Graves’ orbitopathy post-SARS-CoV-2 vaccines: report on six patients

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Received: 8 September 2022 / Accepted: 27 October 2022 / Published online: 15 November 2022
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Abstract
Context Autoimmune and inflammatory thyroid diseases (Graves’ disease, subacute thyroiditis, chronic autoimmune thyroiditis) have been reported following SARS-CoV-2 vaccines but Graves’ orbitopathy (GO) post-COVID-19 vaccination is uncommon.

Methods We describe six new patients seen in Endocrinology Departments with Outpatient Clinics for GO following SARS-CoV-2 vaccines in France.

Results After COVID-19 vaccination, GO was observed in six patients (three men, three women, mean age 53 ± 6 years) with a personal past history of Graves’ disease (5/6) or orbitopathy (4/6). New-onset (n = 2) or recurrence (n = 4) of GO was observed following mRNA vaccines after the first (3/6) or second (3/6) dose, with the mean time from vaccination to GO at 23.8 ± 10.4 days. In one patient, thyrotoxicosis was confirmed by increased free T4 and low TSH concentrations while others had normal TSH levels, during chronic levothyroxine treatment in three patients. Four patients had significant anti-TSH receptor antibodies levels. According to the severity and activity of GO, the patients were treated using selenium (n = 2), intravenous glucocorticoids (n = 2), teprotumumab (n = 1), tocilizumab (n = 2) and orbital decompression (n = 1) with a significant improvement in GO signs and symptoms observed by most patients.

Conclusion In this study, we report the main data from six new patients with GO following SARS-CoV-2 vaccines. Clinicians need to be aware of the risk of new-onset or recurrent GO in predisposed patients with autoimmune thyroid diseases after COVID-19 vaccination. This study should not raise any concerns regarding SARS-CoV-2 vaccination since the risk of COVID-19 undoubtedly outweighs the incidence of uncommon GO after SARS-CoV-2 vaccination.

Keywords Graves’ orbitopathy · Graves’ disease · COVID-19 · SARS-CoV-2 · Vaccine · Autoimmunity

Introduction

Graves’ disease is the most frequent cause of hyperthyroidism due to the stimulation of the TSH-receptor on follicular thyroid cells by autoimmune antibodies which results in thyrotoxicosis, goitre and extra-thyroidal manifestations (Graves’ orbitopathy, pretibial myxoedema). Graves’ hyperthyroidism is characterized by a Th-1 response with a high number of Th-1 CD4 cells and interferon secretion but usually affects genetically predisposed patients in the presence of triggering factors (stress, smoking, infection, post-partum, radioiodine treatment). The overall prevalence of Graves’ orbitopathy (GO) among patients with Graves’ disease is up to 40%, with 3–5% going on to develop severe Graves’ ophthalmopathy [1].

An increasing number of autoimmune and inflammatory-related side effects are being reported following COVID-19 vaccination (thrombotic thrombocytopenia, Guillain–Barré...
A 70-year-old female was treated with oral prednisolone (7.5 mg/day) for frozen shoulder syndrome. Her past thyroid history included Graves’ disease with total thyroidectomy and daily substitutive levothyroxine therapy (137 μg) as well as stable GO after 4 intravenous infusions of tocilizumab. Eighteen weeks after the last infusion of tocilizumab, she received the second dose of the mRNA vaccine. Sixty days later, the woman presented spontaneous and orbital pain upon eye movement, conjunctival irritation and eyelid oedema. Clinical Activity Score (CAS) was 4/7 and an orbital MRI confirmed bilateral proptosis with oedema of the medial and inferior rectus muscles which was indicative of active moderate-to-severe GO. Laboratory investigations confirmed normal thyroid function with normal TSH and free T4 concentrations during stable levothyroxine treatment, and elevated levels of anti-TSH receptor antibodies (> 40 IU/L). In the context of recurrent GO during oral glucocorticoid therapy, the woman was treated with tocilizumab (8 mg/kg monthly intravenous infusions) and reported a significant and rapid (2 weeks) clinical improvement with decreased anti-TSH receptor antibodies levels (25 IU/L) after 5 infusions of tocilizumab.

