Recurring subacute thyroiditis after SARS-CoV-2 mRNA vaccine: A case report

Vasiliki Vasileiou a, Stavroura A. Paschou b,*, Xakousti Tzamali a, Marina Mitropoulou a, Fotini Kanouta a, Theodora Psaltopoulou c, Georgia N. Kassi a

a Department of Endocrinology, Alexandra Hospital, Athens, Greece
b Endocrine Unit and Diabetes Center, Department of Clinical Therapeutics, Alexandra Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece
c Department of Clinical Therapeutics, Alexandra Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

ARTICLE INFO

Keywords:
SARS-CoV-2 vaccination
COVID-19
Vaccination
Thyroiditis
mRNA vaccine

ABSTRACT

SARS-CoV-2 vaccination is the most powerful and promising tool against the COVID-19 pandemic. Millions of people have been vaccinated worldwide. Recently, few cases of subacute thyroiditis following SARS-CoV-2 vaccination with various types of vaccine have been reported. We describe here a 36-year-old woman who presented with subacute thyroiditis 10 days after she had received her first dose of the SARS-CoV-2 mRNA vaccine COMIRNATY (Pfizer/BioNTech); the condition receded but then recurred 10 days after she received her second dose. As vaccination programmes proceed, clinicians' attention and vigilance for such cases will be increased. Physicians need to know that subacute thyroiditis is a mild and self-limiting condition in the majority of cases. Last but not least, the benefits of vaccination against COVID-19 outweigh the side-effects reported so far.

1. Introduction

Subacute thyroiditis (SAT) is a self-limiting inflammatory thyroid disorder. The presenting symptoms usually appear 2–8 weeks after an acute symptomatic or asymptomatic viral infection. Clinical presentation may include general signs of infection, fatigue, front-neck pain and thyroid dysfunction, usually with transient thyrotoxicosis [1].

Many types of virus have been suggested as possible causative agents for SAT, [2] including SARS-CoV-2 [3–6]. In addition, SAT has been described following influenza or hepatitis B vaccination [7–12]. Recently, cases have been reported of SAT following SARS-CoV-2 vaccination with CoronaVac (Sinovac Life Sciences, China) [13–15], Vaxzevria (AstraZeneca, Sweden) [16–20], Spikevax (Moderna Biotech, Spain) [20], Covaxin (Bharat Biotech, India) [21], and Pfizer-BioNTech SARS-CoV-2 mRNA vaccine (BioNTech, Fosun Pharma, Pfizer, Germany and USA) [22–28].

We report here the case of a 36-year-old woman who presented with SAT 10 days after she had received her first dose of the SARS-CoV-2 mRNA vaccine COMIRNATY (Pfizer/BioNTech); the condition receded but then recurred 10 days after the patient had received her second dose.

2. Case presentation

A 36-year-old Caucasian woman was admitted to the outpatient clinic complaining of anterior neck pain that radiated to the ear and jaw, mostly on the left side. She also had fever of up to 37.8 °C, fatigue and palpitations. Her symptoms first appeared 10 days after she had received her first dose of the SARS-CoV-2 mRNA vaccine COMIRNATY (Pfizer/BioNTech) but the condition remitted a few days later without medication. Therefore, the patient did not seek medical attention and proceeded with her second dose of the same vaccine. Ten days after that second dose, the symptoms recurred, with greater intensity of the neck pain and fatigue.

She had no medical history of thyroid disease, nor did she report any viral infection, including SARS-CoV-2 infection, during the previous 3 months. She had had recent diagnoses of ulcerative gastritis and intraocular hypertension. She was being treated for endometriosis with progesterone on a daily basis. Otherwise, her personal and family history were not remarkable. She did not report any adverse events after vaccination in the past. Her clinical examination revealed tenderness in the thyroid region and a mild tremor. Her blood pressure was 115/75

* Corresponding author at: Endocrine Unit and Diabetes Center, Department of Clinical Therapeutics, Alexandra Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece.
E-mail address: s.a.paschou@gmail.com (S.A. Paschou).

https://doi.org/10.1016/j.crwh.2021.e00378
Received 23 November 2021; Received in revised form 19 December 2021; Accepted 21 December 2021
Available online 28 December 2021
2214-9112/© 2021 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license
mmHg and heart rate 100 beats/min; her body temperature was normal. The patient weighed 56.5 kg and her height was 1.61 m and she reported no weight loss over the preceding months.

