

## The role of PET/CT in Cogan's syndrome

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**Abstract** We report on the case of a 60-year-old woman with complaints of fatigue, coughing, anorexia, atypical chest pain, recurrent fever, and also ear pain and hearing loss. A test for anti-neutrophil cytoplasmic antibody (ANCA) was myeloperoxidase positive with p-ANCA specificity. Laboratory acute phase parameters were increased. A 2-deoxy-2-[<sup>18</sup>F]fluoro-D-glucose positron emission tomography/computed tomography investigation showed pathological uptake in the aorta ascendens, with no other involvement of the large vessels. After therapy with methylprednisolon intravenously and later prednisolon orally with methothrexate, her general condition and hearing loss improved both subjectively and objectively. "Atypical" Cogan's syndrome was diagnosed on the basis of sensorineural deafness with improvement on steroids and large-vessel vasculitis of the aortic arch.

**Keywords** Cogan's syndrome · F18-FDG PET/CT · Hearing loss · Large-vessel vasculitis

### Introduction

The association of nonsyphilitic interstitial keratitis and audiovestibular involvement was first reported in 1934 by

Mogan and Baumgartner. Their description was extended several years later by Cogan [1].

In "typical" Cogan's syndrome, the presence of interstitial keratitis is necessary, the term "atypical" Cogan's syndrome is used when other types of inflammatory eye disease, including conjunctivitis, uveitis, scleritis, and choroiditis are associated with the vestibuloauditory abnormalities [2]. In many cases, the symptomatology is not only restricted to the eyes and the ears but also other organs, thus resembling systemic vasculitis in one third of the patients. The most common symptoms are cardiovascular, musculoskeletal, neurological, gastrointestinal, and mucocutaneous [3].

Positron emission tomography (PET) with 2-deoxy-2-[<sup>18</sup>F]fluoro-D-glucose (FDG) is becoming increasingly important in diagnosis, staging, and therapy monitoring in clinical oncology and has recently been used in the diagnosis of infectious diseases with elevated intracellular glucose metabolism. Activated inflammatory cells have been shown to overexpress glucose transporters and to accumulate increased amounts of glucose and structurally related substances such as F18-FDG [4, 5].

Therefore FDG-PET is also introduced as a diagnostic means to assess involvement in large vessel vasculitis [6]. In this report, we report the use of FDG-PET/computed tomography (CT) scanning in the diagnosis of Cogan's syndrome.

### Case report

A 60-year-old Caucasian woman was admitted to the hospital with a 4-month history of excessive fatigue, coughing, anorexia and weight loss, night sweats, and atypical chest pain. She also experienced short periods of fever. She experienced headaches and ear pain and hearing

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loss for over the last month, mainly on the left side, and felt sometimes dizzy. No blurred vision complaints or eye problems were noted. She was not known with any allergies.

For her hypothyroidism (multinodular goiter), she used Thyrax (L-thyroxine) 150 mcg once a day. She did not smoke and consumed alcohol only moderately.

The family history revealed a daughter with systemic lupus erythematosus.

Physical examination revealed a pulse of 104, and bloodpressure was 125/85 mmHg and the temperature 37.1°C. Heart sounds were normal, and the lungs were clear. The outer ears were normal. No lymphadenopathy was detected and no scalp tenderness or decreased pulsation at the temporal arteries was noted.

Laboratory tests revealed an erythrocyte sedimentation rate (ESR) of 51 mm/h and C-reactive protein (CRP) of 53 mg/L. Test for rheumatoid factor was 42 kU/L (<10), and tests for antinuclear factor and double-stranded DNA antibodies were negative.

A test for anti-neutrophil cytoplasmic antibody (ANCA) appeared to be myeloperoxidase positive with p-ANCA specificity.

Serum electrolytes and creatinine were normal. Her differential blood count, alkaline phosphatase, and transaminases were normal. The urine gave a negative test for protein, and the sediment contained no white cells, red cells, or casts in the urine.

Initially arteritis temporalis was suspected, but Doppler ultrasonography of the temporal arteries showed no abnormalities. A chest X-ray revealed no interstitial or focal

abnormalities. Subsequently, a PET/CT was performed, which showed pathological uptake in the wall of the aortic arch. More intense pathological uptake was seen at the beginning of the aorta descendens in the lateral wall, most likely a sign of perivascular inflammation. Maximum standard uptake value (SUV max) measured 11.9. No other involvement of large vessels was noted (Fig. 1). A magnetic resonance imaging (MRI) scan of the cerebrum showed abnormalities suspicious for bilateral mastoiditis, possibly as a consequence of bilateral otitis media.

After placing inner ear tubes, her hearing loss improved only little. Culture of the ear secretion was negative for pathogenic microorganisms. Audiograms confirmed sensorineural hearing loss, particularly in the left ear.

