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Post COVID19 Vaccine - Thyroid Dysfunctions: A Case Report and Review of the Literature

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Abstract

Background: According to the WHO dash board 2021, it has been estimated that more than 234 million who confirmed COVID-19 cases, have been reported, and more than 6 billion vaccine doses have been administered worldwide, where thyroid dysfunction appeared to be a growing event, which might be associated with SARS-CoV-2 infection; raising the issue for proper evaluation and highlights a path for a new challenge, and novel research field.

Patients and Methods: A young teenager male with no history of any previous medical condition or any special habit of medical importance, developed thyroid dysfunction post COVID-19 vaccination with viral vector vaccine diagnosed by multidisciplinary approach and evaluated by clinical examination, laboratory investigations and thyroid imaging, in Egypt. For 1-2 days post vaccination, he developed the normal expected side effects of the vaccine, in the form of low-grade fever reaching up to 38ºC, mild myalgia, infrequent headache. So, antipyretic was given in the form of paracetamol. 7-10 days following COVID-19 viral Vector vaccine, he started to develop palpitation, progressed through a whole one and half month post vaccination to appear on moderate exertion, then on very mild exertion, progressed to occur at rest, accompanied by an increase sensation to hot weather. On examination: Regular pulse but at rate of 120/min at rest, temperature 37ºC, no lymphadenopathy, normal thyroid without any swellings on palpation, tachycardia, while other systems were normal. There was mild to moderate cervical pain, and anterior neck pain region.

Results: Laboratory investigations revealed elevated liver enzymes 2-3 folds, TSH=0.002Uiu, T3=15.95pg/ml, T4= 2.7ng/dl, with other labs within normal values. Cardiography showed hyperdynamic circulation, thyroid ultrasonography detected a picture suggestive of Graves' disease, while Tcm thyroid scan confirmed the diagnoses. The teenager male was confirmed to have Graves' disease/thyroid dysfunction and elevated liver enzymes as well, under follow-up.

Conclusions: It seems that the viral vector vaccine for COVID-19 may be a possible initiator and/or triggering factor for susceptible subjects with either a family history or not. It could be also, causing flaring up a hidden inactive disease with rapid activation to these susceptible subjects.

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Key Words: *Post COVID-19 vaccine – Thyroid dysfunction – Graves' disease.*

Introduction

SEVERAL types of vaccines with different mechanisms of action such as: Inactivated vaccine, adenovirus vectored, or mRNA have been manufactured and directed against COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV-2), they have initially shown apparent safety with partial protection [1]. According to the WHO dashboard 2021, it has been estimated that more than 234 million who confirmed COVID-19 cases, have been reported, and more than 6 billion vaccine doses have been administered worldwide, where thyroid dysfunction appeared to be a growing event, which might be associated with SARS-CoV-2 infection; raising the issue for prober evaluation and highlights a path for a new challenge [2].

Case Presentation

A Young teenager male 18 years old and 1-day, normal body built, normotensive 110/70, pulse 65/ minutes, afebrile, excellent general condition, no history of any previous medical issue, and no special habits of medical importance; non-smoker or excessive coffee or tea habits. This was his condition before giving the viral Vector vaccine Ad26. cov2-s (J &J/Janssen) for COVID-19 on the 20th of September 2021, Egypt. For 1-2 days post vaccination, he developed the normal expected side effects of the vaccine, in the form of low-grade fever reaching up to 38ºC, mild myalgia, infrequent headache. So, antipyretic was given in the form of paracetamol. 7-10 days following COVID-19 viral Vector vaccine, he started to develop palpitation, progressed through a whole one and half month post vaccination to appear on moderate exertion, then on very mild exertion,