Her laboratory tests 26 days after 2nd dose of vaccine revealed low TSH concentrations, with slightly elevated FT4 and normal T3 levels. ESR and CRP levels were increased, while blood count was normal. Anti-thyroid peroxidase (anti-TPO) and thyroid stimulating hormone receptor antibodies (TRAb or TSI) were negative. There was an elevation of anti-thyroglobulin (anti-TG) antibodies levels (Table 1). Ultrasound of the neck showed slightly elevated dimensions of the thyroid gland with heterogeneous echogenicity and bilateral hypoechoic areas (Fig. 1). Cervical lymph nodes were not obvious. The Tc99 pertechnetate radionuclide thyroid scan showed poor thyroid uptake (Fig. 2). A diagnosis of subacute thyroiditis was made.

Due to the mildness of symptoms, the patient commenced treatment with paracetamol and ibuprofen. Ten days later, she appeared at the endocrine department complaining of worsening of her neck pain, fever, myalgia and fatigue. Her symptoms were no longer relieved by treatment with NSAIDs. She also reported 1 kg weight loss and cough. TSH was suppressed, FT4 and T3 levels were clearly elevated, and CRP was still high. Her thyroid was enlarged and was tender on palpitation. Treatment with methylprednisolone (16 mg twice a day) was initiated.

The pain and tenderness resolved completely within 48 h and 2 weeks later TSH, FT4 and T3 levels were within normal limits (Table 1). The patient was followed-up on tapering treatment with methylprednisolone. Follow-up was performed by clinical examination and measurement of thyroid hormones.

3. Discussion

SAT is a self-limiting thyroid disorder, commonly associated with upper respiratory viral infection [1]. Several viruses have been considered as causes of SAT, including adenovirus, enterovirus, influenza virus, cytomegalovirus, rubella virus, Epstein Barr virus, Coxsackie virus, and measles virus [2]. SAT may be rarely associated with SARS-CoV-2 infection, as a few cases have been reported recently in the literature [3-6]. Moreover, several cases of SAT after viral vaccines have been reported. Most of them are related to influenza, H1N1 or HBV vaccines [7-12].

Recently, following the massive vaccination programme worldwide, there have been a few reports of thyroid dysfunction after SARS-CoV-2 vaccination, including SAT [13-28] and Graves’ disease [19,29-31]. All types of vaccines have been involved, namely inactivated virus SARS-CoV-2 vaccines CORONAVAC [13-15] and COVAXIN [21], viral vector-based vaccines VAXZEVRIA [16-20,31] and Janssen [19] and

| Case Reports in Women’s Health 33 (2022) e00378 |

**Table 1**

| Laboratory blood tests. |
|-------------------------|
| TSH | T4 | FT4 | T3 | CRP | ESR | anti-TPO | anti-Tg | TRAb (TSI) |
|-------------------------|
| 26 days after 2nd dose | 0.225 mIU/ml | 149 nmol/l | 22.01 pmol/l | 1.96 mg/dl | 59 | 15.72 | 292 | 0.1 |
| 40 days after 2nd dose | 0.028 mIU/ml | 185 nmol/l | 31.67 pmol/l | 6.46 mg/dl | – | – | – | – |
| 54 days after 2nd dose | 0.173 mIU/ml | – | 16.42 pmol/l | 0.773 mIU/ml | – | – | – | – |
| Normal range | 0.4-4 mIU/ml | 58-161 nmol/l | 12-22 pmol/l | < 0.5 mg/dl | 0-20 mm/h | < 34 IU/ml | < 40 IU/ml | < 1.75 U/L |

Fig. 1. Thyroid ultrasound.

Fig. 2. Radionuclide thyroid scan.
mRNA-based vaccines COMIRNATY [22–28] and MODERNA [20].

