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TAKAYASU ARTERITIS: RECENT ADVANCES AND CLINICAL PITFALLS

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ABSTRACT – Takayasu arteritis (TA) is a rare idiopathic inflammatory disease of large size arteries, primarily affecting young women. Vasculitic lesions might cause arterial steno-occlusions or dilatation with significant morbidity and mortality. TA rarity may result in its frequent under-recognition and diagnostic delays. Key disease features are systemic inflammation, arterial inflammation and remodelling. They may not always occur together and are differentially targeted by therapies. Accordingly, serial imaging studies are required for exhaustive activity assessment and patient follow-up. The present review provides a practical approach to most frequent clinical pitfalls, including diagnosis, activity assessment, the use of imaging, and the therapeutic approaches, and highlighs the most important unmet needs.

KEYWORDS: Takayasu arteritis, Vasculitis, Vascular remodelling, Magnetic resonance, Positron emission tomography.

INTRODUCTION

Takayasu arteritis (TA) is an idiopathic systemic disease characterised by patchy wall inflammation and thickening of large-sized arteries such as the aorta, the pulmonary arteries and their main branches[1-3]. Vasculitic lesions might undergo luminal remodelling resulting in arterial steno-occlusions (in more than 90% of patients) or, more rarely, in dilatations such as ectasias or aneurysms (in up to a quarter of patients)[4-8].

TA is a rare disease, frequently overlooked in the general medical audience and for which scarce good-quality evidence available. The scope of the present review is to summarise the state-of-the-art of the clinical practice of patients with TA, and to highlight the most important unmet needs.

NATURAL HISTORY

The traditional view of the natural history of TA identifies three phases: i) a systemic inflammatory phase, characterised by constitutional symptoms, ii) the vascular phase, characterised by vascular symptoms due to inflammation and progressive stenoses or dilatations, and ii) the fibrotic phase, characterised by burn-out disease. However, these phases may not be present or be consequential in all patients, and different arterial lesions in different phases frequently coexist in the same patients. Rather than distinct disease phases, they might be viewed as different pathogenic features, represented by systemic inflam-

mation, vascular inflammation and tissue remodelling. Accordingly, TA history might be simplified as an inflammatory phase that spontaneously tends to enter into a long-lasting remission.

The active, inflammatory phase has variable time-length and tendency to recur, being monophasic in about a quarter of patients and polyphasic in the remaining subjects, where it typically lasts months to many years[4]. It is believed that luminal remodelling typically occurs during the phases of active disease and persists during subsequent remission. However, there are exceptions to this general rule, that will be detailed below.

EPIDEMIOLOGY AND GENETICS

TA is a rare condition, with an average incidence of about 0.5-3/10^6*year[20,21]. Young females in the reproductive age are most frequently affected, with a male to female ratio of about 1:8. The peak incidence occurs in the third decade of life, and TA is classically view as a young-limited condition. Accordingly, the American College of Rheumatology (ACR) 1990 classification criteria recognize an age below 40 years old as an important criterion for prototypic TA. Paediatric-onset TA represents the third most incident vasculitis in this age group[22]. Evidence shows that paediatric patients more frequently have constitutional symptoms and involvement in the aorta and renal arteries[23,24], and might have a more severe course[25]. At the other end of the spectrum, the age at onset of 50 years has been proposed as a watershed to distinguish TA and giant-cell arteritis (GCA), which is an elderly-limited condition. However, there are subjects in which large-vessel vasculitis ensued beyond this age that lack specific features of GCA (such as cephalic involvement or polymyalgia rheumatica), while presenting clinical features similar to TA patients. These patients with elderly-onset TA might represent up to 15-20% in some TA cohorts[26,27].

TA is diffuse across all ethnic groups, although a higher disease prevalence is described in the Asian countries[20]. Familiar clustering of TA is rare, although relatives of affected patients may suffer from other systemic autoimmune conditions including systemic lupus erythematosus or rheumatoid arthritis. Genetic studies have identified risk factors for TA: some of these might depends on the population of interest, whereas others -most notably HLA B-52- have been confirmed in multiple ethnicities[28,29].

