Association of Giant Cell Arteritis with Papillary Thyroid Carcinoma

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ABSTRACT

Previous studies suggest that there may be an association between cancer and autoimmune diseases. We describe the case of a 59-year-old patient who did not have any significant diseases in the last year. She had new onset of fever of unknown aetiology, headache, fatigue and night sweats. We used laboratory methods to rule out infectious diseases. Significant laboratory findings reported increased signs of inflammation and anti-nuclear antibody (ANA) positivity. Positron emission tomography/computed tomography (PET/CT) imaging showed the origin of the patient's difficulties, arteritis, with increased metabolic activity in the aortic wall and other arteries. Doppler ultrasonography of the arteries did not show pathology in the temporal arteries but found accelerated blood flow in the superior mesenteric artery (AMS). Another finding from PET/CT was a tumour in the thyroid gland, later verified histologically as papillary thyroid carcinoma (PTC). We investigated the link between rheumatological disease and papillary carcinoma, applying similar therapy, corticosteroids and immunosuppressants.

KEYWORDS

giant cell arteritis; thyroid gland; papillary thyroid carcinoma; corticosteroids; fever; PET/CT; vasculitis

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INTRODUCTION

Giant cell arteritis (GCA) is one of the primary systemic vasculitis affecting medium and large arteries. GCA's clinical manifestations include general non-specific symptoms (fever, night sweats, fatigue, weight loss). Classification criteria are age greater than or equal to 50 years at disease onset, new onset of headaches, decreased pulsation and tenderness of the temporal arteries, elevated erythrocyte sedimentation rate greater than or equal to 50 mm/hour, and abnormal temporal artery biopsy (1, 2). The diagnosis is based on having at least 3 of these 5 criteria met (2).

Furthermore, the diagnosis can be confirmed by imaging or histology (3). Because of non-specific symptoms, the diagnosis can be delayed. This report describes our clinical case of a patient whose symptoms were non-specific. We were looking for cases associated with GCA and papillary thyroid carcinoma (PTC), but none have been reported to date. We present a case of a middle-aged woman who had GCA concomitantly with PTC.

CASE REPORT

In April 2021, a 59-year-old patient was admitted to our hospital after a previous investigation of fever of unknown origin. Since February 2021, the patient has had a headache, night sweats, fever over 39 °C, small and large joint pain, and lost over 10 kg of weight from February to April 2021. She took ibuprofen as an analgesic and antipyretic multiple times per day without results. Before we admitted the patient to our hospital, she was treated by a general practitioner (GP) and in her local hospital. GP treated her with two broad-spectrum antibiotics, but the treatment was ineffective. Afterwards, the GP sent her to her local hospital, that further investigated the cause of her symptoms. The hospital provided laboratory tests, microbiology (blood culture) and immunology, radiology tests, X-ray of the chest, ultrasonography (USG) of the abdomen, computed tomography (CT) of the head and chest and transoesophageal echocardiography (TEE). However, the results of the tests presented no new findings. Because of the patient's headaches, the neurologist performed an examination but did not find any source of pain. She was given another broad-spectrum antibiotic, but the fever remained while headaches and joint pain worsened. The local hospital reached out to us for consultations, and we recommended that the patient undergoes positron emission tomography/computed tomography (PET/CT). After the PET/CT, the patient was admitted to our hospital in April with her complete medical history.

On admission, her temperature was 35.8 °C, her heart rate was regular at 110/minute, her respiratory rate was 16/minute, and her blood pressure in the supine position was 116/78 mmHg. Her height was 178 cm, and she weighed 78 kg. She reported that she is subfebrile every evening. A physical examination was performed with palpation of the mass in the thyroid gland. Laboratory findings were as follows: C-reactive protein (CRP) 148.9 mg/l, leukocytes 9.68 × 10^9/l, erythrocytes 3.44 × 10^{12}/l, haemoglobin 91 g/l, erythrocyte sedimentation in the first hour was higher, 120 mm/h. The free tetra-iodothyronine (fT4) 17.2 pmol/l and thyroid-stimulating hormone (TSH) 1.02 mU/l were normal. The antineutrophil cytoplasmic antibodies (ANCA) were negative, ANCA myeloperoxidase (MPO) 1.33 U/ml, ANCA proteinase 3 (PR3) 1.13 U/ml, IgG 14.5 g/l, IgG4 0.19 g/l, rapid plasma reagin (RPR) negative, Treponema pallidum hemagglutination assay (TPHA) negative. The anti-nuclear antibodies (ANA) were positive. Creatine level was normal.

