

# Subacute thyroiditis: New entity?

Mara Carsote<sup>1,2</sup>, Claudiu Tupea<sup>1</sup>, Florica Sandru<sup>2,3</sup>, Diana Elena Rentea<sup>1</sup>, Stefania Zugravu<sup>1</sup>,  
Claudia Mehedintu<sup>2,4</sup>, Mihai Cristian Dumitrascu<sup>2,5</sup>

<sup>1</sup> "C.I. Parhon" National Institute of Endocrinology, Bucharest, Romania

<sup>2</sup> "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

<sup>3</sup> Elias Emergency Hospital, Bucharest, Romania

<sup>4</sup> "Nicolae Malaxa" Clinical Hospital, Bucharest, Romania

<sup>5</sup> University Emergency Hospital, Bucharest, Romania

## ABSTRACT

In 2021, the scientific community was marked by the introduction of vaccine against COVID-19. This is major step in overcoming the pandemic, but it does not mean that several side effects or precautions are not related to the immunization; however, the current level of statistical evidence concerning potential negative effects is low, as logically expected at this point. We aim to introduce a female case who was confirmed with subacute thyroiditis after COVID-19 vaccination. Prompt recognition of subacute thyroiditis avoids unnecessary investigations, hospitalizations or even exposure to antibiotics as seen in this case. Early intervention with anti-inflammatory medication releases the symptoms. The association with vaccine against COVID-19 might be incidental or not; more evidence is needed but as far as we might think nowadays, the connection is possible, thus the importance of specific awareness.

**Keywords:** thyroid, thyroiditis, virus, vaccine, subacute thyroiditis, inflammation, COVID-19, coronavirus, vaccination, immunization

## INTRODUCTION

In 2021, the scientific community was marked by the introduction of vaccine against COVID-19 (1,2,3). This is major step in overcoming the pandemic, but it does not mean that several side effects or precautions are not related to the immunization; however, the current level of statistical evidence is low, as logically expected at this point (5,6,7). It has been suggested, but not clearly proven, that immunization against COVID-19 might induce Guillain-Barré syndrome, hepatitis/acute hepatic failure, worsening of some immune-mediated neurological, skin and cardiac conditions etc. (8,9,10).

## AIM

We aim to introduce a female case who was confirmed with subacute thyroiditis after COVID-19 vaccination.

## METHOD

This is case presentation. The patient agreed to anonymously introduce the data below.

## CASE PRESENTATION

### Admission

This is a 54 years old non-smoking female, coming from non-endemic area, who was admitted for the following clinical picture (since last 2-3 weeks): dry cough, odynophagia, fever (maximum 39.4 degrees Celsius). She does not have a relevant medical history, neither a family medical history.

### Recent medical history

Her recent medical history was the following: at first she was treated at home with antibiotics (doxycycline), then she was hospitalized at the Infectious

Corresponding author:

Florica Sandru

E-mail: florysandru@yahoo.com

Article History:

Received: 23 December 2021

Accepted: 29 December 2021

Diseases Service where she received treatment with meropenem and azithromycin without clinical response. The investigations that were performed, including computed tomography of the thorax and abdomen, and blood cultures did not detect any cause of the symptoms. In the meantime, she was tested several times for SARS-CoV-2 PCR and found negative. Then, following an otorhinolaryngology (ORL) consultation, a subacute thyroiditis was suspected and referred to endocrinology. 3 weeks before the first symptoms, the patient had the second dose of vaccine against COVID-19 (Pfizer) (Table 1).

**TABLE 1.** Timing of vaccination, symptoms and medical evaluations until subacute thyroiditis diagnosis was established

Timing	Event
23.09.2021	Pfizer dose 1-no severe adverse reaction
14.10.2021	Pfizer dose 2-no adverse reactions
5-8.11.2021	dry cough, odynophagia
7-8.11.2021	Fever (maximum 38.6 degrees Celsius); initially treatment with doxycycline for 5 days with no improvement
8-20.11.2021	Worsening of odynophagia
22-25.11.2021	Hospitalization at the Infectious Diseases Service; treatment with meropenem and azithromycin without clinical response
25.11.2021	ORL consultation: suspicion of subacute thyroiditis
26.11.2021	Hospitalized (as emergency) at Endocrinology Department: confirmation of subacute thyroiditis

