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LARGE-VESSEL VASCULITIS AND Q FEVER CORRELATION

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ABSTRACT

Q fever is a zoonotic infection caused by the pathogen *Coxiella burnetii*, and patients can present with a wide spectrum of clinical manifestations, depending on whether it is an acute or a chronic infection.

We present the case of a 61-year-old male with fatigue, posterior thoracalgia, intermittent fever, night sweats and weight loss for a month. After an extensive workup, he was diagnosed with acute Q fever with large-vessel vasculitis. The FDG-PET/CT scan suggested an active vasculitis specifically in the thoracic aorta, proximal abdominal aorta, subclavian and carotid vessels, suggesting an immunologic response to acute Q fever infection, barely reported worldwide.

KEYWORDS

Large-vessel vasculitis, Q fever, FDG-PET/CT scan

LEARNING POINTS

- Large-vessel vasculitis is a possible immunologic response to acute Q fever infection.
- There are few data about the management and treatment of patients with Q fever related large-vessel vasculitis.

CASE DESCRIPTION

A 61-year-old male was admitted to the internal medicine department on 16 April 2021 due to fatigue, posterior thoracalgia and intermittent fever, especially at night, for a month. The pain was worsened in orthostatism and was associated with muscle weakness in the limbs. Additionally, he complained of night sweets, anorexia and a weight loss of 16 kg over two months.

The patient denied gastrointestinal or genitourinary symptoms. He also denied foreign travels in the last year, contact with animals and ingestion of unpasteurised dairy products or unpotable water.

The patient's medical history included a gastric ulcer, hypertension, benign prostatic hyperplasia, bilateral glaucoma and occlusion of the left central retina vein. He was a heavy smoker (three packs a day for 40 years). He had stopped drinking alcohol two months before. His daily medication was omeprazole 20 mg *qd*; amlodipine/valsartan 5 mg/160 mg *qd*; doxazosin 8 mg *qd*, alprazolam 0.25 mg *qd*, acetylsalicylic acid 150 mg *qd*, timolol/dorzolamide 5 mg/5 ml+20 mg/ml *bid*, brimonidine 0.7 mg/0.35 ml *bid*, latanoprost 0.05 mg/ml *qd*. The patient denied known allergies.

On examination, he was normotensive with a blood pressure of 110/53 mmHg, heart rate of 90 bpm, peripheral oxygen saturation of 96%, and febrile with a temperature of 37.8ºC. A general examination was unremarkable; no lymphadenopathies or organomegalies were noted.

The patient had already undergone some diagnostic tests

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outside the hospital's care. The blood tests of February 2021 demonstrate normocytic normochromic anaemia with haemoglobin 10.6 g/dl (reference range >14.5 g/dl), erythrocyte sedimentation rate 108 mm/h (reference range <20 mm/h), elevated c-reactive protein of 13.1 mg/dl (reference range <0.5 mg/dl) and gama-glutamyl transpeptidase of 99 U/l (reference range <30 U/l). A thoracic and abdominal CT scan on 5 April shows hepatic steatosis and a lung calcified granuloma. An upper digestive endoscopic study and prostate ultrasound were also performed, without significant changes.

Repeated blood tests confirmed the findings of the February tests. Two sets of blood cultures and sputum cultures were obtained with negative results, including for mycobacteria.

Investigations for the possibility of a systemic autoimmune disease included antinuclear antibodies, anti-neutrophil cytoplasmic antibodies and rheumatoid factor, and were all negative.

Considering the subacute fever, and despite the absence of heart murmurs, a cardiac ultrasound was performed to exclude endocarditis; results were normal.

The interferon-gamma release assay was positive, compatible with latent tuberculosis.

Serological tests for infectious diseases such as hepatitis C and B, HIV, syphilis, *Mycoplasma*, *Borrelia*, *Rickettsia*, *Bartonella*, *Legionella* and *Brucella* were all negative, but confirmed previous infections with cytomegalovirus, Epstein-Barr virus and toxoplasmosis. For *Coxiella burnetii* he was positive with a titre of 1,280 (reference > 80). The confirmatory tests were performed: a phase II IgG of 1,280; phase II IgM, phase I IgG and phase I IgM were negative, thus confirming acute Q fever.

An FDG-PET/CT scan presented high FDG-F18 uptake, suggesting active vasculitis, in the ascending and descending thoracic aorta, proximal abdominal aorta, left and right subclavian, carotid vessels, without suspected adenopathies *(Fig. 1A)*. There was also a calcified micro-nodule in the upper lobe of the right lung, in relation to a granuloma.

