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Opinion

COVID-19 Vaccine Related Painless Reactive Thyroiditis

Dermawan, Andrew[1], Muthucumarana Kalindu[2], Anvardeen Kalilur[3], Chandran Sukesh[4]

[1]*Andrew Dermawan, BMed/MD, SJOG Midland Public & Private Hospital, Perth, Australia*
Muthucumarana, MD, FRACP, SJOG Midland Public & Private Hospital, Perth, Australia
[3]*Kalilur Anvardeen, MBBS, FRACP, SJOG Midland Public & Private Hospital, Perth, Australia*
[4]*Sukesh Chandran, MD, MRCP(UK), FRCP Edin, FRACP, SJOG Midland Public & Private Hospital, Perth, Australia*

***Corresponding author**
Andrew Dermawan, BMed/MD, SJOG Midland Public & Private Hospital, Perth, Australia, andrew.dermawan@health.wa.gov.au , Tel: +61 8 9462 4000

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Abstract

In the second year of the SARS-COV-2 global pandemic, there have been many vaccines that has been produced all around the globe. Despite it being safe to be administered, its side effect profile is not fully understood yet. This report aims to document a case of symptomatic hyperthyroidism developing three days after first dose of the Pfizer-BioNTech vaccine. With undetectable TSH, high free T3 and T4, negative thyroid antibodies and thyroid stimulating immunoglobulins, and zero uptake on his thyroid uptake scan, this is consistent with painless reactive thyroiditis, likely vaccine-related due to the time frame.

ABBREVIATIONS

TFT; thyroid function test, **TSH;** thyroid stimulating hormone, **COVID-19;** coronavirus disease 2019

INTRODUCTION

In the second year of the SARS-COV-2 global pandemic, there have been many vaccines that have been produced all around the globe. Despite it being safe to be administered, its side effect profile is not fully understood yet. This report aims to document a case of symptomatic hyperthyroidism developing three days after first dose of the *Pfizer-BioNTech* vaccine.

CASE PRESENTATION

Mr A is a 43-year-old male who presented with two days history of lethargy, malaise and palpitation, with onset reported three days after his first dose of COVID-19 vaccination (*Pfizer-BioNTech*). There is no tremor, diaphoresis, fever, and weight loss or heat intolerance. There is also no infective symptom such as cough, coryzal symptom, shortness of breath, diarrhoea, dysuria, skin rash, nausea, or vomiting. He does not have any significant past medical history and is not taking any regular medications. He does not use any over the counter medication, or any substance like alcohol or smoking. At time of examination, his heart rate is 90 – 100, with an electrocardiogram showing normal sinus rhythm, and his blood pressure is 135/70. There is no evidence of thyrotoxicosis. There is no neck lump, no exophthalmos, lid lag or hand tremor. At this stage, there are 2 other patients with similar presentations of palpitations occurring within 3 days of receiving COVID-19 vaccination, and they have similar picture of hyperthyroidism on their TFT result, with negative thyroid antibodies. Vaccine-related thyroiditis is again suspected.

Investigation

His thyroid function test (TFT) shows a low TSH of 0.01 mU/L, high free T4 of 22 pmol/L and high free T3 of 9.2 pmol/L. His thyroid antibodies are also negative: anti thyroid peroxidase (anti-TPO) level of <3.0 IU/ml, anti-thyroglobulin (anti-TG) level of <4 IU/ml and thyroid stimulating immunoglobulins (TSI) are negative. His inflammatory markers including white cell count and C-reactive protein are also normal. His nasopharyngeal swab is negative for COVID-19 PCR. He subsequently had a thyroid uptake scan (picture shown below), with a total thyroid uptake of 0%. In the absence of a recent exogenous iodide administration, the features are consistent with thyroiditis, with no evidence of active Grave's disease or a toxic nodule (Figure 1).