In this case, the course of disease did not differ from the usual clinical expression of SAT nor did response to treatment. The patient's age and gender were typical: SAT connected to SARS-CoV-2 vaccination concerns predominantly young and middle-aged women (18 out of 21 cases) (ged 26 to 55 years) while males and one female were older (67 to 75 years old). Reports concerning inactivated virus and mRNA-based SARS-CoV-2 vaccines refer to the appearance of symptoms 4–12 days after the first or second dose of vaccine, SAT has been reported 2 weeks after the first dose of the viral-vector based vaccine VAXZEVRIA. In all cases, rapid improvement of clinical symptoms and laboratory findings was achieved either by administration of NSAIDS in most cases or by short-duration corticosteroid treatment. Follow-up in all cases was consistent with mild and uncomplicated course of disease.

Various hypotheses have been raised regarding thyroid autoimmunity after vaccination, such as autoimmune inflammatory syndrome induced by adjuvants (ASIA) or molecular mimicry. Adjuvants are an essential component of vaccines, used mainly to increase the response to vaccination, and may play a role in producing diverse autoimmune and inflammatory responses. Post-vaccination phenomena have been described, including autoimmune endocrine diseases, mostly after receipt of an HPV, influenza or hepatitis B vaccine. The clinical spectrum of reported thyroid disease includes both Hashimoto’s thyroiditis and Graves’ disease [32]. Regarding molecular mimicry, cross-reactivity between the coronavirus spike protein produced after vaccination and thyroid cell antigens is suggested as underlying mechanism [33].

The fact that SAT may arise a few days after SARS-CoV-2 vaccination requires medical attention for a possible causal relation. Interestingly, in our case, SAT recurrence and deterioration were observed after the second dose of the mRNA vaccine. This manifestation is consistent with the rechallenge criterion for causality assessment according to the WHO-UMC system [34], strongly suggesting a possible cause-and-effect relationship.

SAT after COVID-19 vaccination is a very rare condition taking into consideration the vaccination of millions of people worldwide. On the other hand, because of its mild clinical course, also it may be underreported as an adverse event. As vaccination programmes proceed, clinicians’ attention will be probably increased. However, physicians need to know that SAT is a self-limiting and mild disease with only transient thyroid dysregulation in the vast majority of cases. Last but not least, the benefits of vaccination against COVID-19 outweigh any mild and rare side-effects reported so far.

**Contributors**

Vasiliki Vasileiou wrote the initial draft.
Stavrula A. Paschou wrote the initial draft.
Xakousti Tzamali revised the manuscript.
Fotini Kanouta revised the manuscript.
Theodora Psaltopouli revised the manuscript.
Georgia N. Kassi revised the manuscript.

All authors took care of the patient. All authors approved the final version of the article.

**Funding**
The authors received no funding from an external source for the publication of this case report.

**Patient consent**

Obtained.

**Provenance and peer review**

This article was not commissioned. Peer review was directed by Professor Margaret Rees independently of Stavrula A. Paschou, one of the authors and a member of the *Case Reports in Women’s Health* editorial board, who was blinded to the process.

**Conflict of interest statement**

The authors declare that they have no conflict of interest regarding the publication of this case report.

