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CASE REPORT

A Nearly Missed Hashimoto's Thyroiditis: A Case of Refractory Anaemia

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ABSTRACT

This is a case of a 68-year-old man who was diagnosed late with Hashimoto's thyroiditis following a few admissions for symptomatic anaemia. Although hypothyroidism is common among the elderly, the classic symptoms are less likely to be evident and anaemia can be the first sign of hypothyroidism. This patient had multiple comorbidities including ischaemic heart disease, diabetes and chronic kidney disease which might have contributed to the delay in finding the underlying cause of his anaemia. He initially presented with symptomatic anaemia and received blood transfusions and iron supplementation. On subsequent follow up, his anaemia failed to improve. He was then referred to our primary care clinic. Hashimoto's thyroiditis was diagnosed based on his clinical features, thyroid function test results and anti-thyroid peroxidase level. This case highlights the importance of determining the cause of anaemia as his haemoglobin level improved significantly after thyroxine was commenced. It also serves as a reminder that hypothyroidism should be considered in patients with anaemia, especially in those with uncertain aetiology.

KEYWORDS: Hashimoto's thyroiditis; hypothyroidism; normochromic normocytic anaemia; primary care

INTRODUCTION

Anaemia is a common condition seen in clinical practice. WHO defines anaemia as a haemoglobin (Hb) level below 13.0g/dL in men and below 12.0g/dL in women [1]. In the elderly population, iron deficiency, gastrointestinal blood loss, chronic diseases, vitamin B12 and folate deficiency, and myelodysplastic disease are among the many causes of anaemia. Anaemia can also be the first sign of hypothyroidism even though it is more common in those with overt hyperthyroidism [2]. This case emphasizes the importance of including thyroid function test as part of the work up for anaemia, particularly in elderly patients with refractory anaemia. Identifying and treating this patient's hypothyroidism improved his Hb significantly.

CASE PRESENTATION

A 68-year-old gentleman was referred to our primary care clinic for investigation and management of refractory anaemia. He had underlying ischaemic heart disease with severe mitral regurgitation and had undergone coronary artery bypass grafting (CABG) six months earlier. He also had underlying type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) stage 3b. He was on aspirin, clopidogrel, s/c actrapid, atorvastatin, frusemide, bisoprolol, omeprazole and bisacodyl. Following CABG, he had two admissions. The first admission was a month after CABG and the reason for admission was for symptomatic anaemia during which he presented with chest pain. On admission, his haemoglobin (Hb) was 7.6g/dL, with normal mean cell volume (MCV) at 99.8fL and normal mean cell haemoglobin (MCH) at 31.3pg. The white cell and platelet count were normal at 8.97 x 103/µL and 191 x 103/µL respectively.

He was transfused immediately with two units of packed red blood cells due to the fear that his low Hb would exacerbate his ischaemic heart disease. The

initial differential diagnosis was anaemia of chronic disease due to the underlying CKD.

Inpatient investigations showed a positive faecal occult blood test (FOBT) with low serum iron (7.4µmol/L) but a high ferritin level (673µg/L). The serum transferrin was normal at 3.0 g/L and the total iron binding capacity (TIBC) was also normal at 75.3 µmol/L. However, his Unsaturated Iron Binding Capacity (UIBC) was raised at 46.7 µmol/L by 10% which may suggest a coexisting iron deficiency anaemia and anaemia of chronic disease. Both serum vitamin B12 and folate levels were within normal ranges. A peripheral blood film (PBF) showed normochromic normocytic RBCs with presence of macrocytes. The diagnosis made by the physician at this point was anaemia of chronic disease with underlying infection or inflammation. As his symptom improved, he was discharged with iron tablets and planned for outpatient oesophago-duodenoscopy (OGDS) and colonoscopy to look for any source of gastrointestinal bleeding.

Three months later, he presented with oliguria and was clinically dehydrated. He was admitted for acute renal impairment secondary to dehydration when his serum creatinine was elevated at 444µmol/L. His estimated glomerular filtration rate (eGFR) was 12 mL/min/1.73m2. His Hb level remained low at 9.3g/dL despite iron supplementation. Repeat blood film then showed hyperchromic and macrocytic RBCs with a MCV of 104.7 fL and MCH of 33.6 pg. He was given intravenous rehydration which improved his condition. He was then discharged home with all his regular medications including iron tablets. He was given a referral to our primary care clinic to look into his anaemia. Figure 1 depicts the timeline of his illness.

