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BRIEF REPORT

Enlargement of a metastatic lymph node from differentiated thyroid cancer after COVID-19 vaccination

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Abstract

Background The massive vaccination campaign against COVID-19 has granted a high level of protection against the severe forms of the disease at the price of some mild adverse events.

Objective To underline that COVID-19 vaccination can induce a transient enlargement of lymph-node metastases in differentiated thyroid cancer patients.

Case presentation We describe the clinical, laboratory, and imaging features of a 60-year-old woman affected by paratracheal lymph-node relapse of Hurtle Cell Carcinoma who came to our attention after full COVID-19 vaccination because of neck swelling and pain. In April 2021, after 5 years of stable structural disease, the patient presented an enlargement of the metastatic lymph node, associated with a rise of serum thyroglobulin (from 4.6 to 14.7 pg/mL). Anti-inflammatory treatment was started and pain and swelling remitted after 15 days. At the subsequent evaluation, at neck ultrasound, the right paratracheal lesion was smaller and thyroglobulin dropped to 3.9 pg/mL.

Conclusions We report the case of an enlargement of metastatic lymph node from differentiated thyroid cancer after COVID-19 vaccination. We warn clinicians to identify features of inflammatory response due to COVID-19 vaccination in order to prevent unwarranted surgical treatment.

Keywords Thyroid cancer · Lymph-node metastases · COVID-19 vaccination · Inflammatory response · Lymphadenopathy

Introduction

Thyroid gland is the target of both inflammatory and neoplastic disease, with differentiated thyroid cancer (DTC) being the most frequent histotype. Among DTC subtypes, Hürthle cell carcinoma (HCC) usually presents an aggressive clinical behavior with a significant risk of clinical recurrence [1, 2].

Conventional treatment of HCC is based on total thyroidectomy with dissection of metastatic lymph nodes, when pre-surgically diagnosed, followed by radioiodine treatment for the more aggressive cases [3]. Follow-up is based upon serial measurement of thyroglobulin (Tg), along with thyroglobulin autoantibodies (TgAbs) and neck ultrasound [3]. A rise in Tg or TgAbs values during follow-up is suggestive of disease progression. About 10% prevalence of lymph-node metastases has been reported, with the central and latero-cervical compartments being more frequently involved [2, 4]. According to American Thyroid Association recommendations, in patients with persistent or recurrent lymph-node metastases from DTC, therapeutic dissection is advised when the smallest dimension is ≥8 mm for central and ≥10 mm for latero-cervical lymph-node metastases [3]. Smaller lymph nodes require active surveillance through serial neck ultrasound. However, active surveillance can also be chosen in patients who have already been submitted to multiple neck surgeries and/or are affected by relevant comorbidities, even in the presence of metastatic lymph nodes >8–10 mm. Significant growth of metastatic lymph node, which suggests disease progression, is an indication to prompt surgical treatment [3].