Methods

The 6 patients were seen in the Tertiary Endocrinology Department with Outpatient Clinic for GO with new-onset, recurrent or worsening GO following SARS-CoV-2 vaccination. For every patient, we collected information on demographic data (sex, age), previous history of autoimmune or thyroid disease, type of administered vaccines (mRNA vaccine, inactivated virus or vector vaccine), timing of GO, onset or recurrence following vaccination, signs and symptoms at presentation, laboratory tests (TSH, free T4, anti-TSH receptor antibodies) and other diagnostic examinations (CT scan or MRI scan of the orbits), specific medical or surgical therapies and ophthalmic follow-up.

Patients

(a) A 70-year-old female was treated with oral prednisolone (7.5 mg/day) for frozen shoulder syndrome. Her past thyroid history included Graves’ disease with total thyroidectomy and daily substitutive levothyroxine therapy (137 μg) as well as stable GO after 4 intravenous infusions of tocilizumab. Eighteen weeks after the last infusion of tocilizumab, she received the second dose of the mRNA vaccine. Sixty days later, the woman presented spontaneous and orbital pain upon eye movement, conjunctival irritation and eyelid oedema. Clinical Activity Score (CAS) was 4/7 and an orbital MRI confirmed bilateral proptosis with oedema of the medial and inferior rectus muscles which was indicative of active moderate-to-severe GO. Laboratory investigations confirmed normal thyroid function with normal TSH and free T4 concentrations during stable levothyroxine treatment, and elevated levels of anti-TSH receptor antibodies (> 40 IU/L). In the context of recurrent GO during oral glucocorticoid therapy, the woman was treated with tocilizumab (8 mg/kg monthly intravenous infusions) and reported a significant and rapid (2 weeks) clinical improvement with decreased anti-TSH receptor antibodies levels (25 IU/L) after 5 infusions of tocilizumab.

(b) A 43-year-old male patient had a personal medical history of type-1 diabetes mellitus, psoriasis, Graves’ disease treated with carbimazole (10 mg/day) and sight-threatening GO of the right eye refractory to intravenous glucocorticoids treated by 4 IV infusions of tocilizumab (8 mg/kg) with complete recovery of the dysthyroid optic neuropathy (DON). Forty-five days after the last infusion of tocilizumab, the patient received the first dose of the Moderna mRNA vaccine. The patient reported spontaneous orbital pain and diplopia the next day then decreased visual acuity after the second dose of the COVID-19 vaccine. The CAS was 7/7 and the patient presented sight-threatening GO in relation to recurrent DON on the right eye. During carbimazole therapy, TSH levels were slightly elevated with low free T4 concentrations and absence of anti-TSH receptor antibodies. The patient was once again treated with tocilizumab (8 mg/kg). Significant improvement in inflammatory symptoms (CAS = 1/7) was observed after the first infusion of tocilizumab with recovery of visual acuity after 4 IV infusions.

(c) A 73-year-old male patient with a personal medical history of atrial fibrillation and prostate cancer presented a Graves’ disease treated with carbimazole. Twenty-one days after the first dose of the Pfizer mRNA vaccine, he experienced conjunctival irritation and diplopia. The CAS was 3/7 and an orbital MRI showed oedema of the lower rectus muscle in the right eye favouring mild GO. TSH levels were normal and anti-TSH receptor antibodies were normal. The patient was treated with selenium as well as intravenous methylprednisolone infusions and reported an improvement in symptoms affecting the right eye after the first infusion with absence of inflammatory signs or symptoms after 6 infusions of 500 mg methylprednisolone.