During the first consultation at the primary care clinic, he complained of constipation and feeling of lethargy for the past year. He denied shortness of breath, palpitation or chest pain. He has no family history of thyroid disorders or blood dyscrasias, however, his elder sister had colorectal carcinoma. He did not smoke or drink alcohol. On examination, he looked pale with an apathetic facial expression and thinning of the eyebrows. He was not icteric nor oedematous. His blood pressure was 100/60 mmHg, and pulse rate was 68 beats per minute. He was slow to respond to questions and had slow movements. His skin and hair were dry and his nails were brittle. There was no xanthelasma, tendon xanthoma or goitre seen. There was no thyroid nodule on palpation. Cardiovascular examination revealed a grade four pan-systolic murmur loudest at the apex. Lung examination was unremarkable. Abdominal examination was normal and per rectum examination revealed no mass or malaena. His ankle reflexes were delayed.

His latest blood test results showed a low Hb of 7.4g/dL (macrocytic) with a high MCV of 107.4 fL, high MCH of 35.6 pg with normal total white blood cells, 4.51 x 10^3/µL and platelets, 181 x 10^3/µL. His urea was raised at 12 mmol/L, and his creatinine was 190 µmol/L. A repeat blood film showed a macrocytic picture. Serum vitamin B12 and serum folate were normal. His liver function test was normal. Thyroid function test (TFT) was ordered. Urgent OGDS and colonoscopy were arranged as he was unsure about his previous appointment date for these investigations. Further progress of FBC and TFT is shown in Table 1 below.

At the subsequent follow up, the patient's condition remained the same. His T4 level was low at 2.7 pmol/L (11.5 – 22.7) and TSH was markedly raised at 58.4 mIU/L (0.550 – 4.780). His anti-thyroid Peroxidase (anti-TPO) was also elevated at 783 IU/mL (<35.0 IU/mL). Meanwhile, his OGDS revealed antral and pyloric inflammation, with a healing ulcer near the pylorus. His rapid urease test was negative. On colonoscopy, there were three colonic polyps seen at the transverse colon. Histopathological examination reported the duodenal biopsy was suggestive of peptic duodenitis with reactive Brunner's gland hyperplasia while the hepatic flexure polyp found a tubular adenoma suggestive of low-grade dysplasia.

He was informed of the Hashimoto's disease diagnosis. He understood that he would require lifelong treatment with thyroxine. Thyroxine was started at 50mcg OD and slowly tapered up to 100mcg OD. This improved his Hb level significantly. He was also arranged for three-yearly colonoscopies and was prescribed with Omeprazole 20mg BD for at least two months.

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2017	2018			
1st Dec – 6th Jan	30th Jan – 23rd Feb	Apr	21st May - 24th May	28th June
Admission for CABG 12th Dec 2017	1st admission following CABG		2nd admission following CABG	1st visit to PCM

Figure 1: Timeline of presenting illness

Table 1 Significant blood test results for this patient

	Hb (g/dL) (13.0-17.0)	MCV (fL) (80-100)	MCH (pg) (27.0-34.0)	FT4 (pmol/L) (11.5-22.7)	TSH (mIU/L) (0.55-4.78)	Management
Week 1 (1st visit)	7.4	107.4 (high)	35.6 (high)	2.7	58.40	
Week 3	9.0	104.4 (high)	33.3 (high)			L-Thyroxine started at 50mcg OD
Week 9	8.8	99.9 (normal)	31.1 (normal)			L-thyroxine 50mcg OD
Week 13				14.3	18.96	L-thyroxine 75mcg OD
Week 20	11.0	94.8 (normal)	29.3 (normal)	20.3	9.35	L-thyroxine 100mcg OD
Week 30	12.6	89.4 (normal)	27.9 (normal)			L-thyroxine 100mcg OD

DISCUSSION

This case highlighted the importance of differentiating between the aetiologies of anaemia as the prognosis and treatment are different. It is important to identify and treat anaemia as it is associated with increased risk of hospitalization and mortality in the elderly [3]. In Malaysia, the overall prevalence of anaemia among the elderly is 35.3%. The highest prevalence of anaemia was found among Indians, those with increasing age, those with history of hospital admission, and those with diabetes mellitus [4].

It was a challenge to establish the exact cause of anaemia in this patient because of his multiple comorbidities. The patient was at risk of developing iron deficiency anaemia due to gastrointestinal bleeding as he was on aspirin, which was reflected by the positive FOBT, low iron and raised UIBC at the first admission and a healing ulcer on OGDS. With a diagnosis of CKD, he was also at risk of developing anaemia of chronic disease. Hence, hypothyroidism was not initially considered.

The prevalence of anaemia among hypothyroid patients is higher than the general population (i.e. 75% vs. 32%) [5]. It was also observed that the higher the TSH level, the higher the prevalence of moderate to severe anaemia [6]. One of the causes of hypothyroidism is Hashimoto's thyroiditis. It is an autoimmune disorder in which antibodies directed to the thyroid gland lead to chronic inflammation [7]. The resulting inflammation often leads to an underactive thyroid gland. It is said that it takes about ten years to be diagnosed with Hashimoto's disease between the start of the autoimmune attack and when the person is eventually diagnosed [7]. Hashimoto's disease is common in females, and younger age groups between the age of 30 and 50 years [8,9].