PET/CT showed 18F-fluorodeoxyglucose (18F-FDG) uptake in the aortic wall, subclavian arteries, carotid arteries, common iliac arteries, internal iliac arteries, and left lobe of the thyroid gland. We diagnosed her with GCA because she had increased sedimentation, new onset of headaches, pathological findings on PET/CT and was over 50 years old. We also investigated temporal arteries, but there was no sensitivity or decreased pulsation. Doppler ultrasonography of the arteries did not show pathology in the temporal arteries, but it showed flow acceleration in the proximal part of AMS 200–250 cm/s.

Since we had laboratory findings with signs of inflammation (high CRP, sedimentation) and the results from PET/CT showed inflammation of arteries and no pathological findings in temporal arteries, we did not perform a biopsy of the temporal artery. We started treating the patient's vasculitis with an initial dose of 32 mg/day of methylprednisolone. The patient also had eye and vision examinations. The fundus examination did not show a sign of ischemia, but automated perimetry revealed abnormalities in visual fields in temporal halves. Because of that, we started treatment with a dose of 500 mg/day of methylprednisolone for four days. The corticosteroid treatment promptly resolved the patient's symptoms, which she already had before coming to our hospital.

While she was treated for her vasculitis, we also focused on the mass in the left lobe of her thyroid gland revealed on PET/CT. Thyroid gland USG showed a mildly hypoechoic nodule 12 × 15 × 15 mm with calcifications. USG-guided fine-needle aspiration biopsy was performed and revealed suspicion for papillary thyroid carcinoma (Bethesda V). Immediately after the last dose of methylprednisolone, total thyroidectomy was performed, with no postoperative complications. Histology confirmed the classical variant of PTC, 21 × 19 × 12 mm, with dystrophic calcifications, one site of vascular invasion and no capsular invasion. The patient was discharged home with corticosteroid therapy (methylprednisolone), which we tapered from 16 mg/day to the final dose of 6 mg/day. Two months postoperatively, she received radioactive iodine (131-I) remnant ablation using 3700 MBq (100mCi) activity. The investigation before 131-I ablation revealed a moderate postoperative residuum of thyroid tissue (24-hour iodine neck accumulation of 8.9 % and serum thyroglobulin (TG) level of 18.65 ng/ml in hypothyroidism). Post-therapeutic whole-body scintigraphy and single photon emission CT (SPECT) of the neck and mediastinum, combined with low dose CT (SPECT/CT) confirmed a small residuum of the right lobe of the thyroid, together with one metastatic lymph node close to the right sternoclavicular joint. No distant metastases were found. She was classified as T2N1MO, stage II, and intermediate risk according to American Thyroid Association

(ATA). Subsequently she was treated with levothyroxine (dose adjusted to TSH suppression) and followed up using USG and serum levels of TG and autoantibodies against TG (TG-Ab). There was an excellent treatment response, with no USG signs of relapse and TG level below 0.2 ng/ml (and negative TG-Ab) with suppressed TSH and 0.44 ng/ml (i.e. below 1.0) with non-suppressed TSH. As there was no active residual cancer, while the vasculitis symptoms (joint pain) reoccurred after several months, we conclude that the symptoms were not paraneoplastic.

We added methotrexate to therapy, but the effect was temporal. We then increased the dose of oral methylprednisolone from 6 mg/day to 16mg/day for 7 days. Now she has a dose of 8mg/day of methylprednisolone with a satisfying effect.