(d) A 45-year-old woman had a past medical history of hyperparathyroidism, sickle cell anaemia, total thyroidectomy in the context of Graves’ hyperthyroidism managed with substitutive levothyroxine therapy, GO treated by intravenous infusions of glucocorticoids and subsequent bilateral orbital decompression for inactive GO. During the week following the second dose of the Moderna mRNA vaccine, she presented an eyelid oedema, conjunctival irritation, spontaneous and orbital pain upon eye movement without diplopia. The CAS was 4 and the woman had active moderate-to-severe GO. On stable levothyroxine treatment, TSH levels were in the normal range and anti-TSH receptor antibodies were elevated. The woman received lubricants and reported a spontaneous improvement in orbital inflammation in 5 months.
After SARS-CoV-2 vaccination, GO was observed in 6 new patients (3 men, 3 women, mean age was 53 ± 6 years, ranging from 39 to 73 years). Most patients had a past personal history of Graves’ disease (5/6) or GO (4/6). Newly diagnosed or recurrent GO were reported following mRNA COVID-19 vaccines after the first (3/6) or second (3/6) dose with the mean time from COVID-19 vaccination to onset or worsening of GO at 23.8 ± 10.4 days, ranging from 1 to 60. In one patient, thyrotoxicosis was confirmed by high free T4 and low TSH concentrations while others (5/6) had normal TSH levels during chronic levothyroxine treatment in 3 patients. Autoimmune GO was associated with the presence of anti-TSH receptor antibodies in most patients (4/6). According to the activity and severity of GO, patients were treated using selenium (n = 2), intravenous glucocorticoids (n = 2) or immunosuppressive drugs (tocilizumab n = 2), anti IGF1 receptor monoclonal antibody (teprotumumab n = 1) and orbital decompression (n = 1) with significant improvement in signs and symptoms experienced by most patients.

In all reported patients with GO following COVID-19 vaccination, no triggering events (increased TSH concentrations, changes in smoking status, pregnancy, recent surgeries, radioiodine treatment) were observed in their medical history other than COVID-19 vaccination and the timing between the new-onset or reactivation of GO and SARS-CoV-2 vaccines was similar to that stated in previous reports of autoimmune and inflammatory diseases following COVID-19 vaccination [2]. Considering the high vaccination coverage, it is possible that the relationship between the occurrence of GO and COVID-19 vaccination was coincidental. However, the temporal sequence of the new onset, recurrence or worsening of GO was potentially prompted by exposure to the SARS-CoV-2 vaccines with the COVID-19 vaccination serving as a triggered event in predisposed patients with Graves’ disease and/or GO. In the absence of reports on the total number of patients with GO following SARS-CoV-2 vaccination in a defined population, estimating the incidence of this orbital side effect is difficult.

Autoimmune hyperthyroidism can occur after several vaccines (hepatitis B, human papilloma virus, H1N1) [15–19] and autoimmune thyroid diseases may develop in the hyperimmune environment created after the SARS-CoV-2 immunisation. The exact pathogenetic mechanisms underlying new onset, recurrence or exacerbation of GO following SARS-CoV-2 vaccines are not fully understood and several hypotheses could be put forward:

(a) Molecular mimicry: various SARS-CoV-2 proteins (spike proteins, nucleoproteins and membrane proteins)
Table 1: Main clinical, hormonal and radiological data as well as treatment and ophthalmic follow-up in 6 new patients with GO post-SARS-CoV-2 vaccines

