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Case Report

Potential Application of Diffusion-Weighted Whole-Body Imaging with Background Body Signal Suppression for Disease Activity Assessment in Takayasu Arteritis—In Search of the ''Golden Mean'': Case Report

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The case report describes our first experience of ''diffusion-weighted whole-body imaging with background body signal suppression'' (DWIBS) application for disease activity assessment in a young female patient with Takayasu arteritis (TA). Despite the normal level of inflammatory markers, clinical signs of disease recurrence were present. In our case, DWIBS did not only help to identify the disease recurrence in the patient with false-negative inflammatory markers but also revealed new foci involved in the TA process. DWIBS can be a potentially new imaging method, useful during the follow-up in patients with TA.

Nonspecific aortoarteritis or Takayasu arteritis (TA) is an idiopathic large-vessel vasculitis, affecting predominantly young women. The multifocality of the lesions of the thoracoabdominal aorta in TA causes not only the diversity of the clinic but also the difficulties of diagnosis and assessment of the disease activity in such patients. As a result, noninvasive imaging modalities, such as ultrasonography, magnetic resonance imaging (MRI), multislice computed tomography angiography (MSCTA), and 2-[^{18}F]-fluoro-2-deoxy-D-glucose positron emission tomography (^{18}F-FDG-PET), are used to assess disease activity.[1] Nevertheless, there are a number of objective shortcomings, such as impossibility to examine the vessels of the whole body, radiation, administration of a contrast agent, and a relatively high cost.[2] In 2004, Takahara et al.[3] reported a unique concept of whole-body MRI called ''diffusion-weighted whole-body imaging with background body signal suppression'' (DWIBS). This method provides functional information and plays an important role in whole-body oncological imaging. In this case report, we describe the application of DWIBS for disease activity assessment in a patient with TA.

CASE REPORT

A 32-year-old female was admitted to the Republican Specialized Center of Surgical Angioneurology with complaints of neck pain, vertigo on exertion, and low-grade fever a week before admission. The diagnosis of TA has been confirmed since 2013, according to the criteria of the American College of Rheumatology (1990).[4] On admission, patient was in good general condition, with good logical contact, oriented to person, time, and space. In physical examination, we found absence of pulse on the both radial arteries. Bruits could be heard over the right cervical artery.

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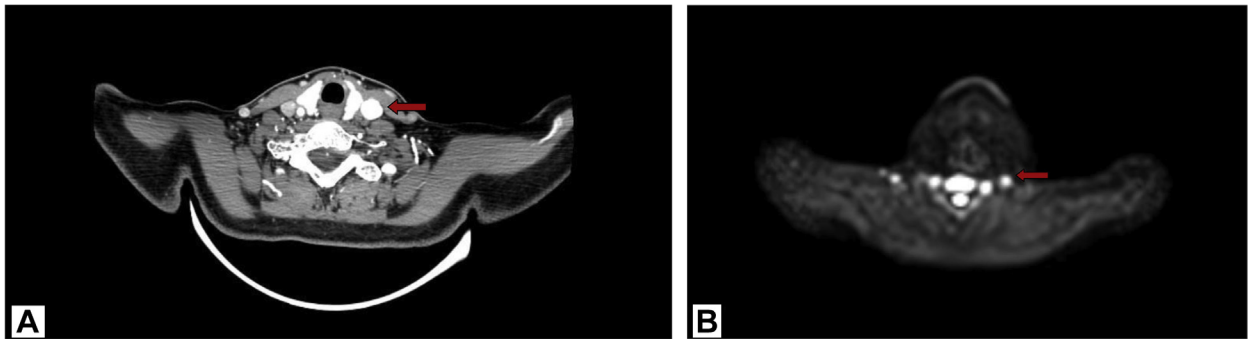

Fig. 1. MSCTA **(A)** and DWIBS **(B)** showing inflammation on the same artery wall (red *arrows*).

Apart from microcytic anemia (hemoglobin, 9.5 g/dL; mean corpuscular volume, 76.1 fl), laboratory studies did not reveal the presence of elevated inflammatory markers (erythrocyte sedimentation rate, 9 mm/h; serum C-reactive protein level $\leq$ 0.2 mg/dL). Hepatic and renal functions and immunoglobulin and serum complement levels were within the normal limits. Antinuclear antibody, antineutrophil cytoplasmic antibodies, and rheumatoid factor were not detected. A serological test for syphilis was negative.