Differential Diagnosis

Mr A's presentation is consistent with COVID-19 vaccine related painless reactive thyroiditis. The likely trigger would be his COVID-19 vaccination as it was administered two days prior to his symptom onset. One possible differential diagnosis would be reactive thyroiditis from a recent infection. However, given that he was asymptomatic prior to his COVID-19 vaccination, and he had a negative swab, therefore an active COVID infection is unlikely. In addition, there are no community transmitted cases of COVID-19 in Perth for over three months at the time of report. Hashimoto's thyroiditis is also a differential diagnosis, but unlikely given that his autoantibodies were negative. He is also not on any medications that can induce thyroiditis, such as amiodarone, lithium, tyrosine kinase inhibitors, and checkpoint inhibitor immunotherapy.

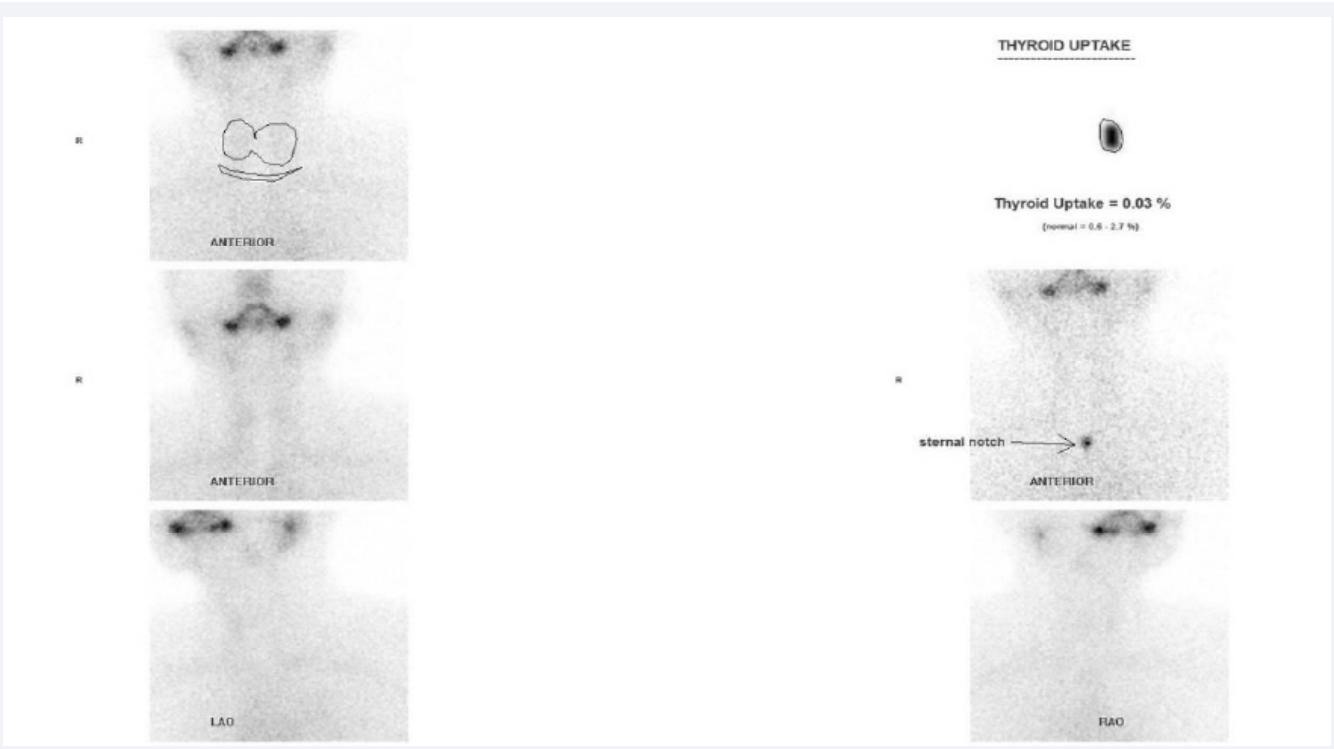

Figure 1 Thyroid uptake scan showing total thyroid uptake of 0%.

Treatment

He is diagnosed with vaccine-related reactive thyroiditis. Propranolol 10mg bd is prescribed for his palpitations, but no steroid treatment is required yet.