A transoesophageal cardiac ultrasound was requested, which excluded the presence of vegetations.

Given the diagnosis of acute Q fever with vascular involvement, he was started on doxycycline 100 mg *bid* and hydroxychloroquine 200 mg tid. He was discharged for ambulatory consultation with prednisolone 60 mg/daily starting dose, to induce remission, and a dose tapering schema to a target dose of 15–20 mg/day within 2 to 3 months. Antimicrobial treatment for latent tuberculosis was started with isoniazid 300 mg *qd* and pyridoxine 150 mg 2 times per week.

After 3 months of isoniazid treatment, the patient was readmitted to the internal medicine department due to peripheral neuropathy and toxic hepatitis. Isoniazid was suspended and replaced with rifampin.

A control FDG-PET/CT scan was performed at 6 months after the treatment initiation, indicating diminished inflammation in the affected vessels *(Fig. 1B)*.

In December 2021, after eight months of treatment, the tests for *C. burnetii* antibodies, phase II and phase I, were all negative. Prednisolone tapering continued to 10 mg daily. The inflammatory parameters (erythrocyte sedimentation

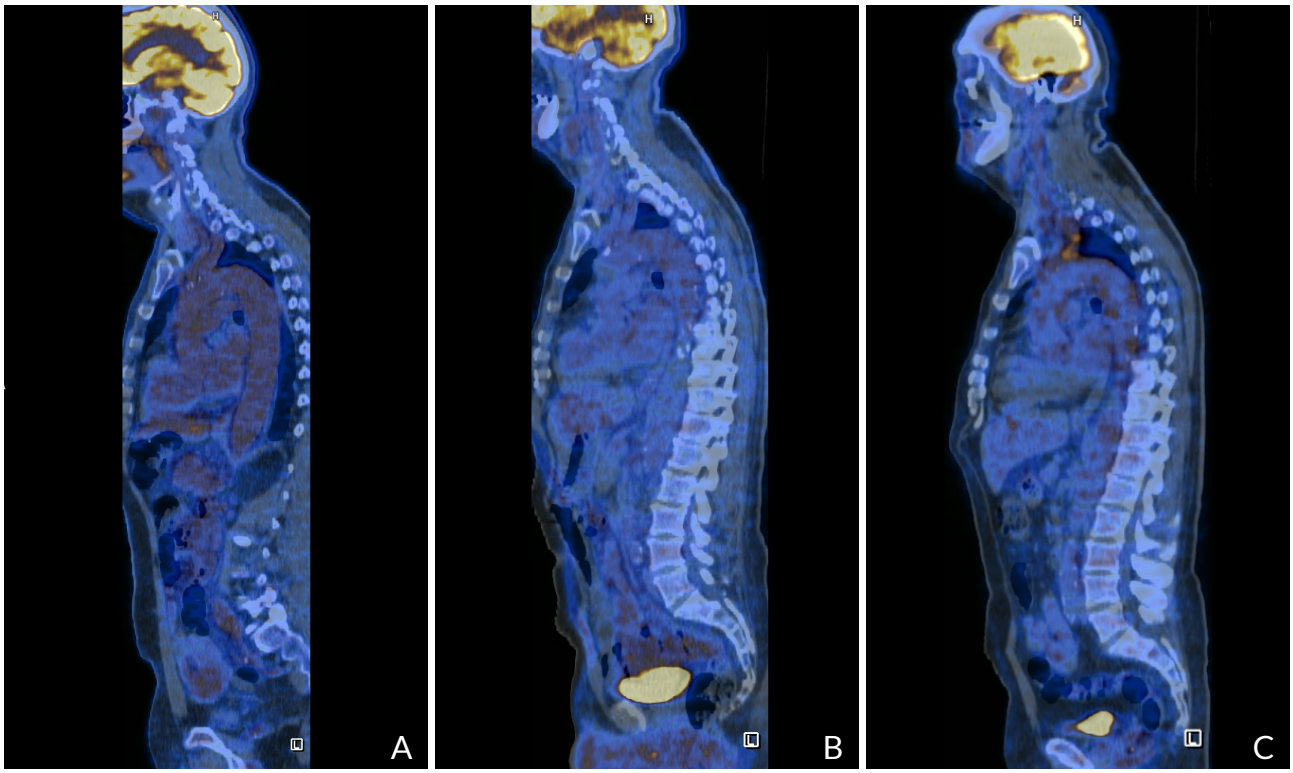

Figure 1. A) FDG-PET/CT scan before initiated treatment suggesting active vasculitis. B) FDG-PET/CT scan 6 months after initiated treatment with corticosteroids, doxycycline and hydroxychloroquine indicating diminished inflammation. C) FDG-PET/CT scan after finishing treatment with doxycycline and hydroxychloroquine and reducing dosage of corticosteroids, demonstrating extended vasculitis.

rate and c-reactive protein) and haemoglobin normalised.