At the time of admission, the patient was on immunosuppressive therapy with prednisone at a dose of 10 mg/day.

Color Doppler ultrasonography (CDUS) examination of cephalad arteries visualized concentric, hypoechogenic thickening of brachiocephalic trunk walls causing stenosis from the right side and total occlusion of common carotid artery from the left. On both sides, we noted occlusion in the proximal part of the subclavian artery. Vertebral arteries were unremarkable bilaterally. CDUS showed no significant changes 2 months before.

The patient had MSCTA of cephalad arteries 2 months before admission, confirming bilateral involvement of carotid and subclavian arteries.

To evaluate the activity of the inflammatory process, DWIBS was used. The examination was performed on a 1.5-T MRI scanner (Achieva; Philips Healthcare), with the patient positioned feet first on an extended anatomical coverage table, based on the rolling-table technology (MobiTrak; Philips). The used sequences were coronal T1-weighted turbo spin echo, coronal short tau inversion recovery sequence (STIR) from the head to the midthigh, and axial DWIBS single-shot echoplanar imaging (ss-EPI). The coronal T1WI was with Q body coil with the following parameters: slice thickness, 4 mm; gap, 1 mm; number of slices for station, 44; field of view, 530 $\times$ 265; acquisition matrix, 208 $\times$ 287, and reconstruction matrix, $\times$ 512. The coronal STIR sequence was acquired with the same parameters as coronal T1WI, except repetition time/echo time 64; inversion time, 165 ms; and acquisition matrix, 336 $\times$ 12. Both T1WI and STIR images were acquired in free breathing. DWIBS was acquired in free breathing and the axial plane using Q body coil with the following parameters: ss-EPI; repetition time/echo time, shortest; inversion time, 180 ms; slice thickness, 6 mm; gap, 0 mm; echo-planar imaging factor, 61; b values, 0—1,000 s$\setminus$mm^2. The total examination time was about 40 min for whole-body DWIBS. No contrast agent was applied. Reconstructed DWIBS images from the axial plane were obtained and merged with T1 and STIR to form fused T1/DWIBS and STIR/DWIBS images. Color-coded fused T1-DWIB images were generated at the Philips workstation.

Signal enhancement was detected from both carotid and subclavian arteries. The foci from both carotid and subclavian arteries detected by the DWIBS MRI study were confirmed by MSCTA (Fig. 1). In addition, foci of an enhanced signal from the both iliac arteries were identified (Fig. 2). Based on the data from the aforementioned studies, we concluded that the patient had type V disease with involvement of the aortic arch vessels and abdominal aortic branches in a phase of active inflammation. So, the patient received treatment with pulses of methylprednisolone at 4-week intervals, together with long-term prednisone therapy (with intention to tamper the doses) and dual antiplatelet therapy.

DISCUSSION

Currently, many new methods of diagnosis and treatment of diseases have appeared at the disposal of medical practitioners. However, with this choice of methods for examining patients, there are a number of objective shortcomings. First, some examination methods, as well as the equipment on which they are conducted, are expensive. Second, conducting some examinations, despite their high technology requirement, is to some extent dangerous to the patient (invasiveness, radiation). Finally, the most important is that these methods do not cancel but only complement the already-existing methods of diagnosis and treatment of diseases.

More often, it concerns to so-called ‘‘difficult’’ diagnoses. These diseases include TA. The task of

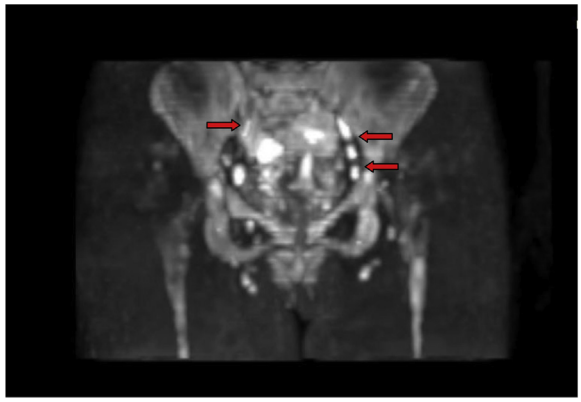

Fig. 2. Pelvic DWIBS: enhanced signal from both iliac arteries (red *arrows*).

the practitioner in examining a patient with TA is to find the ''golden mean'' to set the correct diagnosis and avoid unreasonable methods of examining patients.