Three weeks later, he was followed up with repeat TFT. It showed a similar picture of hyperthyroidism, with TSH of < 0.03 mU/L, free T4 of 24pmol/L and free T3 of 10.5 pmol/L. Due to lack of improvement and persistent symptoms, he is then commenced on prednisolone 20mg daily, to be tapered by 5mg every week once TFT shows improvement.

Outcome

Two months later, Mr A symptoms have completely resolved following commencement of prednisolone. He has weaned off his prednisolone completely. His repeat TFT has also normalised to TSH of 1.49 mIU/L, free T4 of 12.6 pmol/L, and free T3 of 5.9 pmol/L, reflecting a euthyroid state. He is also referred to vaccination safety clinic.

DISCUSSION

COVID-19 is a prevalent global pandemic in the current times and there are many recently developed vaccines administrated around the globe. According to the Centre of Disease Control and Prevention (CDC), there are currently three main types of COVID-19 vaccine that are authorised and recommended or undergoing phase 3 clinical trial.(1) Here in Perth, Western Australia, there are two vaccines currently in use: *Pfizer-BioNTech* and *Oxford-AstraZeneca*. There has not been any new case of COVID-19 in the community for about one year, until one reported case of quarantine hotel worker transmission on 31 January 2021 which prompted a state-wide lockdown for one week.(2) This is followed by a recent community transmitted case on 23 April 2021, which also prompted lockdown for 3 days, with no further new case after.(3) Although the initial stage of testing has deemed them to be safe for use, however the full side effect profile remains unknown. According to the World Health Organisation (WHO), like many vaccines, most side effects are mild and moderate and resolves within a few days, namely injection site reaction, fever, fatigue, headache, muscle pain, chills, and diarrhoea.(4) Rare, but serious, side effects include anaphylaxis.(4) Recently, there have been case reports of Oxford-AstraZeneca vaccine causing increased risk of blood clots.(5) This resulted in 6 EU countries halting the rollout of the vaccine. However, only a small number of cases were reported (37 cases) in people who have received the vaccine.(6) And after an investigation by the European Medicine Agency (EMA), it is concluded that the vaccine is not linked with increased risk of blood clots and is both safe and effective.(7) However, there has been more cases of serious clotting side effects in Western Australia.(8) This prompted the Australian Health Department to only administer the Oxford-AstraZeneca vaccine to adults over 50 years old, while Pfizer-*BioNTech* is preferred in those under 60 years.(9) This report aims to highlight a potential correlation of COVID-19 vaccine with hyperthyroidism. Whether there is a direct link remains unknown. To date, all the published cases of thyroid disease after COVID-19 vaccination do not provide sufficient mechanism to prove that it is not a coincidence. There have been several case reports of COVID-19 infection causing subacute thyroiditis, but not the vaccine.(10) There have also been case reports of hepatitis B vaccine resulting in autoimmune thyroid disorders, such as Grave's disease and Hashimoto's

thyroiditis.(11) However, a 2007 study with a sample size of 1,785 cases showed that there was no observed increased risk.(11) There is also no clear guideline in managing vaccine-related thyroiditis. Our management in this case is based on the treatment recommendation for painless reactive thyroiditis. (12) Many patients with thyroiditis require no treatment during either hyperthyroid or hypothyroid phase because thyroid dysfunction is rarely severe and is transient.(12,13) During the hyperthyroid phase, patients who are symptomatic or at increased risk of atrial fibrillation, should be treated with beta blockers, such as propranolol or atenolol, unless there is contraindication.[17,18] In very rare cases of severely deranged TFTs, glucocorticoids have shown some success.(13,14) There is no role for antithyroid drugs (ie, carbimazole) or radioactive iodine, because the hyperthyroidism is not caused by excess thyroid hormone synthesis and because uptake of radioiodine is very low.(13,14) A repeat thyroid function test should be done in several weeks to ensure that it normalises, and to watch for hypothyroid phase, both supporting the diagnosis of painless reactive thyroiditis.(12,13) Occasionally patients may have sufficient symptoms of hypothyroidism which necessitates thyroxine replacement therapy (levothyroxine,T4) (16,17). The usual dose of levothyroxine is 50-100mcg daily with periodic monitoring of TFT (12).

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