CASE REPORT

Contrast-enhanced ultrasonography in Takayasu arteritis: watching and monitoring the arterial inflammation

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Accepted 23 September 2015

SUMMARY

A 43-year-old man was diagnosed with Takayasu arteritis, and treated with methotrexate and corticosteroids. While under treatment and with normal biological inflammatory parameters, he experienced an ischaemic stroke, successfully treated with intravenous thrombolysis (alteplase). The B-mode ultrasound examination revealed circumferential wall thickening of the left common carotid artery. Contrast-enhanced ultrasonography showed a progressive arterial wall enhancement of the left common carotid artery. This pathological enhancement indicates neovascularisation of the arterial wall, which is supposed to correlate with active vascular inflammation. After an increase in immunosuppressive treatment, follow-up contrast-enhanced ultrasonography no longer showed artery wall enhancement. Contrast-enhanced ultrasound examination is an inexpensive, reproducible and minimally invasive method, providing dynamic information on arterial wall neovascularisation and thus inflammation. This case illustrates that contrast-enhanced ultrasonography can be a useful tool for the management and follow-up of Takayasu arteritis, and its use as a marker of disease activity and arterial inflammation in Takayasu arteritis should be evaluated in further studies.

they do not always correlate with disease activity.³ Imaging methods are used for diagnosis and to determine the extent and evolution of the arterial lesions. Conventional angiography is still considered the gold standard for diagnosis, but non-invasive vascular imaging methods are more frequently used (computerised tomographic angiography, MR angiography and colour Doppler ultrasound). In recent years, interest in positron emission tomography with ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG PET) has risen because it combines anatomical and functional information.⁴ Hypermetabolic artery wall in ¹⁸F-FDG PET seems to correlate with activated inflammatory cells infiltrating the arteries. ¹⁸F-FDG PET may be used to assess and monitor disease activity, but is limited by its cost, availability and radioactivity.

Contrast-enhanced ultrasonography has recently been developed. This uses hyperechogenic microbubbles that are trapped in the vasa vasorum of the intima and media, without diffusion to the interstitium. It is currently used in atherosclerotic disease:⁵ the degree of enhancement correlates with the neovascularisation, which itself correlates with the degree of inflammation of the plaque. Its use in arteritis has yet to be evaluated,⁶ but it is a promising method, as we illustrate with this case.

BACKGROUND

Takayasu arteritis is a rare chronic vasculitis affecting large vessels such as the aorta and its main branches. It is characterised by granulomatous inflammation of the vessel wall. This inflammation leads to wall thickening, stenosis, thrombus formation and, ultimately, to organ ischaemia.¹

The disease mainly affects individuals in their second or third decade of life. Clinical manifestations include fever, weight loss, fatigue and symptoms of organ ischaemia. Diagnosis is based on clinical and angiographic manifestations: blood pressure difference >10 mm Hg between arms; bruits over subclavian arteries; and arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities.

Management of Takayasu arteritis is challenging. The main reason for this is the lack of parameters reflecting disease activity, especially arterial wall inflammation, which is the driving force behind the disease.² Biological inflammatory parameters (serum C reactive protein (CRP) level and erythrocyte sedimentation rate (ESR)) are largely used, but

CASE PRESENTATION

A 43-year-old man with a medical history of hypertension had recurrent amaurosis fugax of the left eye. He had an otherwise normal clinical examination. His blood analyses revealed an elevation of biological inflammatory parameters. A whole-body CT angiography showed multiple arterial stenoses (left common carotid artery, right and left subclavian arteries) and occlusion of the right common carotid artery, with a thickening of the left common carotid artery wall. ¹⁸F-FDG PET showed increased fixation in these arteries. Takayasu arteritis was diagnosed based on clinical, biological and angiographic parameters. The patient fulfilled the American College of Rheumatology 1990 Classification Criteria for Takayasu arteritis.⁷ Treatment with methotrexate (20 mg/week) and corticosteroids (60 mg/day) was started, associated with an antithrombotic agent (aspirin 75 mg/day). After 2 weeks, his biological parameters were normal, and the patient was asymptomatic. The corticosteroids were then slowly decreased to 25 mg/day.

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To cite: Herlin B, Baud J-M, Chadenat M-L, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-211094

Three months later, while he was still under the same treatment, he had a sudden left hemiparesis and dysarthria. MRI showed a right middle cerebral artery (MCA) ischaemic stroke with right M2-MCA occlusion. T2*-weighted gradient echo axial image showed a susceptibility sign at the M2 portion of the left MCA. The patient had a National Institutes of Health Stroke Score (NIHSS) of 9. Because of the M2-MCA occlusion on the MRA during the acute ischaemic event while his intracranial arteries were normal on the previous angiography 3 month before, and the susceptibility sign in T2*-weighted gradient echo axial image at the M2 portion of the left MCA, we evoked a clot in the M2 portion of the left MCA, which can be favoured by the disease activity.⁸ The patient was therefore treated with intravenous recombinant tissue plasminogen activator (rt-PA) 0.9 mg/kg 162 min after the start of the symptoms. He had an excellent clinical recovery: his NIHSS 12 h after thrombolysis was 2, and 24 h after, was 0. Biological inflammatory parameters were normal (CRP<5 mg/L, ESR=1 mm/h).

INVESTIGATIONS

The patient suffered from an acute ischaemic event, which could be related to his Takayasu arteritis, while he was under immunosuppressive treatment and had normal biological inflammatory parameters. To optimise his treatment, it was therefore important to analyse whether this ischaemic event was a consequence of the disease activity.