In patients with thyroid disease, although abnormalities in the haematological parameters have been noted, the exact mechanism of the thyroid hormones actions on human erythropoiesis is not clearly understood. A decreased thyroid hormone is known to adversely affect erythropoiesis, and this alters the RBC morphology. The RBCs in hypothyroid patients may present with a normochromic normocytic (65.9%), microcytic hypochromic (22.72%) or macrocytic (11.36%) picture [6]. It was also found that about 68.9% of anaemic hypothyroid patients had a positive anti-TPO level [6]. In addition, there is a significant positive relationship between the concentrations of free thyroid hormone and haemoglobin, haematocrit, and erythrocyte count, with a simultaneous negative correlation between TSH levels and the serum iron concentration and transferrin saturation [10].

Experimental studies demonstrated an enhanced erythroid colony growth induced by free triiodothyronine, thus, in hypothyroid patients, the number and proliferative activity of erythroid cells in the marrow is reduced [11]. Hypothyroid patients also show a decreased plasma concentration of erythropoietin. All the observed changes are regarded as physiological adaptations to the reduced oxygen requirement of the tissues, due to the diminished basal metabolic rate in hypothyroidism [11]. Successful

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treatment of hypothyroid patients with Hashimoto's thyroiditis and restoration of the euthyroid state is associated with a decrease in hepcidin concentration that follows the observed dynamics of iron homeostasis. This leads to improvement in erythropoeisis [12].

In conclusion, anaemia may be one of the first signs of hypothyroidism. Hence, hypothyroidism should always be considered in patients with anaemia, especially in those with uncertain aetiology.

Conflict of Interest

Authors declare none. Verbal informed consent for patient information was obtained from the patient himself.

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Author's Contribution

SAWA prepared the first draft of the case report. SAR and MSMY contributed to the critical revision of the case report. All authors read and approved the final version.

REFERENCES

1. World Health Organization (WHO). Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitam Miner Nutr Inf Syst Geneva, World Heal Organ 2011. 2011;1–6.

2. M'Rabet-Bensalah K, Aubert CE, Coslovsky M, Collet TH, Baumgartner C, Den Elzen WPJ, et al. Thyroid dysfunction and anaemia in a large population-based study. Clin Endocrinol (Oxf). 2016;84(4):627–31.

3. Culleton BF, Manns BJ, Zhang J, Tonelli M, Klarenbach S, Hemmelgarn BR. Impact of anemia on hospitalization and mortality in older adults. Blood. 2006; 107(10): 3841–6.

4. Institute for Public Health, Ministry of Health Malaysia. National Health and Morbidity Survey 2015. Kuala Lumpur, Ministry of Health. 2015

5. Smith DL. Anemia in the Elderly. Am Fam Physician. 2000; 62(7): 1565-1572.

6. Kulkarni VK, Jadhav DU. A study of anemia in primary hypothyroidism. Int J Adv Med. 2017;4, 383-389. doi: 10.18203/2349-3933.ijam20170522.

7. Wiersinga WM. Hashimoto's Thyroiditis in Thyroid Diseases: Endocrinology. Switzerland. Springer, Cham. 2016.

8. Iddah MA, Macharia BN, Ng'wena AG, Keter A, Ofulla AVO. Thryroid hormones and hematological indices levels in thyroid disorders patients at Moi teaching and referral hospital, Western Kenya. ISRN Endocrinol. 2013; 2015: 1-6.

9. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Arch Intern Med. 2000; 160(4): 526–534.

10. Bremner AP, Feddema P, Joske DJ, Leedman PJ, O'Leary PC, Olynyk JK, et al. Significant association between thyroid hormones and erythrocyte indices in euthyroid subjects. Clin Endocrinol (Oxf). 2012; 76(2): 304–311.

11. Park S, Han CR, Park JW, Zhao L, Zhu X, Willingham M, et al. Defective erythropoiesis caused by mutations of the thyroid hormone receptor α gene. PLoS Genet. 2017; 13(9). e1006991. doi: 10.1371/journal.pgen.1006991

12. Hernik A, Szczepanek-Parulska E, Filipowicz D, Abdolall A, Borowczyk M, Wrotkowska E, et al. The hepcidin concentration decreases in hypothyroid patients with Hashimoto's thyroiditis following restoration of euthyroidism. Sci Rep. 2019; 9: 16222. doi: 10.1038/s41598-019-52715-3