**TABLE 2.** The biochemistry panel of a 54-year-old female confirmed with subacute thyroiditis

Parameter	Value- 26.11.2021	Value- 29.11.2021	Normal ranges	Units
Uric acid	3.2		2.6-6	mg/dl
ALT (Alanine aminotransferase)	9	12.3	0-31	U/l
AST (Aspartat aminotransferase)	14	10.8	0-32	U/l
Conjugated bilirubin	0.13		0-0.5	mg/dl
Total bilirubin	0.3		0.2-1.2	mg/dl
Ionic serum calcium	4.58		3.9-4.9	mg/dl
Total serum calcium	9.6		8.4-10.2	mg/dl
Total cholesterol	109		0-200	mg/dl
Alkaline phosphatase		131	38-105	U/l
Serum phosphorus	3.8		2.3-4.7	mg/dl
Fasting glycaemia	103	74.4	70-105	mg/dl
HDL-cholesterol	18		40-60	mg/dl
LDL-cholesterol	69		60-160	mg/dl
Potassium	4.3		3.5-5.1	mmol/l
Magnesium	2.7		1.6-2.55	mg/dl
Sodium	141		136-145	mmol/l
Total proteins	6.2		6.4-8.3	g/dl
Triglycerides	105		0-149	mg/dl
Urea	29		15-50	mg/dl
Creatinine	0.5		0.5-1.2	mg/dl
CRP (C reactive protein)	7.368	1.229	0-0.5	mg/dl
ESR (erythrocyte sedimentation rate)	105	77.4	1-25	mm/1-h
Fibrinogen	823	624	200-500	mg/dl

## Endocrine evaluation

Clinical examination showed a small goiter, with inhomogeneous consistence, associating local spontaneous pain and at palpation, and also pain when swallow; no signs of hyperthyroidism. Biochemistry panel showed a typical inflammatory picture (Table 2).

Thyroid assays confirmed thyrotoxicosis, but also a component of autoimmune thyroiditis (Table 3). Morning plasma cortisol was 9.75 µg/dl (normal ranges between 4.82 and 19.5 µg/dl).

**TABLE 3.** The endocrine panel of an adult female with subacute thyroiditis

Parameter	Value	Normal ranges	Units
<b>TSH (thyroid stimulating hormone)</b>	<b>0.0081</b>	<b>0.5-4.5</b>	<b>µUI/ml</b>
<b>FT4 (free levothyroxine)</b>	<b>22.84</b>	<b>9-19</b>	<b>pmol/l</b>
T3 (triiodothyronine)	116.4	80-200	ng/dl
ATPO (anti-thyroperoxidase antibodies)	4.99	0-5.61	UI/ml
<b>ATG (anti-thyroglobulin antibodies)</b>	<b>203.6</b>	<b>0-115</b>	<b>UI/ml</b>
TRAB (thyroid stimulating antibody)	0.8	0-1.75	UI/l

Thyroid ultrasound showed hypoechoic, intense inhomogeneous structure, with slightly increased vascularity, and no lymph nodes involvement.

## Therapy

The antibiotics were stopped. Corticotherapy was introduced: prednisone 25 mg/day, 14 days followed by 20 mg/day, 14 days, then 15 mg/day, 14 days, followed by 10 mg/day, 14 days, then 5 mg/day, 14 days, and then 5 mg every other day for 14 days. Periodic check-up is required.

## DISCUSSIONS

We introduce a typical case of subacute thyroiditis without relevant short term and long term prior medical history. On admission at endocrinology, the clinical picture was highly suggestive for the disease, as well as increased inflammatory markers in addition to confirmation of thyrotoxicosis (which was not clinically relevant). But, until the condition was recognized, essential thyroid evaluation was not performed (10,11). Routine TSH and thyroid ultrasound are imperative under these circumstances (during pandemic as well) (12,13). Interestingly, the patient had a complex panel of investigations and she was offered multiple regimes of antibiotics before the actual diagnostic amid pandemic (fever of unknown cause).

Another important aspect which is probably the clue of the case is represented by the close relationship between clinical onset and vaccination against COVID-19. In 2021, a few papers addressed the issue of developing subacute thyroiditis after immunization against coronavirus (14-27). Females are prone to the condition, as generally known; in cases with-

out typical clinical picture, fine needle aspiration-based cytological examination might help, but it is not routinely indicated (28,29,30). A prior thyroid condition or syndromic circumstance does not increase the risk (31,32).