HISTOLOGY AND PATHOGENESIS

Pathogenic insight on TA is scarce and hampered by disease rarity and difficulties in obtaining arterial specimens. Most of knowledge derives from studies on GCA, another vasculitis affecting the wall of large-and medium sized arteries. Unfortunately, relevant clinical and epidemiological differences exist between GCA and TA, and it is debated whether these two conditions should be considered the spectrum of the same disease.

Broadly speaking, the three main pathogenic components of TA are systemic inflammation, arterial inflammation and tissue remodelling. The cellular and molecular events underlying these three occurrences are poorly understood. Most studies have focused on vascular inflammation and have shown that arteries are critical anatomical structures endowed with intrinsic tolerogenic properties that have been collectively referred as “arterial immune privilege”. Despite resting arteries do not contain leukocytes but resident vascular dendritic cells (vDCs), active TA lesions shows inflammatory infiltrates in all the tree vascular tunicas, which are composed of dendritic cells (DCs), CD4+ and CD8+ T cells, $\gamma\sigma$ T cells, NK cells, B cells, and macrophages, frequently structured in typical granulomas, which may contain multinucleated giant-cells[30,31].

Several mechanisms may contribute to overcome arterial tolerance[32]. These include i) activation of vDCs by toll-like receptors, ii) increased permeability and a pro-inflammatory phenotype of *vasa-vasorum* endothelium[33,34], iii) defective PD1/PDL1 inhibitory checkpoint[35], and iv) ineffective anti-inflammatory T_{reg} function[36]. Once arterial tolerance is lost and the arterial wall has become permissive to inflammation and leukocyte recruitment, wall-infiltrating T-cells and macrophages are the main drivers of persistent arterial inflammation, injury, and tissue remodelling. $CD4^+$ cells appear to differentiate towards T_h1 and T_h17 phenotypes. Tissue injury and remodelling might result from the activity of infiltration macrophages producing reactive oxygen species (ROS) and growth factors such as platelet-derived and vascular-endothelial growth factor (PDGF and VEGF). Histologically, this is reflected by *vasa-vasorum* neoangiogenesis, degradation of elastic fibres, laminar necrosis, smooth muscle degeneration, intimal hyperplasia, and wall fibrosis[32,37].

CLINICAL FEATURES

Clinical features of TA (Table 1) can be classified into three main domains, namely systemic inflammation, vascular involvement, and extra-vascular involvement. Vascular manifestations frequently represent the central and most cumbersome features. Here, the clinical features will be described in correlation with the three disease domains:

Table 1. Clinical manifestations of Takayasu arteritis.

Systemic inflammation	Arterial involvement	Extra-arterial involvement
Fever - Fatigue - Serositis - AA amyloidosis	- Arterial steno occlusions - Anisosphygmias/BP inequalities - Vascular bruits - Limb claudication - Atypical aortic coartation - Renovascular hypertension - Angina abdominis - CAD - TIA/stroke - Arterial aneurysms - Arterial inflammation (eg: arteriodynia) - Aortic valvulitis and regurgitation - Secondary (accelerated) atherosclerosis	- Erythema nodosum-like nodules - Pyoderma gangrenous - Peripheral arthritis - Axial arthritis and sacroileitis - Inflammatory-bowel diseases - Mouth ulcers - Uveitis - Scleritis/episcleritis - Myocarditis - Granuloumatous lymphadenitis - Sarcoidosis

Legend: CAD= coronary artery disease, TIA= transient ischemic attack.