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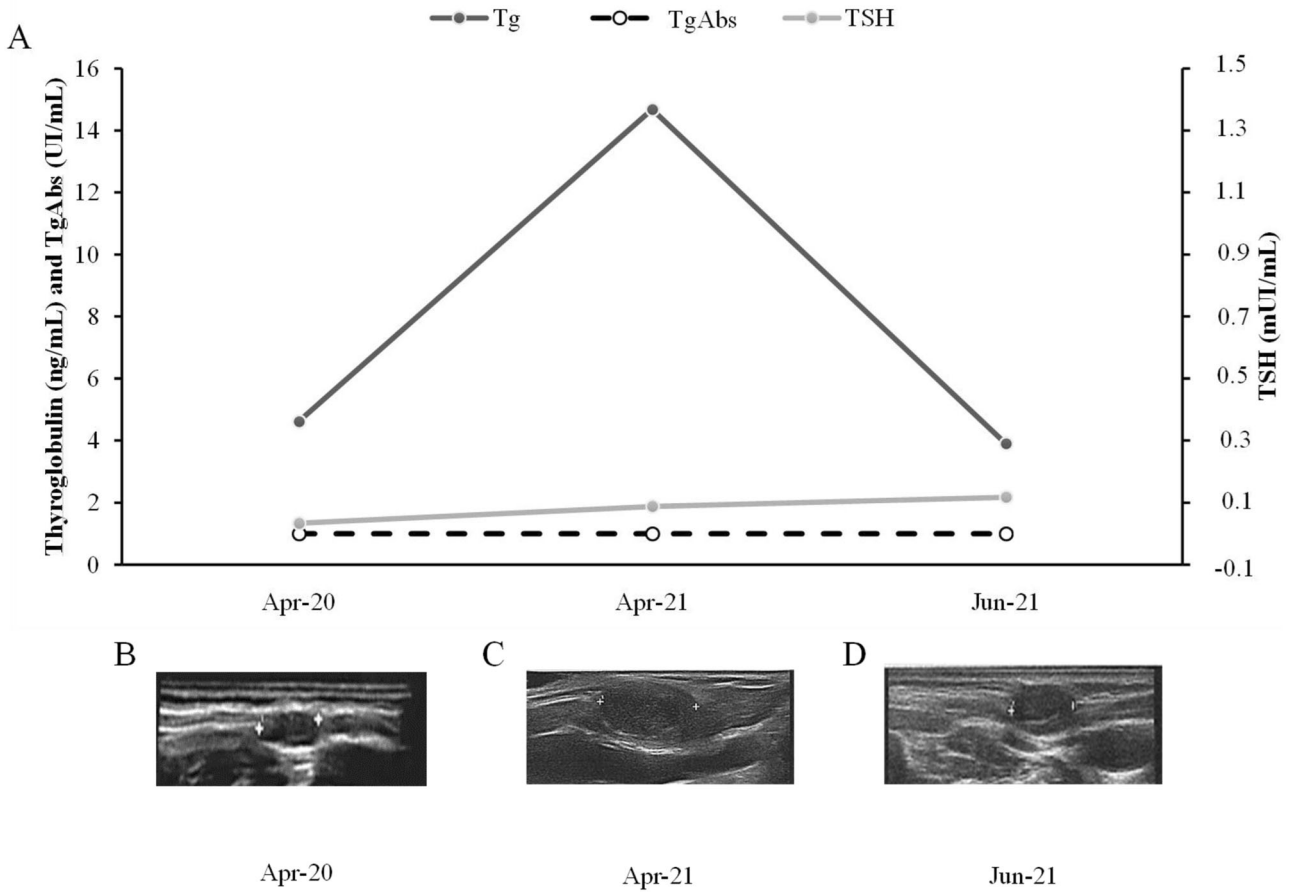

Fig. 1 **A** Thyroglobulin (Tg), Tg autoantibodies (TgAbs), and TSH trend (April 2020, April 2021, and June 2021). **B–D** Ultrasound images of the right paratracheal lymph-node metastasis in longitudinal section in April 2020 (13 mm), April 2021 (17 mm), and June 2021 (11 mm), respectively

Case presentation

A 60-year-old female patient, affected by HCC treated with total thyroidectomy (2006) and radioiodine (total activity 210 mCi, 2007–2010), in 2016, was diagnosed with right paratracheal lymph-node metastasis, which remains stable up to 2020. At that time, Tg was 4.6 pg/mL and neck ultrasound showed a metastatic lymph node, measuring 6 × 7 × 13 mm (Fig. 1A, B).

On April 28, 2021, the patient underwent the second dose of COVID-19 vaccination (Comirnaty). In the evening, she presented with fever, and the next day, she experienced neck swelling and spontaneous pain, which increased at palpation (Fig. 2A). Two days after, serum Tg had risen to 14.7 pg/mL (Fig. 1A). Neck ultrasound disclosed an enlargement of the metastatic lymph node (now 11 × 15 × 17 mm) and the appearance of a large anechoic area inside (Fig. 1C). At neck ultrasound, the only enlarged lymph node was metastatic, with no evidence of inflammatory reaction in the other lymph nodes. Pain and swelling remitted after 15 days of anti-inflammatory treatment (ibuprofen 400 mg daily) (Fig. 2B). In June 2021, Tg values dropped to 3.9 pg/mL (Fig. 1A) and the right paratracheal lesion was smaller (now 7 × 11 × 11 mm) at the neck ultrasound (Fig. 1D). Suppressed TSH values and TgAb values below the level interfering with Tg measurement