Another particular aspect of the case was the co-detection of positive anti-thyroid antibodies. Generally, a person diagnosed with an autoimmune thyroid condition associates a higher risk of another endocrine or non-endocrine autoimmune conditions, but not necessarily of subacute thyroiditis (33,34,35). Limited data are published so far on potential link between vaccination against COVID-19 and thyroid issues which do not limit the indication of immunization according to doses and booster doses that are recommended for general population (36). On the other hand, we already know that the coronavirus infection itself causes subacute thyroiditis (37-50).

## CONCLUSIONS

Prompt recognition of subacute thyroiditis avoids unnecessary investigations, hospitalizations or even exposure to antibiotics as seen in this case. Early intervention with anti-inflammatory medication releases the symptoms. The association with vaccine against COVID-19 might be incidental or not; more evidence is needed but as far as we may think nowadays, the connection is possible, thus the importance of specific awareness.

## REFERENCES

- Rinoldi C, Zargarian SS, Nakielski P, Li X, Liguori A, Petronella F, et al. Nanotechnology-Assisted RNA Delivery: From Nucleic Acid Therapeutics to COVID-19 Vaccines. *Small Methods*. 2021 Sep;5(9):e2100402.
- Smith RG. Clinical data to be used as a foundation to combat Covid-19 vaccine hesitancy. *J Interprof Educ Pract*. 2022 Mar;26:100483.
- Chun JY, Park S, Jung J, Kim SH, Kim TS, Choi YJ, Kim HJ, Eom HS, Hyun JW. Guillain-Barre syndrome after vaccination against COVID-19. *Lancet Neurol*. 2021 Dec 17:S1474-4422(21)00416-6.
- Sohrabi M, Rakhshankhah ES, Ziaei H, Kachuee MA, Zamani F. Acute liver failure after vaccination against of COVID-19; a case report and review literature. *Respir Med Case Rep*. 2021 Dec 14:101568.
- Pauluzzi M, Stinco G, Erichetti E. Bullous pemphigoid in a young male after COVID-19 mRNA vaccine: a report and brief literature review. *J Eur Acad Dermatol Venereol*. 2021 Dec 20.
- Kasi SG, Dhir SK, Shah A, Shivananda S, Verma S, Marathe S, et al.; Indian Academy of Pediatrics Committee on Immunization (IAPCOI). Coronavirus Disease 2019 (COVID-19) Vaccination for Children: Position Statement of Indian Academy of Pediatrics Advisory Committee on Vaccination and Immunization Practices. *Indian Pediatr*. 2021 Dec 17:S097475591600381.
- Shafiq A, Salameh MA, Laswi I, Mohammed I, Mhameed O, et al. Neurological Immune Related Adverse Events Post-COVID-19 Vaccination: A Systematic Review. *J Clin Pharmacol*. 2021 Dec 18.
- Fazlollahi A, Zahmatyar M, Noori M, Nejadghaderi SA, Sullman MJM, Shekarriz-Foumani R, Kolahi AA, Singh K, Safiri S. Cardiac complications following mRNA COVID-19 vaccines: A systematic review of case reports and case series. *Rev Med Virol*. 2021 Dec 17:e2318.
- Magro C, Nuovo G, Mulvey JJ, Laurence J, Harp J, Crowson AN. The skin as a critical window in unveiling the pathophysiologic principles of COVID-19. *Clin Dermatol*. 2021 Nov-Dec;39(6):934-965.
- Dumitru N, Ghemigian A, Carsote M, Albu SE, Terzea D, Valea A. Thyroid nodules after initial evaluation by primary health care practitioners: an ultrasound pictorial essay. *Arch Balk Med Union*. 2016;51(3):434-438.
- Vasiliiu C, Albu SE, Carsote M, Valea A, Ghemigian A, Gheorghisan-Galateanu AA. Thyroid nodules: a puzzle in gynecological endocrinology. *Arch Balk Med Union*. 2019;54(2):363-367.
- Xu J, Li Y, Xia Q, Shi Q. Association between Thyroid Disease and Severe Coronavirus Disease 2019 (COVID-19) Infection: A Meta-Analysis. *Iran J Public Health*. 2021 Aug;50(8):1517-1525.
- Ladani AP, Loganathan M, Kolikonda MK, Lippmann S. COVID-19 Legacy. *South Med J*. 2021 Dec;114(12):751-759.
- Siolos A, Gartzonika K, Tigas S. Thyroiditis following vaccination against COVID-19: Report of two cases and review of the literature. *Metabol Open*. 2021 Dec;12:100136.
- Kyriacou A, Ioakim S, Syed AA. COVID-19 vaccination and a severe pain in the neck. *Eur J Intern Med*. 2021 Oct 18:S0953-6205(21)00338

