antibodies.

The patient was started on carbimazole (CMZ). However, her illness was characterised by poor response to medical management and a fluctuating course. The serial reports and dose of CMZ are shown in the 'investigations' section. In view of her condition, the patient was further investigated, revealing positive IgA tissue transglutaminase antibodies. An upper gastrointestinal endoscopy was performed along with duodenal biopsy, which were suggestive of coeliac disease (figure 1).

INVESTIGATIONS

IgA level: 324 mg/dL (90–450 mg/dL)

IgA tissue transglutaminase (March 2012): positive
168 µ/mL (<15)

The upper gastrointestinal endoscopy was suggestive of atrophy of the villi in the stomach and the duodenum, with a few erosions, and reduced folds fissuring and scalloping, all pointing to coeliac disease (figure 1). The biopsy from the duodenum was suggestive of total villous atrophy with crypts that were hyperplastic with increased intraepithelial lymphocytes (30–100). The lamina propria was inflamed with occasional Brunner's gland (April 2012).

Additional tests:

Antithyroid peroxidase and anti-TSH receptor antibody: positive.

Glutamic acid decarboxylase antibody: negative

Serum cortisol: 8:00–180 (50–250 ng/mL)

Serum prolactin: 16 (5–25 ng/mL)

Follicle stimulating hormone (day 4 of menstrual cycle): 3.4 (1.8–9.6 µIU/mL)

25 hydroxyvitamin D3: 11 (30–100 ng/mL)

Serum calcium: 8.8 (8.9–11 mg%); phosphorus: 2.4 (3.5–5.5 mg%); albumin: 3.4 (3.5–6.5 g%); alkaline phosphatase: 328 (70–180 IU/mL)

Bone mineral density: Z score

Total body=−3.7; lumbar spine=−4.2; left femur=−4.1

DIFFERENTIAL DIAGNOSIS

The common gastrointestinal features make distinction between CD and GD blurred. Other causes of malabsorption such as ulcerative colitis, irritable bowel syndrome, etc, can coexist with GD and should be included in the differential diagnosis.

TREATMENT

The patient was started on GFD. The CMZ dose was adjusted according to serial thyroid function tests. The patient was given radioiodine therapy, after which she became hypothyroid; she is currently on 100 µg of thyroxine with euthyroid status on medications (tables 1 and 2). The patient was given vitamin D correction and calcium and vitamin D replacement.

OUTCOME AND FOLLOW-UP

Currently, the patient is hypothyroid on 100 µg of thyroxine with normal thyroid function test. Her weight has increased from 35 kg at initiation of

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To cite: Joshi AS, Varthakavi PK, Bhagwat NM, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-201386

ESOPHAGUS- NORMAL
GE JN- 36 CMS
FUNDUS- MILD ATROPHY SEEN
BODY, ANTRUM- NORMAL
D1- FEW EROSIONS SEEN
D2- REDUCED FOLDS, FISSURING AND SCALLOPING SEEN, BIOPSY TAKEN
IMP- FEATURES S/O CELIAC DISEASE

Figure 1 Patient's upper gastrointestinal endoscopy photograph.

GFD to 51 kg currently. Her menses has regularised and her quality of life has improved.

DISCUSSION

The association of AITD with CD has been well described. It is a part of polyglandular autoimmune disorders type II.³ HLA

DR3 has been proposed to be responsible for the association between GD and CD.⁴ However, most of the discussion related to CA and AITD is restricted to hypothyroidism. Although it is easy to recognise CD in patients with hypothyroid by noting the symptoms of weight loss, diarrhoea, high dosage requirement of thyroxine, abdominal discomfort, etc, it is difficult to point out

Table 1 Serial thyroid function tests with treatment of the patient before diagnosis of coeliac disease

Test analyte (normal range)	04/09/2011	05/11/2011	28/12/2011	23/03/2012
T3 (70–200 ng/mL)	>800	496	567	321
T4 (4.5–12.6 µg/dL)	>30	28	29	24
TSH (0.2–4.5 µIU/mL)	<0.01	<0.01	<0.01	<0.01
Medication	30 mg CMZ	40 mg CMZ	60 mg CMZ	60 mg CMZ
Weight (kg)	34	35	33	35

Table 2 Serial thyroid function tests with treatment of the patient after diagnosis of coeliac disease and initiation of gluten free diet