| N  | Sex | Age  | Family history | Personal history | Past thyroid disease | Treatment | Name of vaccine | Type of vaccine | Dose | Time (days) | History of GO | Signs of ophthalmopathy | CAS Severity of GO | FT4 (pmol/l) | TSH (mIU/L) | TSHr-Ab | Radiological signs | Treatment | Follow-up |
|----|-----|------|----------------|------------------|---------------------|-----------|----------------|----------------|------|-------------|---------------|------------------------|----------------|-------------|-------------|---------|----------------------|-----------|----------|
| 1  | F   | 70   | N              | Adhesive capsulitis (frozen shoulder) | Graves' disease treated by thyroidectomy, Graves' orbitopathy treated with tocilizumab, pretibial myxoedema | Levothyroxine, prednisolone | Pfizer mRNA | 2nd | 60 | Recurrence after 7 years | Spontaneous and orbital pain with eye movement, oedema | 4 | Moderately-to-severely GO | 1.65 | 20 | > 40 | Bilateral proptosis, oedema of medial and inferior rectus muscles | Prednisolone, tocilizumab | Significant clinical improvement, decreased anti-TSH receptor Ab (25 IU/L) |
| 2  | M   | 43   | N              | Diabetes mellitus type 1, psoriasis | Graves' disease, dysthyroid optic neuropathy treated with tocilizumab with complete recovery | Insulin therapy, carbimazole, inhibitor proton pump | Moderna mRNA | 1st | 1 | Recurrence after 11 months | Spontaneous orbital pain, diplopia, abnormal visual acuity after the 2nd dose | 7 | Sight-threatening GO | 4.04 | 6.2 | N | Tocilizumab (8 mg/kg x 4) | Significant improvement in symptoms, normal visual acuity after tocilizumab |
| 3  | M   | 73   | N              | Prostate cancer, atrial fibrillation | Graves' disease | Carbimazole, beta blockers, apixaban | Pfizer mRNA | 1st | 21 | New | Conunctival irritation, diplopia | 3 | Mild GO | 2.4 | N | *** | Oedema of lower rectus muscle in the right eye | Selenium, IV methylprednisolone | Improvement in inflammation of lower rectus muscle in the right eye |
| 4  | F   | 45   | N              | Hyperparathyroidism, sickle cell anemia | Total thyroidectomy, Graves' orbitopathy treated with steroid therapy (EUGOGO protocol) and orbital decompression | Levothyroxine | Moderna mRNA | 2nd | NA | Recurrence after 18 months | Spontaneous and orbital pain with eye movement, conjunctival irritation, eyelid oedema | 4 | Moderately-to-severely GO | 0.76 | NA | 151 IU/L | NA | Lubricants | Improvement in orbital inflammation at 5 months |
Table 1 (continued)

| N | Sex | Age | Family history | Past thyroid disease | Treatment | Name of vaccine | Type of vaccine | Dose | Time (days) | History of GO | Signs of ophthalmopathy | CAS | Severity of GO | TSH (mU/L) | FT4 (pmol/l) | TSHr-Ab | Radiological signs | Treatment | Follow-up |
|---|-----|-----|----------------|---------------------|-----------|----------------|---------------|------|-------------|---------------|-------------------------|------|---------------|------------|-------------|--------|------------------|-----------|----------|
| 5 | M   | 48  | N              | Diabetes mellitus, obesity, schizophrenia | Total thyroidectomy, dysthyroid optic neuropathy in 2020 | Levotheroxine, metformin, propranolol, risperidone, diazepam | Moderna mRNA | 2nd  | 30          | Recurrence after 12 months | Orbital pain, conjunctival irritation, decreased visual acuity | 5    | <0.01         | 21         | 28 IU/L     | 5      | Significant and bilateral proptosis, enlargement of extraocular muscles (lower rectus muscle) | IV methylprednisolone, bilateral orbital decompression, teprotumumab | Normal visual acuity and CAS 0/7 after 1 IV infusion of teprotumumab, anti-TSH receptor 9 IU/L |
| 6 | F   | 39  | Y N N          | No treatment | Pfizer mRNA | 1st  | 7              | Left proptosis, conjunctival irritation | Mild GO | 0.30 | NA          | 5 IU/L        | Enlargement and inflammatory aspect of extraocular muscles (lower rectus muscle) | Selenium |