progressed to occur at rest. On the 26 th of November, he went to a cardiologist at a private hospital asking for prober evaluation and thorough medical advice. But only D-dimer was asked and found to be 0.27/0.5U/ml, excluding embolism. So, the cardiologist gave the patient a beta- blocker (Indral) 10mg/d, and to be re-assessed after ten days. Actually, the patient did not take the prescribed medication, and sought a second medical opinion same day evening with a rheumatologist consultant. A detailed history was taken with specific questions focusing on general body temperature; where an increase sensation to hot weather (hyperthermia), even during this cold autumn-winter seasonal variation, besides, the palpitation annoying the patient with a progressive course. The patient came, complaining from mild to moderate cervical pain, and anterior neck pain region. On a more detailed local cervical spine examination, it was found that: no abnormality detected except anterior at the region of C4,5 where tenderness at the level of thyroid gland. Cervical joint movements and range of motion was normal, except for mild limitation on rotation and paracervical tenderness, as well. No evidence of disc disorders or herniation on clinical and neurological examination. Extra-articular examination has shown pulse was regular but at rate of 120/min at rest ! !, temperature 37ºC, no lymphadenopathy, normal thyroid without any swellings on palpation, tachycardia, while other systems were normal.

For a wider scope management, fast multidisciplinary approach was sought to evaluate the patient's general condition. On 27 th of November 2021, a consultant cardiologist, who performed a meticulous clinical examination and imaging by both E.C.G: Which revealed sinus rhythm and possible acute pericarditis. Echocardiography was done twice showing: A picture of severe hyperdynamic circulation, mild aortic and tricuspid incompetence, good systolic function, ejection fraction (EF) 60% within normal range, no evidence of pulmonary hypertension with pulmonary artery systolic pressure (PASP) 25mmgh, dilated right ventricle with preserved function and right ventricle apical hyper trabiculations and impaired apical motion. No pericardial effusion, no intracardiac thrombi. A hepatologist and gastroenterologist to assess the abdominal organs excluding further abnormalities. Two endocrinologists were sought: A consultant who ordered all thyroid functions, in addition to routine labs including: Complete blood picture, liver enzymes, and serology: T3, T4 and TSH, also, auto antibodies for any thyroid abnormalities. Table (1).

Table (1): Laboratory investigations of the male teenager.

Laboratory investigations:	
ESR (mm/1 st hr)	5
TLC (x10^3/mm^3)	5.2
Platelets (x10^3/mm^3)	209
Hemoglobin (g/dl)	14.3
CRP (mg/dl)	0.9
Creatinine (mg/dl)	^0.68 (0.7-1.3)
ALT (U/L)	153/50
AST (U/L)	65/34
D-dimer (U/ml)	0.27/0.5
Ferritin ng /ml	152 (30-400)
CPK (U/L)	156 (32-294)
CK-MB (ng/ml)	0.6 (0-5)
Troponin I	0.01 (0.004)
S. albumin (g/dl)	4 (3.5-5.2)
Gamma GT (U/L)	35(0-55)
Bilirubin (Total) mg/dl	0.63 (0.3-1.2)
Bilirubin (Direct) mg/dl	0.13 (0-0.2)
TSH Uiu	^0.002 (0.48-4.17)
T3 (pg/ml)	T 15.95 (2.3- 3.7)
T4 (ng/dl)	2.7 (0.89-1.37)
Anti TG Abs. (IU/ml)	3 (<4,1)
Anti-APO (U/ml)	1.2 (<5.6)

ESR Erythrocyte sedimentation rate.
TLC Total leucocytic count.
CRP C-reactive protein.
ALT Alanine transaminase.
AST Aspartate transaminase.
CPK Creatine phosphokinase.
S Serum.
GT Glutamate.
TSH Thyroid stimulating hormone.
T3 Triiodothyronine.
T4 Thyroxine.
Anti TG Abs : Anti thyroglobulin antibodies.
Anti-APO : Anti thyroid.

The second endocrinologist and Internal Medicine: Ordered urgent: Thyroid ultrasonographic imaging (U/ S) and Tc-99m pertechnetate thyroid scanning. Ultrasonographic examination of the thyroid gland revealed that, both thyroid lobes and isthmus are relatively prominent in size with inhomogenous parenchymal texture. No definite masses or calcifications. Right lobe measures about 2.3x 2.4x5.4cm, left lobe measures about 1.3x1.7x4.5cm, and isthmus measures about 0.4cm; A picture suggestive of thyroiditis. No other abnormalities were detected. Tcm thyroid scanning has shown an increase uptake 8.5% (normal values: 0.5-4%). Hyperthyroid state attributed to primary diffuse toxic goiter (Graves' disease). Fig. (1).