**References**

[1] A. Tabassom, V. Chippa, M.A. Edens, StatPearls [Internet], StatPearls Publishing, Treasure Island (FL), 2021.
[2] R. Desaiilloud, D. Hober, Viruses and thyroiditis: an update, Virol. J. 6 (2009) 5, https://doi.org/10.1186/1743-4226-6-5.
[3] D. Dworakowska, S. Morley, N. Mulholland, A.B. Grossman, COVID-19-related thyroiditis: a novel disease entity? 95 (3) (2021 Sep) 369–377, https://doi.org/10.1111/cen.14453.
[4] A. Brancatella, D. Ricci, D. Cappellani, et al., Is subacute thyroiditis an underestimated manifestation of SARS-CoV-2 infection? Insights From a Case Series, J. Clin. Endocrinol. Metab. (2020 Aug 11), https://doi.org/10.1210/clinem/dgaa537.
[5] I. Muller, D. Cannavaro, B. Dazzi, D. Govelli, G. Mantovani, A. Muc sabotello, E. Ferrante, E. Ori, V. Resti, V. Longari, M. Guzzocora, A. Bandera, E. Lazzaroni, A. Dolci, F. Ceriotti, T.E. Re, A. Gori, M. Arosio, M. Salvi, SARS-CoV-2-related atypical thyroidsitis, Lancet Diabetes Endocrinol. 8 (9) (2020) 739–741, https://doi.org/10.1016/S2213-8587(20)30266-7.
[6] P. Caron, Thyroiditis and SARS-CoV-2 pandemic: a review, Endocrin. 72 (2021) 326–331, https://doi.org/10.1007/s12021-020-02689-y.
[7] C.M. Giris, R.R. Russo, K. Benson, Subacute thyroiditis following the H1N1 vaccine, J. Endocrinol. Invest. 33 (2010) 506, https://doi.org/10.3881/jei.2010.46633.
[8] J. Herran Martinez, E. Corder, M. Uzcategui, M. Garcia, S. Sostre, A. Garcia, Subacute thyroiditis and dysrythrophesia after influenza vaccination suggesting immune dysregulation, Bol. Asoc. Med. P R. 103 (2) (Apr-Jun 2011) 48–52.
[9] F.A. Altay, G. Altay, M. Altay, Subacute thyroiditis following seasonal influenza vaccination, Hum. Vaccin Immunother. 12 (2016) 1033–1034, https://doi.org/10.1080/21645515.2015.1171716.
[10] A. Passah, S. Arora, N.A. Damle, K.S. Reddy, D. Khandelwal, S. Aggarwal, Occurrence of subacute thyroiditis following influenza vaccination, Indian J. Endocrinol. Metab. 22 (2018) 713–714, https://doi.org/10.4103/ijem.IJEM.237_18.
[11] J. Toft, S. Larsen, H. Toft, Subacute thyroiditis after hepatitis B vaccination, Endocr. J. 45 (1998) 135.
[12] J.Y. Hsiao, S.C. Hsin, M.C. Hsieh, P.J. Hsia, S.J. Shin, Subacute thyroiditis following influenza vaccine (Vaxigrip) in a young female, Kaohsiung J. Med. Sci. 22 (2006) 297–300, https://doi.org/10.1016/s1607-5316(09)70131-5.
[13] B.G. Iremili, S.N. Sendur, Ul. Unlurturk, Three cases of subacute thyroiditis following SARS-CoV-2 vaccine: post-vaccination ASIA syndrome, J. Clin. Endocrinol. Metab. (2021), https://doi.org/10.1210/clinem/dgaa572.
[14] E.S. Saygılı, E. Karalıklı, Subacute thyroiditis after inactiv SARS-CoV-2 vaccine, BMJ Case Rep. 14 (10) (2021 Oct 1), e244711, https://doi.org/10.1136/bcr-2021-244711.
[15] M. Şahin Tekin, S. Şahinsoy, G. Yorulmaz, Subacute thyroiditis following COVID-19 vaccination in a 67-year-old male patient: a case report, Hum. Vaccin Immunother. (2021 Jul 1) 1–3, https://doi.org/10.1080/21645515.2021.1947102.
[16] S. Dyibo, Subacute thyroiditis after receiving the adenovirus vectored vaccine for coronavirus disease (COVID-19), Cureus. 13 (2021), e16045, https://doi.org/10.7759/cureus.16045.
[17] G.M. Ratnayake, D. Dworakowska, A.B. Grossman, Can COVID-19 immunisation cause subacute thyroiditis? Clin. Endocrinol. (2021) 1–2, https://doi.org/10.1111/cen.14555.
[18] L. Das, S.K. Bhadada, A. Sood, post-COVID-vaccine autoimmune/inflammatory syndrome in response to adjuvants (ASIA syndrome) manifesting as subacute thyroiditis, J. Endocrinol. Invest. (2021 Sep 28) 1–3, https://doi.org/10.1007/s40618-021-01681-7.
[19] K.A. Lee, Y.J. Kim, H.Y. Jin, Thyrotoxicosis after COVID-19 vaccination: seven case reports and a literature review, Endocrin 74 (3) (2021) 470–472, https://doi.org/10.1007/s12020-021-02896-z.
[20] C. Bornemann, K. Woyk, C. Bouter, Case report: two cases of subacute thyroiditis following SARS-CoV-2 Vaccination, Front. Med. (Lausanne). (8) (2021 Aug 24), 737142, https://doi.org/10.3389/fmed.2021.737142.
[21] P. Soltanpoor, G. Norouzi, Subacute thyroiditis following COVID-19 vaccination, Clin. Case Rep. 9 (110) (2021 Oct 4), e04812, https://doi.org/10.1002/ccr3.4812.
[22] F. Franquemont, J. Galvez, Subacute thyroiditis after mRNA vaccine for Covid-19, J. Endocrine Soc. 5 (2021), https://doi.org/10.1002/jendso.bvah048.1954, A956–7.
[23] J. Schimmel, E.L. Alba, A. Chen, M. Russell, R. Srinath, Letter to the editor: thyroiditis and thyrotoxicosis after the SARS-CoV-2 mRNA vaccine, Thyroid. (2021), https://doi.org/10.1089/thy.2021.0184.