Footnote: Sex F female, M male. Age (years). Time (days). Y yes, N not present. TSH (mU/L). FT4 (pmol/l). TSHr-Ab: TSH receptor antibody. NA not available
Table 2: Main clinical, hormonal and radiological data as well as treatment and ophthalmic follow-up in 12 patients with GO post SARS-CoV-2 vaccines from literature

| N  | Ref | Sex | Age | Sex | Family history | Personal history | Past thyroid disease | Treatment | Name of vaccine | Type of vaccine | Dose | Time (days) | History of GO | Signs of ophthalmopathy | CAS | Severity of GO | TSH (mIU/L) | FT4 (pmol/l) | TSHr-Ab | Radiological signs | Treatment | Follow-up |
|----|-----|-----|-----|-----|----------------|------------------|---------------------|-----------|----------------|----------------|------|-------------|---------------|---------------------------|-----|---------------|-------------|-------------|---------|----------------------|-----------|-----------|
| 1  | 8   | F   | 50  | NA  | NA             | Graves’ disease treated with I131 | Levothyroxine | Pfizer   | mRNA 2nd        | 3              | New | 5/7         | Moderate-to-severe GO | Eye irritation, tearing, orbital pain, bilateral proptosis | Y | Normal | Y            | NA          | NA      | CT: enlargement of inferior and medial recti muscles | Teprotumumab | After 2 doses: improvement in congestive symptoms, significant reduction in proptosis |
| 2  | 9   | F   | 34  | NA  | NA             | Graves’ disease treated with thiamazole | No treatment | Pfizer   | mRNA 1st        | 10             | New | NA          | Mild GO       | Swelling and oedema of the eyelids | NA | NA          | Y            | NA          | Thiamazole | NA                       | NA         |                       |
| 3  | 10  | F   | 71  | NA  | NA             | Breast cancer, struma ovarii | Multinodular goiter | No treatment | Pfizer   | mRNA 2nd        | > 70           | New | NA          | Moderate-to-severe GO | 10 weeks after treatment of Graves’ disease | NA | <0.02       | 92.67       | Y           | NA      | Methimazole | NA                       | NA         |                       |
| 4  | 11  | F   | 51  | NA  | NA             | Diabetes melilitus, hypertension | N               | Pfizer   | mRNA 2nd        | 4              | New | 3/7         | Active and mild GO | Proptosis, irritation, dryness | NA | <0.01       | 47.88       | Y           | NA      | Methimazole, propranolol, then thyroid surgery | Significant clinical regression after thyroidectomy |                           |
| 5  | 12  | F   | 58  | NA  | NA             | Graves’ disease treated with I131 | No treatment | Pfizer   | mRNA 2nd        | 3              | Worsening of 3-year GO | 6/10         | Moderate-to-severe GO | 1.17         | Chemosis, redness of eyelids, peri-orbital oedema, pain, diplopia, foreign object sensation | 16.22 | Y           | NA      | Planned teprotumumab | NA                       |                         |
| N | Ref | Sex | Age | Family history | Personal history | Past thyroid disease | Treatment | Name of vaccine | Type of vaccine | Dose | Time (days) | History of GO | Signs of ophthalmopathy | CAS | Severity of GO | TSH (mIU/L) | FT4 (pmol/l) | TSHr-Ab | Radiological signs | Treatment | Follow-up |
|---|-----|-----|-----|----------------|------------------|---------------------|-----------|----------------|----------------|------|-------------|---------------|----------------------------|------|----------------|------------|-------------|---------|-------------------|-----------|------------|
| 6 | 12  | M   | 43  | NA            | NA               | Graves’ disease, Graves’ orbitopathy treated with steroid and external orbital radiation | No treatment | Pfizer mRNA | NA           | 14             | Recurrence of GO | Proposis, diplopia, keratopathy, dysthyroid optic neuropathy | NA | NA            | 2.31       | 9.78        | Y       | NA               | NA        | NA         |
| 7 | 13  | F   | 66  | NA            | NA               | Graves’ disease treated with I131, Graves’ orbitopathy treated with bilateral orbital decompression | No treatment | Moderna mRNA | 2nd | 21            | Recurrence after 15 years | Bilateral peri-orbital oedema, proposis, pain with eye movement | NA | Moderate-to-severe GO | 0.04       | 21.88       | Y       | Oedema and enlargement of the inferior rectus muscles | Teprotumumab | Improvement in symptoms at 5 months |
| 8 | 13  | F   | 53  | NA            | NA               | Methimazole | Pfizer mRNA | 1st | 1            | New                        | Peri-orbital oedema, proposis, upper and lower eyelid retraction in the right eye | NA | Moderate-to-severe GO | 0.99       | 11.58       | Y       | Mild oedema, enlargement of bilateral inferior rectus muscles and lacrimal gland | Teprotumumab | Improvement in symptoms at 8 months |
Table 2 (continued)