TA, also known as ''pulseless disease,'' is a chronic inflammatory disease of large arteries. The name comes from a Japanese ophthalmologist, Mikito Takayasu, who described characteristic symptoms of this disease in 1908.[5]

TA can lead to significant morbidity and mortality, with the degree of arterial damage closely correlated with the prognosis of the disease.[6–8] Arterial thrombosis, occlusion, and aneurysms with end-organ ischemia are common complications.[9,10]

According to a long-term follow-up study published recently, half of patients with TA relapse and experience a vascular complication in 10 years from diagnosis.[11] However, the nonspecific clinical symptoms, varying according to the arteries and related blood supply areas involved, made the diagnosis and activity assessment of TA difficult and often ambiguous.

The current understanding of the pathogenesis of the disease is significantly limited by the relative inaccuracies of the physical examination in assessing the lesion of large vessels and the lack of available biopsy material.[12,13] At the same time, methods for accurate assessment of disease activity are another important unmet need, and data from various authors show that laboratory markers of inflammatory activity are inaccurate in 50% of cases.[14] There is no single clinical study that accurately reflects the activity of the disease, and therefore, it was proposed to determine the activity index by several parameters. These include activity criteria of the National Institutes of Health[15] and the Indian Takayasu Disease Activity Indicator.[16] However, based on clinical and laboratory data, their accuracy remains suboptimal.

CDUS examination is one of widely available and noninvasive diagnostic methods. CDUS studies can help to establish a diagnosis of TA and may reveal those with prestenotic disease.[17] If it is performed by an experienced operator, CDUS would be the method of choice but is known to be rather observer dependent. Also it may be impossible to perform in some patients because of technical reasons (e.g., due to bowel gasses, obesity, ascites).[1]

Through its ability to evaluate a wide range of vascular territories, MRI has become one of the most important imaging techniques for TA, which allows multiple evaluations in young patients and pregnant women.[1] The predominant role of MRI in the follow-up of patients with TA is to provide a safe, noninvasive mean of assessing changes in vascular anatomy over time. It is still a matter of debate whether MRI can add useful information to disease activity assessment.[18,19]

To date, TA has been diagnosed using MSCTA, which allows an accurate assessment of the morphology and lumen of the vessel.[19] The great advantage of this method is the ability to plan endovascular treatment accurately. However, the patient is exposed to more ionizing radiation and may have contrast medium allergy. The frequent false-negative results in patients in the early stages of the disease should also be remembered, as well as the difficulties of visualizing vascular segments distal to stenosis.[20,21]

Although widely used, the precise role of ^{18}F-FDG-PET in the management of TA remains to be determined. First, these scans are very expensive, there is limited access to them outside oncology indications in many parts of the world, and the typical radiation exposure during an ^{18}F-FDG-PET/computerized tomography scan is between 10 and 15 mSv. Second, in addition to the radiation exposure involved, questions persist regarding its sensitivity and specificity for the detection of low-grade relapsing or partially treated arteritis.[22–24]

DWIBS images are acquired using multiple-signal averaging, prepulse fat suppression and heavy diffusion weighting during free breathing.[3] DWIBS is based on diffusion-weighted imaging that visualizes and assesses the random movement of water at the molecular level (Brownian motion) and its diffusion through the tissues.[3,25] An advantage of DWIBS is that it provides a strong contrast of cancerous tissues against surrounding noncancerous tissues, which is useful for the detection, staging, and monitoring of the response to therapy.[25] Failure of the Na+/K+ ATPase pump during inflammatory cell death may

also lead to restricted diffusion. In addition, intracellular edema also increases diffusion because of increased water content. So, the same principle can be used in case of acute inflammatory processes such as TA. Whole-body evaluation, relatively low cost, observer independency, avoidance of radiation exposure, contrast-medium allergy, and contrast-induced nephropathy make this method potentially preferable for disease activity assessment and monitoring. Currently, there is only one article describing the use of DWIBS for patients with TA, published by Oguro et al.[26]

In our case, DWIBS not only helped to identify the recurrence phase in a patient with false-negative inflammatory markers but also visualized new active foci well away from the symptomatic areas. DWIBS can be the potentially new imaging modality, useful during follow-up at patients with TA; however, further studies are needed.

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