- *Systemic inflammation.* Systemic inflammatory features such as fever, fatigue and raised acute-phase reactants frequently characterise the active phases of TA, both at disease onset and during flares. However, systemic inflammation has generally the maximal intensity at disease onset and before implementation of adequate therapies. Subjects with very high spiking systemic inflammation might experience serositis or serosal effusions. At the other end of the disease spectrum, up to 10-15% of subjects with typical arterial involvement fail to show a demonstrable systemic inflammation or a flu-like syndrome at disease onset or during previous months[2]. If significant systemic inflammation persists long enough, secondary amyloidosis (AA-amyloidosis) may ensue[9]. However, this occurrence is becoming anecdotal due to advances in therapy and diagnosis.
- *Vascular involvement*. Patchy arterial wall lesions characterised by inflammation and wall thickening represent the core feature of TA. Their distribution in the arterial tree is variable from patient to patient with obvious consequences on the clinical picture. Arterial wall thickening is *per se* asymptomatic, and vascular manifestations derive from active arterial inflammation or from luminal abnormalities (either steno-occlusion or dilatation). Arterial wall inflammation might result in pain in the actively inflamed arteries (known as “arteriodynia”). Arterial steno-occlusions might lead to anisosphygmias/inequalities in blood pressure among different arterial districts, vascular bruits, pulmonary hypertension or end-organ ischemia manifested by limb claudication, myocardial infarction, stroke, angina abdominis or renovascular hypertension. Collateral circulation is an important protective mechanism in specific arterial districts, most notably the limbs, the splanchnic organs and the CNS. A third group of vascular manifestation is a consequence of arterial ectasias or aneurysms. The aorta is the most frequent and clinically relevant site of arterial dilatation in TA. Associated clinical features might be aortic valve regurgitation, aneurysm rupture/dissection and compression of adjacent structures. In a minority of subjects, aortic valve regurgitation is independent of dilatation of the aortic root and is due to valvulitis and fibrous retraction of the valve cups[10]. Despite most vascular features of TA are directly related to arterial lesions, some complications may have a more complex, multifactorial pathogenesis: TA patients have an increased prevalence of arterial hypertension and suffer from accelerated atherosclerosis. For both conditions, multiple mechanisms have been proposed, ranging from concomitant therapies such as steroids, renin secretion by hypoperfused kidneys, abnormal baroreceptor reflex and reduced arterial compliance to local flow disturbances and the pro-atherogenic effect of paracrine and systemic inflammation.

- *Extra-vascular involvement*. Some patients with TA show extra-arterial involvement such as myocarditis[11], non-erosive arthritis[12], granulomatous lymphadenitis, uveitis/scleritis, or skin disorders such as erythema nodosum-like inflammatory nodules or pyoderma gangrenosum during active vasculitis phases[13]. Other patients (about 15-20% of TA) may experience the coexistence of other autoimmune conditions, whose clinical course might not parallel that of vasculitis[12]. These conditions include inflammatory bowel diseases such as ulcerative colitis or Crohn's disease[14-16], sacroileitis/spondylitis[17], sarcoidosis[18,19], relapsing polycondritis, and anti-phospholipid syndrome[12]. It is unclear whether large-vessel vasculitis in these subjects has a specific clinical course or response to medications, implying a differentiation from "typical" TA. Behcet's disease (BD) has been reported among comorbidity of TA, although this condition is known to affect vessels of variable size and, therefore, large-vessel vasculitis can be considered a manifestation of the primary disease.

DISEASE HETEROGENEITY

Major heterogeneity exists among affected patients, in terms of severity of arterial involvement, distribution of lesions within the arterial tree, coexistence of systemic and arterial inflammation, and response to medications.

The subclavian arteries are the most frequently involved vessels, followed by the aorta and the carotid arteries, with a tendency towards a paired bilateral involvement of symmetric vessels[4,5,38,39]. The mechanisms explaining disease heterogeneity are poorly understood. A puzzling feature is the segmental nature of arterial inflammation and its profound heterogeneity between patients. Definitive explanation for these findings is lacking, but it has been hypothesized that these might reflect the spatial differences existing among resident vDCs and among their surface expression of activating innate immunity receptors. Indeed, it has been shown that the portfolio of receptors expressed by resident vDCs has spatial specificity[40]. Accordingly, experimental vasculitis elicited by specific vDCs-activating stimuli has a spatial distribution consistent with the expression of cognate receptors by these cells[40].

DIAGNOSIS

TA patients frequently experience substantial diagnostic delays with detrimental effects on prognosis[41]. Lack of clinical suspicion is a frequent cause of delays and thus it is important to improve disease's knowledge among physicians. Table 2 lists the red flags for TA that should trigger further diagnostic workup.

Table 2. Red flags for TA.