| N  | Ref | Sex | Age | History | Treatment | Name of Vaccine | Type of Vaccine | Dose | Time (days) | History of GO | Signs of Thyroiditis | CAS | Severity of GO | TSH (mU/L) | FT4 (pmol/l) | TSHr-Ab | Radiological Signs | Treatment | Follow-up |
|----|-----|-----|-----|---------|-----------|----------------|----------------|------|-------------|---------------|---------------------|-----|---------------|------------|--------------|---------|-------------------|-----------|-----------|
| 9  | 13  | F   | 45  | NA      | No treatment | Hashimoto's thyroiditis with TED | mRNA | 1st | 21 | Recurrence after 5 years | Proptosis, mild bilateral eyelid oedema, worsening of eyelid swelling after the 2nd dose | NA | Mild-to-moderate GO | NA | NA | NA | No treatment | Spontaneous reduction in eyelid swelling at 4 months |
| 10 | 14  | F   | 37  | NA      | No treatment | mRNA | 2nd | 21 | New | Mild-to-moderate GO | 0.01 | 72 | Y | NA | Carbimazole, propranolol | NA |
| 11 | 14  | F   | 34  | NA      | No treatment | mRNA | 1st | 26 | New | Mild-to-moderate GO | 0.01 | 68 | Y | NA | Carbimazole, propranolol | NA |
| 12 | 14  | M   | 59  | NA      | No treatment | mRNA | 1st | 21 | New | Mild-to-moderate GO | 0.01 | 49 | Y | NA | Carbimazole, propranolol | NA |

Mean ± SE 50 ± 3 18 ± 5 0.5 ± 0.23 42.2 ± 9.0

Footnote: Sex F female, M male. Age (years). Time (days). Y yes, N not present. TSH (mU/L). FT4 (pmol/l). TSHr-Ab: TSH receptor antibody. NA not available.
share a genetic similarity or homology with human proteins [20]. After polyclonal activation of B lymphocytes by COVID-19 vaccines, antibodies directed against SARS-CoV-2 proteins might cross-react with thyroid antigens located on the follicular cells of the thyroid and the cells of peribital tissues to cause Graves’ hyperthyroidism and autoimmune GO, respectively, in rare patients.

(b) Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) is the consequence of the dysregulation of the immune system following exposure to adjuvants. Adjuvants enhance the immunogenicity of vaccines, increase both innate and adaptive immune responses and can induce the formation of autoantibodies. Autoimmune thyroid diseases have been reported to be related to ASIA syndrome after human papillomavirus, influenza, hepatitis B vaccination [21–26] and most recently after COVID-19 vaccines [2, 5, 27–29]. In the BNT162b2 mRNA vaccine, polyethylene glycol (PEG) conjugates stabilise the lipid nanoparticles and may act as adjuvants to trigger an autoimmune reaction following SARS-CoV-2 vaccination.

(c) Autoimmune hyperthyroidism and TED are related to stimulating anti-TSH receptor antibodies and produced secondary to a Th-1 immune response in which interferon gamma plays a key role [30]. As COVID-19 vaccines lead to a production of Th-1 cells, a similar mechanism could be involved in vaccine-induced Graves’ hyperthyroidism or orbitopathy.