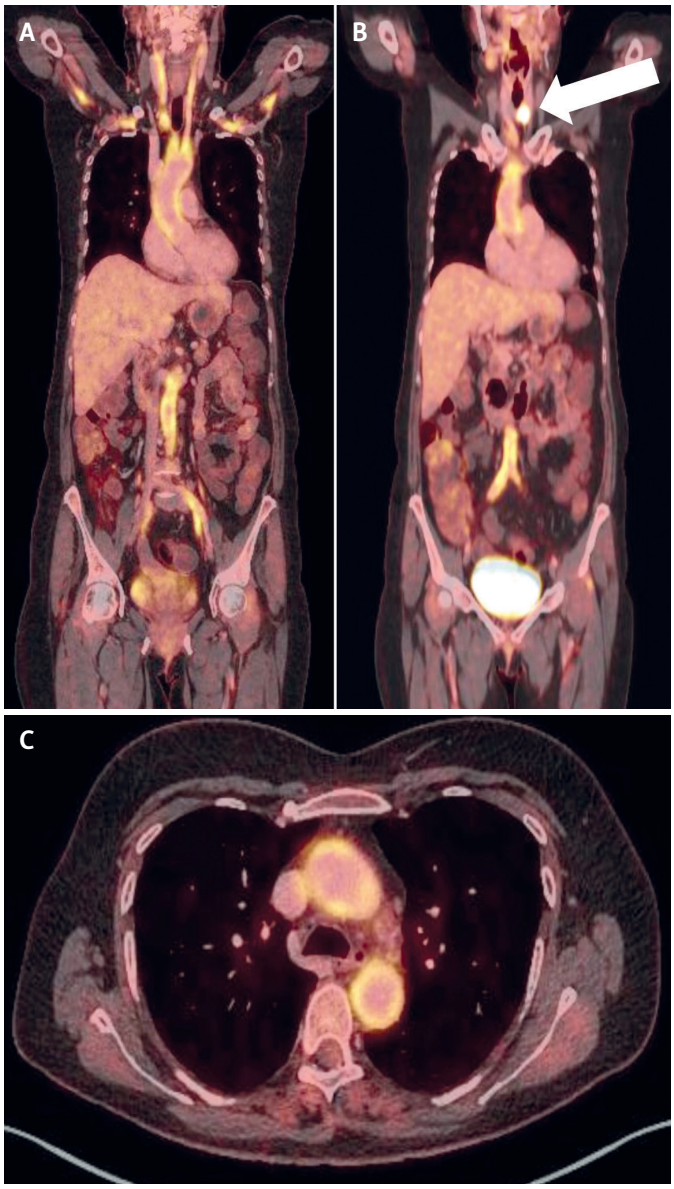

Fig. 1 PET/CT performed before patient was admitted to our hospital (with permission of Multiscan, s.r.o. database).
A: An uptake of ^{18}F-FDG in the aortic wall, subclavian arteries, carotid arteries, common iliac arteries, internal iliac arteries; B: An uptake of ^{18}F-FDG in the left lobe of the thyroid gland in the left lobe of the thyroid gland. Arrow points to a tumour in the thyroid gland; C: Axial view.

The patient will continue with regular check-ups at our hospital's rheumatology and endocrinology outpatient clinic.

DISCUSSION

As mentioned, no case report has been published with a patient treated simultaneously for GCA and PC of the thyroid gland. On the other hand, other interesting cases connect rheumatology and endocrinology. We used the database PubMed and studied a total of ten cases that included patients with rheumatological diseases and papillary carcinoma of the thyroid gland (see table) (4–13). The cases consisted of three men and seven women aged 31 to 69 years and tumour sizes from 19 to 40 mm. We compared our treatment procedure with the previously studied cases (4–13) and found similarities. Seven patients were treated with corticosteroids (4–8, 10, 13), and six of them had corticosteroid treatment before thyroidectomy (5–8, 10, 13). Only four patients had a fever (5–7, 13). It is known that GCA can exhibit non-specific symptoms, including fever of unknown origin (FUO) (14). Many case reports described patients examined for the aetiology of FUO, followed by PET/CT examinations that showed the cause of FUO (15–17). Our case was similar as we did not know the origin of the symptoms, and PET/CT helped us with the diagnosis.