So, medical treatment based on both clinical, laboratory and imaging started at once on 4 th of December 2021. Treatment given: Neomercazole 5mg 3x3=45m/d; a total of nine tablets daily, and Concor 2.5mg/d. An advice of complete rest was given to the young teenager, and to do non- exertional activities with adequate healthy daily living. Also, laboratory investigations repeated after 1.5

months from the start of medical treatment, for re-evaluation. Follow-up was done on the 16 th of December 2021, and middle of January 2022, still on the previously mentioned medications with normal cervical mobility and range of motion, monitoring his pulse which was slowly improving reaching to be 80/min, regular with less palpitation. Although he stopped Bisoprolol (Concor) intake, however hyperthermia is still a complaint. TSH low 0.02 Uiu and elevated liver enzymes by two folds. Last laboratory done on the 23 rd of February 2022 has shown normalized liver enzymes. However, still a picture of thyroid dysfunction and for a close follow-up.

Family history:

His grandmother, his uncle and aunt (from side of his father) had history of thyroid dysfunctions (hypothyroidism/hyperthyroidism) and, all of them were on treatment.

Table (2): Baseline characteristics, laboratory & imaging of the recorded cases Post COVID-19 viral vector vaccination with prominent thyroid dysfunctions [adapted from Lee et al., 2021].

Age/ Sex	Vacci-ne	Main Com-plaint	Sym-ptom onset PV/d	T4	TSH	Anti TPO Ab	Anti-TG Ab	TSHR-Ab	ESR/ CRP	Thyroid Scan	TH.US	Diagnosis
46/F	Vector/AZ-1st	Chest pain-Dyspnea	1	33.9	0.01	77.7	137.5	6.4	5/–ve	38.6	↑vascularity	GD + HT Failure
73/F	Vector/AZ-2nd	Weight loss Dyspnea	14	73.8	<0.008	41.03	NA	6.3	NA	54.2	↑vascularity	GD
34/M	Vector/Janssen	Weight loss Palpitation	14	26.6	<0.008	NA	NA	4.2	NA	NA	↑vascularity	Recurrent GD
39/F	Vector/AZ-2nd	Neck Pain	4	31.4	0.11	<15	NA	<1.1	63/28.6	3.2	Ill-defined hypoechoic lesions	SAT
73/ F	Vector/AZ-1st	Fever Neck Pain	11	94.7	0.012	<15	39.7	1.41	85/34.6	NA	Ill-defined hypoechoic lesions	SAT
39/M	Vector/Janssen	Fever Neck Pain	14	36.9	<0.012	<15	295	2.9	74/36.5	13.8	Diffuse goiter Ill-defined hypoechoic lesion	GD/SAT
33/M	Vector/Janssen	Bilateral Leg Weakness	10	37.4	0.012	<15	203	<1.1	37/5.1	3.4	Heterogenous echogenicity, ↑vascularity	PT with TPP

GD : Grave's disease.
TH : Thyroid.
SAT : Subacute thyroiditis.
PT : Painless thyroiditis.
TSH : Thyroid stimulating hormone.
TPO : Thyroid peroxidase.
TPP : Thyrotoxic periodic paralysis.
Tg : Thyroglobulin.
TSHR-Ab : TSH receptor antibody.
AZ : Astrazenica.
PV : Post vaccinated.
HT : Heart.

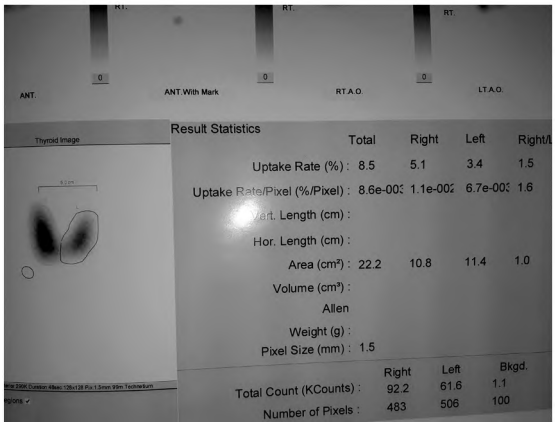

Fig. (1): Tcm thyroid Scanning of the male patient with Hyperthyroidism.