16. Mungmunpantipantip R, Wiwanitkit V. Abnormal Thyroid Function Following COVID-19 Vaccination. *Indian J Endocrinol Metab.* 2021 Mar-Apr;25(2):169.
17. Joob B, Wiwanitkit V. Expected viscosity after COVID-19 vaccination, hyperviscosity and previous COVID-19. *Clin Appl Thromb Hemost.* 2021;27:10760296211020833.
18. Saygili ES, Karakilic E. Subacute thyroiditis after inactive SARS-CoV-2 vaccine. *BMJ Case Rep.* 2021 Oct 1;14(10):e244711.
19. Soltanpoor P, Norouzi G. Subacute thyroiditis following COVID-19 vaccination. *Clin Case Rep.* 2021 Oct 4;9(10):e04812.
20. Chatzi S, Karampela A, Spiliopoulou C, Boutzios G. Subacute thyroiditis after SARS-CoV-2 vaccination: a report of two sisters and summary of the literature. *Hormones (Athens).* 2021 Oct 22:1-3.
21. Sigstad E, Grøholt KK, Westerheim O. Subacute thyroiditis after vaccination against SARS-CoV-2. *Tidsskr Nor Laegeforen.* 2021 Oct 11;141(2021-14).
22. Bornemann C, Woyk K, Bouter C. Case Report: Two Cases of Subacute Thyroiditis Following SARS-CoV-2 Vaccination. *Front Med (Lausanne).* 2021 Aug 24;8:737142.
23. Patel KR, Cunnane ME, Deschler DG. SARS-CoV-2 vaccine-induced subacute thyroiditis. *Am J Otolaryngol.* 2021 Sep 9;43(1):103211.
24. Tekin SM, Şaylısoy S, Yorulmaz G. Subacute thyroiditis following COVID-19 vaccination in a 67-year-old male patient: a case report. *Hum Vaccines Immunother.* 2021:1-3.
25. Oyibo SO. Subacute Thyroiditis After Receiving the Adenovirus-Vectored Vaccine for Coronavirus Disease (COVID-19). *Cureus.* 2021 Jun 29;13(6):e16045.
26. Schimmel J, Alba EL, Chen A, Russell M, Srinath R. Letter to the Editor: Thyroiditis and Thyrotoxicosis After the SARS-CoV-2 mRNA Vaccine. *Thyroid.* 2021 Sep;31(9):1440.
27. İremli BG, Şendur SN, Ünlütürk U. Three Cases of Subacute Thyroiditis Following SARS-CoV-2 Vaccine: Postvaccination ASIA Syndrome. *J Clin Endocrinol Metab.* 2021 Aug 18;106(9):2600-2605.
28. Rusu DM, Musat F, Carsote M, Andronic O. Current evidence on core-needle biopsy (CNB) versus fine-needle aspiration (FNA) for evaluation of thyroid nodules. *Research and Clinical Medicine.* 2020;4(3):36-8.
29. Reyna VF, Broniatowski DA, Edelson SM. Viruses, Vaccines, and COVID-19: Explaining and Improving Risky Decision-making. *J Appl Res Mem Cogn.* 2021 Dec;10(4):491-509.
30. Singla RK, He X, Chopra H, Tsagkaris C, Shen L, Kamal MA, Shen B. Natural Products for the Prevention and Control of the COVID-19 Pandemic: Sustainable Bioresources. *Front Pharmacol.* 2021 Dec 1;12:758159.
31. Carsote M, Paun S, Neamtu MC, Avramescu ET, Iosif C, Terzea D, Constantinoiu S, Danculescu Miulescu R, Neamtu OM, Poiana C. The immunohistochemistry aspects in two cases of neurofibromatosis-associated abdominal tumors. *Rom Journal Morphol Embryol.* 2012;53(2):401-405.
32. Hassanin AA, Haidar Abbas Raza S, Ahmed Ujjan J, Aysh ALrashidi A, et al. Emergence, evolution, and vaccine production approaches of SARS-CoV-2 virus: benefits of getting vaccinated and common questions. *Saudi J Biol Sci.* 2021 Dec 13.
33. Sandru F, Carsote M, Albu SE, Dumitrascu MC, Valea A. Vitiligo and chronic autoimmune thyroiditis. *Journal of Medicine and Life.* 2021;14(2):1-4.