[24] A. Kyriacou, S. Ioakim, A.A. Syed, COVID-19 vaccination and a severe pain in the neck, Eur. J. Intern. Med. S0953-6205 (21) (2021 Oct 18), https://doi.org/10.1016/j.ejim.2021.10.008, 00338–1.

[25] A. Siolos, K. Gartzonika, S. Tigas, Thyroiditis following vaccination against COVID-19: report of two cases and review of the literature, Metabol. Open. 12 (2021 Dec), 100136, https://doi.org/10.1016/j.metop.2021.100136.

[26] S. Chatzi, A. Karampela, C. Spiliopoulou, G. Boutzios, Subacute thyroiditis after SARS-CoV-2 vaccination: a report of two sisters and summary of the literature, Hormones (Athens). (2021 Oct 22) 1–3, https://doi.org/10.1007/s42000-021-00332-z.

[27] M.S. Jeeyavudeen, A.W. Patrick, F.W. Gibb, A.R. Dover, COVID-19 vaccine-associated subacute thyroiditis: an unusual suspect for de Quervain’s thyroiditis, BMJ Case Rep. 14 (11) (2021), e246425, https://doi.org/10.1136/bcr-2021-246425.

[28] L.M. Raven, A.I. McCormack, J.R. Greenfield, Letter to the editor from Raven: three cases of subacute thyroiditis following SARS-CoV-2 vaccine, J. Clin. Endocrinol. Metab. (2021 Nov 9) dgab822, https://doi.org/10.1210/clinem/dgab822.

[29] O. Vera-Lastra, A. Ordinola Navarro, M.P. Cruz Domínguez, G. Medina, T.I. Sánchez Valadez, L.J. Jara, Two cases of Graves’ disease following SARS-CoV-2 vaccination: an autoimmune/inflammatory syndrome induced by adjuvants, Thyroid. 31 (9) (2021 Sep) 1436–1439, https://doi.org/10.1089/thy.2021.0142.

[30] G. Zettinig, M. Krebs, Two further cases of Graves’ disease following SARS-CoV-2 vaccination, J. Endocrinol. Invest. (2021 Aug 3) 1–2, https://doi.org/10.1007/s40618-021-01650-0.

[31] L. di Filippo, L. Castellino, A. Giustina, Occurrence and response to treatment of Graves’ disease after COVID vaccination in two male patients, Endocrine (2021 Nov 2) 1–3, https://doi.org/10.1007/s12020-021-02919-3.

[32] A. Watad, P. David, S. Brown, Y. Shoenfeld, Autoimmune/inflammatory syndrome induced by adjuvants and thyroid autoimmunity, Front. Endocrinol. (Lausanne). 7 (2016) 150, https://doi.org/10.3389/fendo.2016.00150.

[33] A. Vojdani, D. Kharrazian, Potential antigenic cross-reactivity between SARS-CoV-2 and human tissue with a possible link to an increase in autoimmune diseases, Clin. Immunol. 217 (2020), 108480, https://doi.org/10.1016/j.clim.2020.108480.

[34] The use of the WHO-UMC system for standardised case causality assessment, The Upala Monitoring Center, https://www.who.int/medicines/areas/quality_safety/safety_efficacy/WHOcausality_assessment.pdf [Last accessed on 18 December 2021].