Discussion

The pathogenesis of COVID-19 induced thyroid dysfunction might be related to either direct viral infection or abnormal inflammatory-immune responses. Abundant expression of the SARS-CoV-2 receptor (angiotensin-converting enzyme 2) mRNA in thyroid cells might suggest that the thyroid gland could be a target organ of COVID-19 infection [3]. It was reported that, twenty-two cases of subacute thyroiditis were associated with COVID-19 infection [4], and thyrotoxicosis has been reported in up to 20.2% of patients hospitalized for COVID-19 in a single-center retrospective study [5].

Seven cases were detected during a time interval between March to July 2021, as been shown in Table (2) adapted from Lee and others. All of the reported cases were presenting with thyrotoxicosis after COVID-19 vaccination; three cases were diagnosed to have Graves' disease (GD), two had subacute painful thyroiditis (SAT), one patient was diagnosed with concurrent GD and SAT, while the seventh patient had painless thyroiditis with periodic paralysis (PTT). The first three cases had normal thyroid functions before they were giving the vaccination. While the other cases although, they did not do the thyroid functions before vaccination, but have shown no symptoms before [1]. It was speculated that one of possible mechanisms, an autoimmune response after COVID-19 vaccination due to the spike glycoprotein of SARS-CoV-2 sharing a genetic similarity with a human protein [6].

Hyperthyroidim/Graves' disease is on the autoimmune thyroiditis (AIT) caused by autoantibodies binding to the thyroid stimulating hormone receptor antibody (TSHR-Ab), stimulating the thyroid with overproduction to thyroid hormones. Thus, from the previously reviewed case reports, it could be presumed that COVID-19 vaccines can cause not only destructive thyroiditis but also AIT, as well [1].

Conclusions:

It is speculated and observed from that documented and detailed history that Vector vaccine Ad26. cov2-s (Janssen) seems to be a triggering factor for susceptible subjects with either a family history or not, as well and flaring up a hidden inactive disease with rapid activation to these subjects. It is known that Benefits may over weigh risks in any medical condition. But is it the condition here that giving this Vector vaccine that is supposed to be effective after 28 days from its intake? It is expected to raise immunity against COVID-19 for a period up to 3-4 months mostly! Although, not giving a full protection, but seemed to be a possible triggering factor, to cause these major side effects, that the patient is still under treatment, and we don't know the prognosis in the near or far future. Thus, non-biased bioethical research should be directed towards investigating the prevalence and pathogenesis of thyroid dysfunctions following COVID-19 vaccination, with its different mechanisms of action.

Recommendations:

1- A meticulous proper history and/or possible investigations should be directed towards those with a family history of thyroid dysfunctions before giving Vector Vaccine (Janssen) especially teenager 18 years old or below. Also, to be clearly labelled in the panflet of this vaccine in the form of precautions and contraindications.

2- A transparent meticulous and non-biased research should be done on the outcome and possible major side effects of the Vaccine. Its' possible hazard effects on susceptible age groups.

3- The unexplained elevated liver enzymes, and whether this is due to a sort of a drug/vaccine injury to the liver with further evaluation.

4- A clear, non-biased scientific research whether these damages, newly discovered, and occurred post vaccination are reversible or not.

5- It worth to finalize recommendations with a wider scope vision: To highlight and raise the natural immunity defence mechanisms by a proper diet rich in zinc, vitamin C, vitamin D, vitamin B and proper water hydration/Proper and safe sun exposure, open air in a non polluted natural green or seaside areas and change to a healthy lifestyle with high spiritual efforts to guard a normal healthy individual, non-phobic from exaggeration in media about COVID-19. As far as I know that any virus, which is naturally made and not laboratory designed, by any new mutations it is weakened and not the opposite as it fades gradually throughout time.