To assess the existence of vascular inflammation, we performed contrast-enhanced ultrasonography. The ultrasound equipment used was an Acuson S2000 (Siemens, Germany), equipped with a 9–4 MHz linear-array transducer for carotid examination. The B-mode ultrasound examination revealed occlusion of the right common carotid artery and a circumferential wall thickening of the left common carotid artery, as seen in the initial vascular imaging performed at the diagnosis of the arteritis. This ultrasound examination was completed with contrast-enhanced ultrasonography. The contrast agent (Sonovue; Bracco SpA, Milan, Italy) is used by intravenous injection of one bolus of 2.5 mL, followed by a 10 mL saline flush. Contrast-enhanced ultrasound examination was performed using Cadence CPS (Contrast Pulse Sequencing) technology, which is a real-time non-linear imaging technique with a low mechanical index (0.07) allowing a good contrast/tissue specificity. Thirty seconds after the intravenous contrast agent injection (hyperechogenic microbubbles), there was a progressive arterial wall enhancement of the left common carotid artery (figure 1A, B; videos 1 and 2). Microbubbles were visible in the far and near wall, with a circumferential pattern on transversal view. We deduced that the presence of microbubbles in the artery wall was not an artefact arising from pseudo enhancement.⁹ This pathological enhancement was due to the infiltration of microbubbles into the wall thickness, which were then trapped in the vasa vasorum, indicating neovascularisation of the arterial wall and, we hypothesised, active vascular inflammation.

TREATMENT

Based on the clinical ischaemic event and the ultrasound examination, which suggested an active vascular inflammation despite normal biological inflammatory parameters, the dose of corticosteroids was increased to 60 mg/day.

OUTCOME AND FOLLOW-UP

Follow-up ultrasonography was performed to monitor the arterial enhancement 1 and 3 months after the ischaemic event.

Figure 1 Initial contrast-enhanced ultrasonography of the left common carotid artery; (A) longitudinal and (B) transverse sections. Star indicates arterial lumen filled with contrast agent and arrows show microbubbles in the wall thickness, trapped in the vasa vasorum, indicating neovascularisation of the arterial wall, which correlates with the degree of vascular inflammation.

The B-mode ultrasound Doppler appearance did not change. On contrast-enhanced ultrasonography, 1 month after the event, the artery wall enhancement was less pronounced. Three months after the event, no artery wall enhancement was observed after the contrast agent injection (figure 2A, B; video 3).

DISCUSSION

This case illustrates a patient with Takayasu disease with normal biological inflammatory parameters who experienced a clinical ischaemic event. Contrast-enhanced ultrasonography depicted an arterial wall enhancement highly suggestive, in this context, of active arterial inflammation.

Contrast-enhanced ultrasound examination of carotid arteries is an inexpensive, reproducible and minimally invasive method

Video 1 Initial contrast-enhanced ultrasonography of the left common carotid artery, longitudinal view. Intravenous contrast agent was injected at t=0 s; it resulted in arterial lumen opacification, which highlights the concentric thickening of the arterial wall; and then a progressive arterial wall enhancement due to microbubbles in the wall thickness, trapped in the vasa vasorum. This enhancement indicates neovascularisation of the arterial wall, which correlates with the degree of vascular inflammation.

Video 2 Initial contrast-enhanced ultrasonography of the left common carotid artery, transverse view. Intravenous contrast agent was injected at $t=0$ s; it resulted in arterial lumen opacification, which highlights the concentric thickening of the arterial wall; and then a progressive arterial wall enhancement due to microbubbles in the wall thickness, trapped in the vasa vasorum. This enhancement indicates neovascularisation of the arterial wall, which correlates with the degree of vascular inflammation.

that visualises neovascularisation associated with arterial inflammation in patients with Takayasu disease. Two previous reports^{10 11} have used this technique in this setting. The authors reported using it for diagnosis in patients with elevated biological parameters of inflammation. The interest of our case is that our patient had already been diagnosed and treated, and

Video 3 Three-month follow-up contrast-enhanced ultrasonography of the left common carotid artery, transverse view. Intravenous contrast agent was injected at $t=0$ s; it resulted in arterial lumen opacification, which highlights the concentric thickening of the arterial wall; and no further arterial wall enhancement.

had normal biological markers of inflammation when he experienced a thrombotic event. The mismatch between biological and contrast-enhanced ultrasonography could suggest that the latter technique was more sensitive in this case. The value of contrast-enhanced ultrasonography as a marker of disease activity and arterial inflammation in Takayasu disease should be evaluated in larger, specific studies.

Learning points

- ▶ Ischaemic stroke due to a clot occurring in a patient with Takayasu disease can be successfully treated by intravenous thrombolysis (alteplase).
- ▶ Management of Takayasu arteritis is difficult because of the lack of standard parameters reflecting arterial wall inflammation.
- ▶ Contrast-enhanced ultrasonography is an additional technique to B-mode and Doppler mode ultrasonography, which enable a functional approach to microcirculation by highlighting arterial wall neovascularisation.
- ▶ This case suggests that contrast-enhanced ultrasonography could be a useful tool for the management and follow-up of Takayasu arteritis.

Figure 2 Follow-up contrast-enhanced ultrasonography of the left common carotid artery 3 months after the ischaemic event; (A) longitudinal and (B) transverse sections. Star indicates arterial lumen filled with contrast agent and triangles show no microbubbles in the wall thickness.

Acknowledgements The authors are thankful to Jean Emmanuel Kahn and Olivier Blety for their help in manuscript revision and patient care.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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