Red flags for Takayasu arteritis in a young patient
Arterial wall thickening at imaging
Arterial bruits/BP inequalities
Arterial occlusions
Multifocal arterial stenosis and/or dilatation
Smooth arterial wall thickening
Arterial wall inflammation

There is no diagnostic marker for TA and multiple diagnostic or classification criteria have been proposed for TA[42]. However, their utility in the clinical practice is limited, as they are designed mainly for studies or for patients with advanced disease and significant arterial remodelling. Accordingly, diagnosis is obtained by the combination of clinical features and imaging findings (Figure 1). Diagnosis might be puzzled by the high heterogeneity in the potential presentation of TA[43]. However, in our experience, TA presentation can be ascribed to the following three main clinical patterns:

1) Fever or a systemic inflammatory syndrome of unknown origin in a young patient.
2) Arterial stenosis or occlusion unrelated to atherosclerosis or fibromuscular dysplasia.
3) Imaging findings of arterial wall thickening or inflammation.

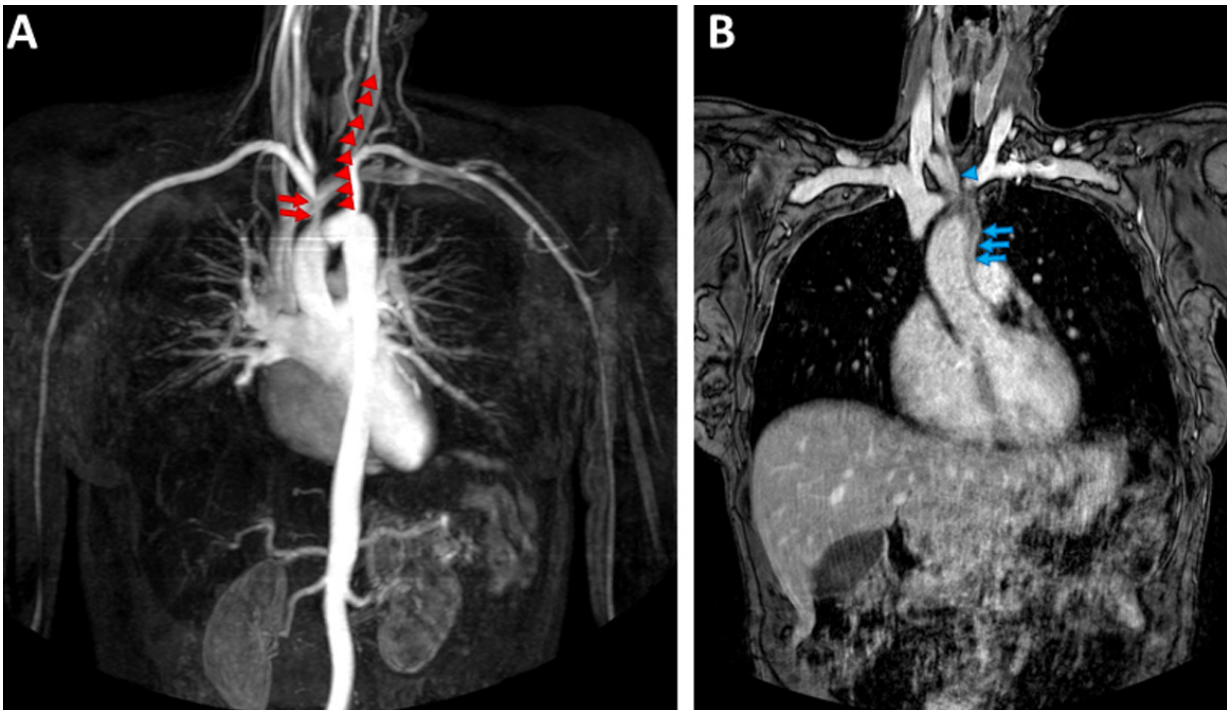

Figure 1.