34. Martinez Quintero B, Yazbeck C, Sweeney LB. Thyroiditis: Evaluation and Treatment. *Am Fam Physician.* 2021 Dec 1;104(6):609-617.
35. Falkowski B, Szczepanek-Parulska E, Krygier A, Wrotkowska E, Ruchala M. Evaluation of interleukin-29 in autoimmune and inflammatory thyroid diseases. *Clin Endocrinol (Oxf).* 2021 Jun;94(6):998-1003.
36. Costa S, Romão M, Mendes M, Horta MR, Rodrigues AT, Carneiro AV, Martins AP, Mallarini E, Naci H, Babar ZU. Pharmacy interventions on COVID-19 in Europe: Mapping current practices and a scoping review. *Res Social Adm Pharm.* 2021 Dec 14;S1551-7411(21)00388-0.
37. Ruano R, Zorzano-Martinez M, Campos A, Rius F, Hernández M. Subacute thyroiditis might be a complication triggered by SARS-CoV-2. *Endocrinol Diabetes Nutr (Engl Ed).* 2021 Dec;68(10):755-756.
38. Álvarez Martín MC, Del Peso Gilsanz C, Hernández López A. Subacute De Quervain thyroiditis after SARS-CoV-2 infection. *Endocrinol Diabetes Nutr (Engl Ed).* 2021 Dec;68(10):754-755.
39. Semikov VI, Aghayan DL, Shulutko AM, Khorobrykh TV, Aleksandrov YK, Mansurova GT, Kazaryan AM. Subacute thyroiditis after SARS-CoV-2 infection. *Clin Case Rep.* 2021 Nov 22;9(11):e05109.
40. Trimboli P, Cappelli C, Croce L, Scappaticcio L, Chiovato L, Rotondi M. COVID-19-Associated Subacute Thyroiditis: Evidence-Based Data From a Systematic Review. *Front Endocrinol (Lausanne).* 2021 Sep 29;12:707726.
41. Brancatella A, Viola N, Rutigliano G, Sgrò D, Santini F, Latrofa F. Subacute Thyroiditis During the SARS-CoV-2 Pandemic. *J Endocr Soc.* 2021 Jul 28;5(10):bvab130.
42. Pirola I, Gandossi E, Rotondi M, Marini F, Cristiano A, Chiovato L, Castellano M, Ferlin A, Cappelli C. Incidence of De Quervain's thyroiditis during the COVID-19 pandemic in an area heavily affected by Sars-CoV-2 infection. *Endocrine.* 2021 Nov;74(2):215-218.
43. Ratnayake GM, Dworakowska D, Grossman AB. Can COVID-19 immunisation cause subacute thyroiditis? *Clin Endocrinol (Oxf).* 2021 Jul 17:10.1111/cen.14555.
44. Tjønnfjord E, Moe RB, Ghanima W, Aballi S. Subacute thyroiditis after COVID-19. *Tidsskr Nor Laegeforen.* 2021 Jun 28;141(10).
45. Christensen J, O'Callaghan K, Sinclair H, Hawke K, Love A, Hajkowicz K, Stewart AG. Risk factors, Treatment and Outcomes of Subacute Thyroiditis Secondary to COVID-19: A Systematic Review. *Intern Med J.* 2021 Jun 17:10.1111/imj.15432.
46. Osorio Martínez A, González-Razo VT, Navarro-Sánchez V, Souto Meiriño CA, Ahumada-Ayala M. SARS-CoV-2-Related Subacute Thyroiditis, Myocarditis, and Hepatitis After Full Resolution of COVID-19 Serum Markers. *Am J Case Rep.* 2021 Jun 17;22:e932321.
47. Whiting A, Reyes JVM, Ahmad S, Lieber J. Post-COVID-19 Fatigue: A Case of Infectious Hypothyroidism. *Cureus.* 2021 May 3;13(5):e14815.
48. de la Higuera López-Frías M, Perdomo CM, Galofré JC. Subacute thyroiditis following COVID-19 infection. *Rev Clin Esp (Barc).* 2021 Jun-Jul;221(6):370-372.
49. Ashraf S, Imran MA, Ashraf S, Hafsa HT, Khalid S, Akram MK, Ghufuran M, Cheema KK, Ahmad A, Izhar M. COVID-19: A Potential Trigger for Thyroid Dysfunction. *Am J Med Sci.* 2021 Sep;362(3):303-307.
50. Seyed Resuli A, Bezgal M. Subacute Thyroiditis in COVID-19 Patients. *Ear Nose Throat J.* 2021 May 11:1455613211012114.