Some cases reported that thyroidectomy resolved all rheumatic symptoms. These findings suggest that thyroid carcinoma caused paraneoplastic syndrome, demonstrated as rheumatic symptoms (9, 10). Thus, we can conclude that thyroidectomy was a crucial moment in therapy. It was unclear if PCL induced rheumatic manifestation in patients in other cases (4, 7, 13). Our patient's symptoms resolved for some time after treatment with corticosteroids. Unfortunately, after several months, when the patient had a lower dose of corticosteroids than at the beginning of treatment, the symptoms returned. This finding excludes the possibility that the symptoms were paraneoplastic. If the patient's symptoms would rapidly progress, we would consider changing the therapy to biological therapy, e.g., interleukin-6 inhibitors (tocilizumab) (18).

PTC, the most common thyroid malignancy, is associated with an excellent prognosis. Overall survival is more than 90% (19). A study was published in 2019 that studied the tumour volume doubling time (TVDT) in a group of 196 with a median patient age of 51 years. The findings of the study uncovered that 71.8% had a TVDT of five years or more (20). Another study was published in 2017 with similar results with intrathyroidal tumours ≤1.5 cm in a group of 291 patients with the median patient age 52 (21). Therefore, it is not necessary to rush with providing thyroidectomy. However, the endocrinology department at our hospital could perform a thyroidectomy in a very short time.

CONCLUSION

In conclusion, the relationship between rheumatology diseases and PTC is still unclear, and further studies are

Tab. 1 Overview of published case reports of patients with connective tissue diseases and papillary thyroid carcinoma.

Age	Sex	Size of PTC	Fever	Therapy	Disease	Corticosteroid therapy before thyroidectomy	Reference
31 years	Female	35 mm	no	Corticosteroids, azathioprine	Polymyositis	no	(1)
64 years	Female	20 × 20 mm	yes	Corticosteroids	Polymyalgia rheumatica	yes	(2)
59 years	Female	not specified	yes	Corticosteroids, cyclophosphamide	Granulomatosis with polyangiitis	yes	(3)
68 years	Male	not specified	yes	Corticosteroids	Still's disease	yes	(4)
69 years	Male	not specified	yes	Corticosteroids	Granulomatosis with polyangiitis	yes	(5)
55 years	Female	19 × 8 mm	no	without corticosteroid therapy	Paraneoplastic vasculitis	no	(6)
64 years	Female	35 mm	no	Corticosteroids	Panuveitis	yes	(7)
46 years	Female	40 mm	no	Azathioprine	Granulomatosis with polyangiitis	no	(8)
51 years	Male	40 mm	no	not specified	Cutaneous and renal vasculitis	No	(9)
32 years	Female	not specified	yes	Corticosteroids	Still's disease	yes	(10)

needed. A convincing association has not been found between PTC and rheumatic diseases, which does not necessarily mean that there is no association. In some patients, the connection between PTC and rheumatological disease is based on paraneoplastic symptoms, which was ruled out in our patient. So far, only a few cases with similar concomitant diseases have been published, and further investigation is required.

ABBREVATIONS

^{18}F-FDG – ^{18}F-fluorodeoxyglucose
AMS – superior mesenteric artery
ANA – anti-nuclear antibody
ANCA – antineutrophil cytoplasmic antibodies
CRP – C-reactive protein
CT – computed tomography
fT4 – free tetra-iodothyronine
FUO – fever of unknown origin
GCA – giant cell arteritis
GP – general practitioner
MPO – myeloperoxidase
PET/CT – positron emission tomography/computed tomography
PTC – papillary thyroid carcinoma
RPR – rapid plasma reagin
TEE – transoesophageal echocardiography
TSH – thyroid-stimulating hormone
TPHA – Treponema pallidum hemagglutination assay
TVDT – tumour volume doubling time
USG – ultrasonography

CONSENT

We obtained signed informed consent in the Czech language from the patient to publish a case report and pictures from imaging examinations.

CONFLICT OF INTEREST

None.

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