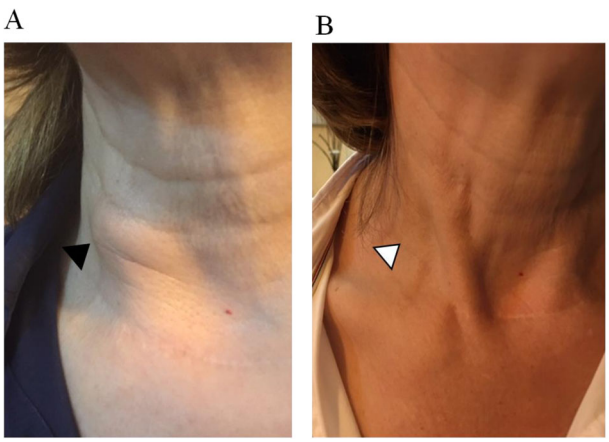

Fig. 2 **A** Clinical evidence of swelling corresponding to the right paratracheal lymph-node metastasis in April 2021 (black triangle). **B** Disappearance of swelling corresponding to the right paratracheal lymph-node metastasis in June 2021 (white triangle)

(<9.3 IU/mL) [5] were retrieved throughout all evaluations (from April 2020 to June 2021).

Discussion

The high morbidity and mortality rate of COVID-19 claimed for a prompt development of vaccines and a massive vaccination campaign. As of January 1, 2023, 13,165,031,710 doses of vaccine against COVID-19 have been administrated worldwide [6]. Most COVID-19 vaccines attain a high level of protection, with mild adverse events, namely local reaction at the injection site, muscle or joint pain, fever, lymphadenopathies and, as recently reported, a mild form of myocarditis [7, 8]. As reported by a recent review, after COVID-19 vaccination, 56 cases of lymphadenopathies, none diagnosed as metastatic, in patients with active or previous oncologic history have been described [9]. In particular, Mitchell et al. showed a 5% prevalence of COVID-19 vaccine-related neck lymphadenopathies with reactive features, at neck ultrasound, in a quite large cohort of patients ($n = 80$) [10]. Likewise, Robinson et al. showed that 3% of women performing breast imaging presented reactive axillary adenopathy upon COVID-19 vaccination [11]. However, this phenomenon has been described in non-metastatic lymph nodes, so far.

Here, we report the case of an HCC patient with metastatic lymph node, who, immediately after full COVID-19 vaccination, experienced an enlargement of lymph node associated with a rise in Tg values, which, according to the current guidelines [3], should have suggested a prompt surgical dissection. However, the clinical features, i.e., fever, pain, and swelling nodule, were suggestive of inflammatory and not metastatic growth. Over 3 months, Tg values trend was characterized by a significant raise followed by a drop up to initial values (Fig. 1A); this swing of Tg values was more suggestive of an inflammatory reaction, causing DTC cell membrane disruption with a "temporary" Tg release, rather than a metastatic progression that induces a persistent Tg release during the time [3].

The clinical, biochemical, and ultrasound features as well as the response to non-steroidal anti-inflammatory drugs resembled an intense inflammatory response, similar to that usually observed in subacute thyroiditis [12]. Indeed, subacute thyroiditis has been described after SARS-CoV-2 infection and COVID-19 vaccination [12, 13].

In conclusion, an enlargement of metastatic lymph node in thyroid cancer can be observed after COVID-19 vaccination. We suggest a careful clinical evaluation to identify features of inflammatory response due to COVID-19 vaccination in order to avoid unnecessary surgical treatment.

Author contributions L.V. and A.P. are the young endocrinologists who took care of the clinical management of the patient, collected and interpreted data, and were involved in the preparation and submission of the manuscript. L.A. is the endocrinologist who took care of the clinical management of the patient. F.S., R.E., and F.L. are the senior endocrinologists who were responsible for the clinical management of the patient and supervisor of manuscript preparation.

Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

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