As been asked by the FDA; after a phone call to their HOT LINE, on 16th of December, 2021. This detailed document and notification was transformed to be a written petition about the previously given vaccine to the male patient, and clearly signed to be added as a document alerting, a global warning for a possible major side effect of the COVID-19 Vector vaccine that should be labelled.

This case report is the first recorded case in Egypt, suffered from hyperthyroidism (Grave's

disease)/thyroid dysfunction, caused by Vector Viral Vaccine; Ad26.cov2-s (Janssen), and one of the eight recorded cases around the world just before the end of 2021, post COVID-19 vaccination.

Declarations:

Availability of supportive data Data are available upon request from the authors.

Competing interests: None to declare.

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Consent: An informed consent has been obtained from the patient guardian's and consented to the submission of the case report to the journal.

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A whole respect and appreciation to the case and his parents for sharing the data to give a message about the value of the medical event that needed not to be ignored and thus, be recorded.

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لقاح ما بعد كوفيد ١٩ - اختلالات الغدة الدرقية: تقرير حالة ومراجعة مصادر بحثية أخرى

وفقاً لمعلومات منظمة الصحة العالمية ٢٠٢١، تشير التقديرات إلى أنه تم الإبلاغ عن أكثر من ٢٣٤ مليون شخص أكدوا حالات كوفيد ١٩، وتم إعطاء أكثر من ٦ مليارات جرعة لقاح فى جميع أنحاء العالم، حيث بدأ أن ضعف الغدة الدرقية حدث متزايد، والتى قد تكون مرتبطة بعدوى SARS-CoV2، إثارة القضية من أجل التقييم المناسب وإبراز مسار تحدٍ جديد و مجال بحثى جديد

الطرق: شاب مراهق ليس لديه تاريخ لأى حالة طبية سابقة، طور اختلال وظيفى فى الغدة الدرقية بعد تطعيم كوفيد ١٩ بلقاح ناقل فيروسى تم تشخيصه من خلال التشخيص متعدد التخصصات وتقييمه بالفحص السريرى والفحوصات المخبرية وتصوير الغدة الدرقية، فى مصر. لمدة يوم أو يومين بعد التطعيم، ظهرت عليه الآثار الجانبية الطبيعية المتوقعة للقاح. بعد ٧–١٠ أيام من لقاح ناقل الفيروس كوفيد ١٩، بدأ فى تطوير الخفقان فتطور خلال شهر ونصف بعد التطعيم ليظهر فى مجهود معتدل، ثم فى مجهود خفيف للغاية، ثم فى حالة راحة، مصحوب بزيادة الإحساس بالطقس الحار.

عند الفحص: كان النبض منتظماً، ولكن بمعدل ١٢٠/دقيقة عند الراحة، ودرجة الحرارة ٣٧°، ولا يوجد اعتلال عقد ليمفاوية، وغدة درقية طبيعية دون أى تورم، مع عدم انتظار دقات القلب، بينما كانت الأنظمة الأخرى طبيعية. كان هناك ألم خفيف إلى معتدل فى العنق، وآلام فى الرقبة الأمامية.

النتائج: أظهرت الفحوصات المخبرية ارتفاع إنزيمات الكبد بمقدار ٢–٣ أضعاف مع اختلال بوظائف الغدة الدرقية. ظهر تخطيط القلب الدورة الدموية شديدة الديناميكية، واكتشف التصوير بالموجات فوق الصوتية للغدة الدرقية صورة توحى بمرض جريفز، بينما أكد فحص الغدة الدرقية Tcm التشخيص. تم التأكد من إصابة الفتى المراهق بمرض جريفز / خلل الغدة الدرقية وارتفاع إنزيمات الكبد أيضاً، وتحت المتابعة.

الاستنتاجات: يبدو أن لقاح الناقل الفيروسى للكوفيد ١٩ قد يكون بادئاً محتملاً / أو عاملاً محفزاً للأشخاص المعرضين للإصابة إما بتاريخ عائلى أم لا. يمكن أن يتسبب أيضاً فى اندلاع مرض خفى غير نشط مع تنشيط سريع لهؤلاء الأشخاص المعرضين للإصابة.