Test analyte (normal range)	24/06/2012	21/08/2012	16/10/2012	10/12/2012
T3 (70–200 ng/mL)	176	64	280	144
T4 (4.5–12.6 µg/dL)	8	1.5	12	6.4
TSH (0.2–4.5 µIU/mL)	<0.01	64	<0.01	<0.01
Medication (gluten free diet continued)	30 mg CMZ	10 mg CMZ	10 mg CMZ Given radioiodine 10 mci dose	CMZ stopped
Weight (kg)	38	44	43	47
	24/01/2013	15/03/2013		
T3 (70–200 ng/mL)	48	134		
T4 (4.5–12.6 mcg/dL)	4.2	9.3		
TSH (0.2–4.5 µIU/mL)	74	3.6		
Medication (gluten free diet continued)	Started on LT4 100 µg/day	LT4 100 µg/day		
Weight (kg)	51	49		

CD in hyperthyroidism, as weight loss and diarrhoea as well as malabsorption are present in both. Also, although the classic description states that GD causes hyperdefaecation and CD causes diarrhoea and/or steatorrhoea, in adults this distinction is all the more blurred in milder/subclinical forms of GD and CD, where occasional loose stools/subclinical malabsorption are more common; and, steatorrhoea has also been reported in isolated GD cases.²

The literature is also divided regarding prevalence of CD in AITD. Some studies found no evidence of CD in GD, but significant prevalence in hypothyroidism, whereas others have found nearly equal prevalence of CD in GD as well as hypothyroidism. The prevalence of CD in AITD ranged from 0–7.8%, while prevalence of autoimmune hypothyroidism and GD in cases of CD ranged from 0–7% and 0–10%, respectively, with the subclinical forms being more common.²

There are no definite recommendations/guidelines for screening for CD in a case of GD. Also, of the various screening tests used for CD, transient false positive antiendomysial antibodies have been documented in GD.⁵ There are no reports regarding false positivity to tissue transglutaminase antibodies to date. Also, as GD and CD are autoimmune disorders, an IgA based test should be performed only after serum IgA estimation because of the variably noted increased prevalence of IgA deficiency in both.⁶

Data are also varied regarding impact of GFD in cases of CD with AITD. Some of the literature reported no significant impact, while others reported a reduction in the dose of thyroxine and reversal of subclinical hypothyroidism. No concrete impact data is reported in GD with CD to the best of our knowledge. However, since reduction in antithyroid autoimmunity has been reported, whether it could translate into better management of GD with CD needs to be assessed.² Also, treatment of CD will result in more predictable absorption of medications (antithyroid drugs) and better response, as is evident in our case.

Another rarely discussed subject is the impact of concomitant presence GD and CD on bone. GD can cause bone loss by creation of a hypermetabolic state, with resorption predominating over formation. CD can worsen bone health not only through nutritional deficiencies but also by the underlying inflammatory state, associated hypogonadism and reduction in insulin-like growth factor-1 levels. Concomitant presence of both disorders can double the negative prognosis for bone health. Only one earlier case report discusses this issue, however, that case was further complicated by primary hyperparathyroidism.⁷ There are no recommendations for routine monitoring and screening for bone health treatment or measures to prevent osteoporosis in these cases.

The dilemmas posed after managing our case are: (1) Should we screen all cases of GD for CD? (2) Is the course of GD

altered by concomitant presence of CD? (3) The lack of data/recommendations for protecting bone health in these cases. No recommendations advocate for these issues as of now, and there are no definite pointers to suggest CD in cases of GD. Minimally, we can consider screening all GD cases with poor response to medical management for CD. The response to treatment of GD can be variable in CD cases due to unpredictable absorption of medication. Definitive treatment can be considered (radioiodine or surgery, as indicated) as early as possible. Also, attention needs to be paid to bone health in cases of CD and GD.

Learning points

- ▶ Coeliac disease is an important autoimmune disorder associated with autoimmune thyroid disease, which includes hyperthyroidism, apart from well described hypothyroidism.
- ▶ Though there are no well-defined guidelines on screening for coeliac disease in a case of Graves' disease, and because symptoms can be common, screening should be considered in symptomatic or in those who do not respond satisfactorily to medical management.
- ▶ A high index of suspicion is needed to diagnose a new autoimmune disorder in the presence of an existing condition, as demonstrated in this case.
- ▶ Concomitant presence of coeliac disease and Graves' disease can adversely affect bone health.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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