One month after the doxycycline and hydroxychloroquine 12 months' treatment ended, a new control of phase II and phase I antibodies was performed, demonstrating an elevation of phase II IgG up to 800 *(Fig. 2)*. The IgM of phase II or phase I and phase I IgG were always negative.

A subsequent FDG-PET/CT scan showed extended vasculitis in the carotid arteries, subclavian arteries, ascending and descending thoracic aortic, aortic arch, abdominal aorta (not present before), and iliac and femoral arteries (not present before) *(Fig. 1C)*.

A second transoesophageal echocardiography was requested, excluding endocarditis. A PCR test was performed on the patient's blood to amplify *C. burnetii* DNA, but nothing was detected. The inflammatory markers were normal and haemoglobin was stable at 14.8 g/dl.

The patient's symptoms restarted with fatigue and thoracic discomfort. Despite low inflammatory markers, the prednisolone was increased to 40 mg/day.

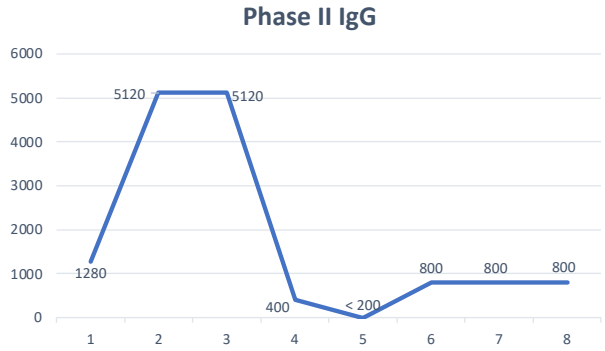

Figure 2. Evolution of the title of phase II IgG antibodies

DISCUSSION

Q fever is a zoonotic infection caused by the pathogen *C. burnetii*, and patients can present with a wide spectrum of clinical manifestations, depending on whether it is an acute or chronic infection[1,2]. Normally, in acute Q fever phase II IgG titres are over 200 and IgM over 50[3]. However, in this case only phase II IgG was present, which was sufficient to conclude a recent infection by *C. burnetii*.

Despite most endocarditis cases being related to chronic Q fever, in patients above 60 years old such as our patient, it is recommended to exclude endocarditis even if they present with acute Q fever, especially in those with vascular involvement[1,3].

The FDG-PET/CT scan has been used for estimation of vascular involvement mostly in chronic Q fever[4]. Nevertheless, in this case it seems that acute Q fever triggered an immunologic process which resulted in the inflammation of the thoracic aorta, proximal abdominal aorta, and subclavian and carotid vessels, with imaging from the FDG-PET/CT scan identical to that of Takayasu's arteritis.

It is well known that in Q fever endocarditis the preferred course of treatment is doxycycline and hydroxychloroquine for 12 to 18 months[3]. In this case, endocarditis was not present; however, due to large-vessel involvement, we based the treatment on the same scheme with the addition of steroids to reduce the inflammatory activity.

Serology tests are recommended 3 and 6 months after the acute infection. If antibodies against phase I antigens remain low and if the patient does not have underlying valvular disease, follow-up can be stopped. In patients with a rapid increase in antibodies against phase I antigens, in men over 40 years and/or those with antiphospholipid antibodies, it is recommended that a transoesophageal echocardiogram is performed[2]. There are no recommendations in case of reactivation of phase II IgG antibodies, which occurred in this patient. Therefore, we assumed endocarditis or reactivation of the vasculitis as being possible, as the patient had thoracic discomfort, and a transoesophageal echocardiogram and FDG-PET/CT were repeated.

In a recent review of cases, only four involving large-vessel vasculitis related to *C. burnetii* infection were described, with one death[5]. The patients received different treatments: two patients received hydroxychloroquine and methotrexate, one patient only received hydroxychloroquine and another only received methotrexate; all patients received steroids but in different dosages. This shows that are not enough data related to the management and treatment of patients with Q fever related large-vessel vasculitis.

Since vasculitis is a rare complication of Q fever, the publication of different cases with distinctive therapies and prognosis may help the management of these patients in the future.

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