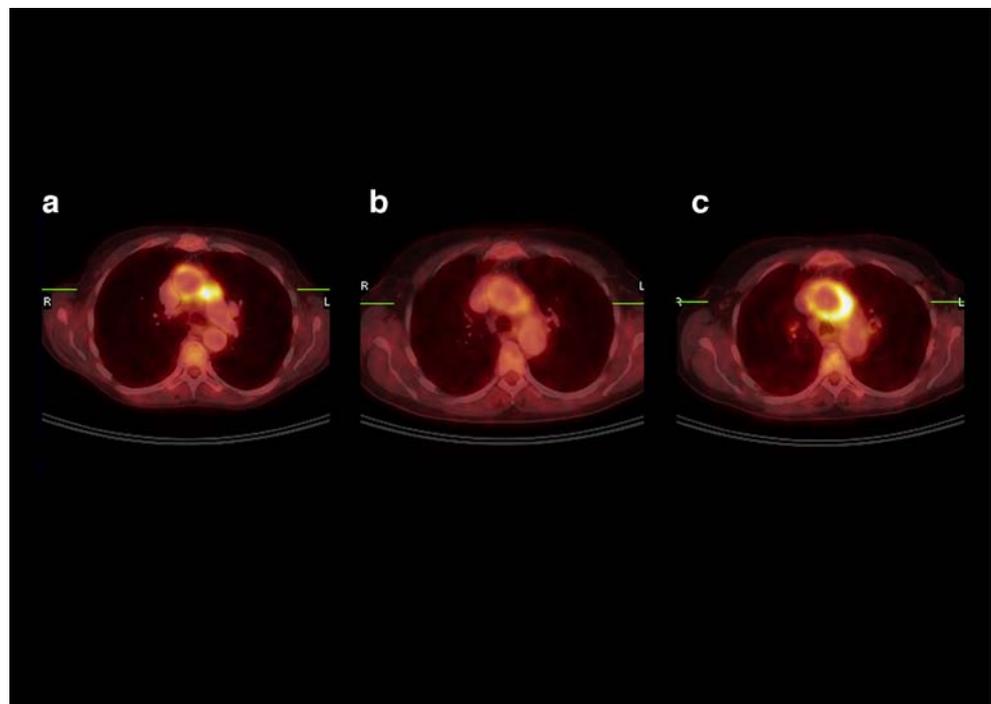
Investigation of the eyes revealed no abnormalities, especially no keratitis.

Therapy was started with three cycles of 1,000 mg methylprednisolone intravenously and later 60 mg prednisolone daily orally. Her general condition and hearing loss improved subjectively. Audiograms 6 weeks later showed also objective improvement of hearing. A control CT scan showed improvement of the abnormalities in both mastoid regions.

As a consequence of the high doses of steroids, risedronate and calcium supplementation were started, and also methotrexate was added for the reason of its steroid-sparing effect. “Atypical” Cogan’s syndrome was diagnosed on the basis of sensorineural deafness with improvement on steroids and large-vessel vasculitis of the aortic arch.

A follow-up PET/CT investigation 3 weeks later showed clearly decreased uptake in the aortic arch, especially a

**Fig. 1** **a** Transverse fused PET/CT slice showing pathological uptake in the wall of the aortic arch and particularly in the lateral wall and perivascular space adjacent to the truncus pulmonalis (SUV max 11.9). **b** Follow-up PET/CT 3 weeks later, after treatment with methylprednisolone i.v. and prednisolone orally, showing clearly decreased uptake in the aortic arch (SUV max 4.3). **c** Second follow-up PET/CT 6 months later, while patient was in a stable condition with methotrexate and low-dose prednisone. Again, high pathological uptake in the aortic arch with higher intensity in the lateral wall and perivascular space adjacent to the truncus pulmonalis (SUV max 12.9)



dramatic decrease at the location of the focal uptake in the lateral wall, compared to the first PET/CT. The SUV max was calculated 4.3. ESR and CRP after 2 weeks of therapy were, respectively, 11 mm/h and <2 mg/L. White cell count was still elevated ( $16.9 \cdot 10^9$  L).

Six months later, she was in a stable condition with methotrexate and low-dose prednisone, and her ESR, CRP, and white cell count were now, respectively, 24 mm/h, 14 mg/L, and  $13.7 \cdot 10^9$  L.

A third PET/CT showed higher pathological activity, compared to the first PET/CT, in the wall of the aortic arch and in the perivascular space adjacent to the truncus pulmonalis (the SUV max was 12.9 compared to the SUV max of 11.9 of the first pretherapy PET/CT investigation). Consequently, the dose of methotrexate and prednisone were both increased to 20 mg/day.

## Discussion

The etiology of Cogan's syndrome is unknown; a minority of patients have rheumatoid factor, antinuclear bodies, and diminished complement levels. Histology of biopsies shows often vasculitis and perivascular inflammation. Giant cells may be present [7]. Specific involvement of large arteries has been reported in Cogan's syndrome [8]. Aortitis in Cogan's syndrome is indistinguishable from Takayasu's arteritis. Cardiac involvement during the course of Cogan's syndrome is, above all, aortic insufficiency. It is a severe complication that may require valve replacement, without which left ventricle involvement insufficiency develops, which can be fatal [9, 10].

Standard diagnostic modalities such as biopsy, angiography, ultrasound, and MRI are commonly unable to demonstrate the full extent of vascular involvement in large-vessel vasculitis. PET investigations might play an important role here as large-vessel F18-FDG uptake is positively correlated with the level of acute phase reactant markers in patients with large vessel vasculitis. In a study of 18 patients with Takayasu's arteritis, the F18-FDG-PET examination showed a sensitivity of 92% and a specificity of 100% [11].

This is, to the best of our knowledge, the first report of Cogan's syndrome diagnosed by the use of FDG-PET/CT scanning. This case report is also supportive in the hypothesis that with PET, the inflammatory activity of large-vessel vasculitis is more accurately assessed compared

to laboratory acute phase parameters [12]. The CT component of PET/CT is useful in the precise anatomical localization of the PET abnormalities and may provide information about changes in the wall structure or luminal flow [13].

The conclusion seems justified that F18-FDG-PET/CT is helpful in risk assessment of large-vessel vasculitis, as it provides intrinsically fused morphologic and functional data in a single examination.

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