Despite a mass immunisation campaign against COVID-19 infection, autoimmune thyroid adverse effects such as Graves’ disease and GO appear to be rare, suggesting they are probably under-reported side effects of COVID-19 vaccination or usually occur with individual predisposition or genetic susceptibility. In genetically susceptible individuals, T lymphocytes are excessively sensitised to the TSH receptor antigen and vaccines activating B lymphocytes may produce autoantibodies against the TSH receptor thereby causing Graves’ hyperthyroidism and GO [31, 32]. On the other hand, inflammatory recurrence of GO in some patients is also a possibility after previous immunomodulating treatments unrelated to SARS-CoV-2 vaccination. Therefore, systematic reporting of patients with GO following COVID-19 vaccination will add information on the frequency and potential mechanism(s) between SARS-CoV-2 vaccines and autoimmune GO.

After clinical and ophthalmic assessment, all grades of severity (mild, moderate-to-severe, sight-threatening) were observed in patients with GO following SARS-CoV-2 vaccination [33]. In patients with mild GO, local (lubricants) and lifestyle measures were sufficient and 2 patients had also selenium (200 μg/day) therapy. In patients with moderate-to-severe GO, immunomodulatory therapy was indicated (intravenous glucocorticoids, tocilizumab) or anti IGF1 receptor monoclonal antibody (teprotumumab), and associated with a significant improvement in most patients. For patients with sight-threatening GO, urgent treatment was instituted with close monitoring of response to immunosuppressive therapies and restoration of visual acuity. The response to immunomodulatory therapy in patients with GO following COVID-19 vaccination may be related to the rapidity of treatment in such patients with a past history of autoimmune thyroid diseases or to a possible brief autoimmune reaction following SARS-CoV-2 vaccination. Finally, vitamin D supplements inhibit Th-1 type immune activity and induce suppression of B cells while selenium supplements decrease the B cell-activating factor. Therefore, these class 2 micronutrient (vitamin D, selenium) supplements have the potential to reduce and modulate autoimmune thyroid activity as well as protect against activation or relapse of autoimmune adverse events due to SARS-CoV-2 vaccination, particularly in predisposed patients with a past history of Graves’ disease and/or GO [34].

Conclusion

All vaccinations are risky but the benefits of SARS-CoV-2 vaccines outweigh any theoretical risks of immunisation. COVID-19 vaccines may be recommended to all patients who are eligible for COVID-19 vaccination or booster doses, including those with autoimmune-mediated diseases such as Graves’ hyperthyroidism and GO. Clinicians should remain vigilant for recurrence or aggravation in patients with a known history of Graves’ disease or GO following SARS-CoV-2 vaccination. In such patients with a prior history of thyroid or orbital autoimmune diseases, a baseline pre-COVID-19 vaccine examination and ophthalmic monitoring is required to diagnose rapidly autoimmune hyperthyroidism or orbitopathy. Concomitantly, class 2 micronutrient (vitamin D, selenium) supplements can be prescribed to prevent more severe forms of GO in patients with a past history of Graves’ disease and/or orbitopathy.

Author contributions All authors have been involved in the medical care of the patients. Material preparation, data collection and analysis were performed by all the Authors. The first draft of the manuscript was written by PC and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript to be published and agreed to be accountable for all aspects of the study.

Funding This research did not receive any specific grants or support from any funding agencies in the public, commercial or not-for-profit sector.
Data sharing statement All authors confirm that all data and materials reported in this manuscript support their published claims and comply with field standards. The data that support the findings of the study are available on request from the corresponding author.

Declarations

Conflict of interest The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Ethical standards Informed consent was obtained from the patients and the work conforms with the 1964 Declaration of Helsinki Good Clinical Practice Guidelines.

Author disclosure The authors report no conflict of interest regarding the data shown in this article.

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