Irrespectively of the pattern of presentation and of the recognition of red flags that trigger the suspicion of TA, the crucial finding for its diagnosis is arterial involvement. In other words, systemic inflammation is unspecific, and the diagnosis of TA requires a careful assessment of arterial findings and its characteristics, which need to be considered at the light of demographics and other clinical features. In general, some important features in the diagnostic process are:

a) Coexistence of otherwise unexplained systemic inflammation in a patient with arterial steno-occlusion or aneurysms. This occurrence is highly suspicious for idiopathic vasculitis, being infective aortic aneurysm one of the prominent differential diagnosis;
b) Presence of intense arterial wall inflammation, which heralds idiopathic or secondary vasculitis;
c) The distribution of arterial lesions in the arterial tree. Confidence for TA is increased if arterial lesions are multifocal and affect sites typically involved by TA but not by atherosclerosis or fibromuscular dysplasia. Coexistence of multiple stenoses and dilatations in different arterial sites is considered to have the highest specificity although it is present only in a minority of subjects. Post-stenotic dilatations are unspecific and should not be considered at the purpose;
d) The features of vascular lesions at imaging. Despite a patchy distribution, TA lesions are typically long (eg, more than 2-4 cm) and smooth (Figure 1). Arterial wall thickening is another important feature, and it is typically circumferential and symmetric or mildly eccentric in TA;
e) Young age at onset. Vascular abnormalities consistent with TA but developed after 50 years of age should be carefully differentiated from atherosclerosis or giant-cell arteritis;
f) Absence of peri-arterial inflammation, which might be a marker of peri-arteritis such as chronic peri-aortitis, IgG4 related disease or Erdheim-Chester disease.

Differential diagnosis of TA includes other vascular such as including atherosclerosis, fibromuscular dysplasia, and primary or secondary vasculitis like giant-cell arteritis, Behcet's disease, Cogan's disease, and infective vasculitis. The latter should be considered in the presence of systemic inflammation and specific risk factors such as an immunocompromised status or concomitant infections. The most common aetiology is bacterial, including luetic and tubercular aetiologies[44,45]. Differentiation from infective vasculitis requires blood cultures (which have sensitivity of about 10%), serology or mycobacterium test, assessment of imaging features (localised involvement with arterial wall erosion, mycotic aneurysms, intraluminal thrombus, perivascular inflammation and lymphadenopathies are suggestive of infectious aetiology) as well as screening for other infectious foci.

Atherosclerosis is a chronic inflammatory disease of arteries and may present grumbling arterial inflammation and arterial wall thickening at imaging. Differentiation from TA is based on age at onset, assessment of atherosclerosis risk factors, patterns of distribution in the arterial tree and imaging characteristics (focal involvement, with highly eccentric wall thickening, wall calcification, evidence of a lipid core, and absence of intense mural inflammation are suggestive of atherosclerosis)[46].

Fibromuscular dysplasia is a segmental, idiopathic, non-inflammatory disease of the medium-sized arteries primarily affecting young women[47]. Arterial stenosis is the most typical feature, while associated manifestations include aneurysms, dissection and tortuosity which can be ascribed to fibromuscular dysplasia only if in the presence of a typical stenosis in another arterial district. Segmental stenosis is either focal or multifocal (in this case typically arranged in a string of beads alternation of stenosis and dilatation). Although all medium-sized arteries might be involved, renal and extra-cranial cerebrovascular circulation are the districts most frequently involved[47]. Multivessel involvement may occur in 30-55% of subjects[47]. Differentiation from TA is based on a) the absence of systemic or arterial inflammation, b) absence of involvement of the aorta and the main pulmonary artery, and on the presence of c) highly asymmetric wall thickening and d) focal or multifocal stenoses, compared to tapered stenoses and aneurysms and long and smooth arterial wall thickening of TA.

PROGNOSIS

TA impacts significantly on patients' prognosis with significant morbidity and mortality. Morbidity is mainly related to fatigue, arterial hypertension, ischemic complications (affecting limbs, the heart, the CNS/eye, the kidney, the splanchnic circulation, or the lung with pre-capillary pulmonary hypertension), heart failure due to multiple mechanisms (valvular, ischemic, hypertensive), and consequences of chronic therapies and a sedentary lifestyle[5,48]. Mortality in the US is about 15% at 15 years[48], which is highly than expected considering the young age of patients. In Europe a better survival rate has been observed, although at a shorter follow-up[49]. Deaths are primarily attributed to cardiovascular complications (myocardial infarction, stroke or arterial rupture/dissection)[48].

THERAPEUTIC STRATEGIES

TA is a systemic condition. Accordingly, medical therapy represents the cornerstone of active disease, while interventional and surgical procedures have an ancillary role limited to specific situations.
Evidence about TA management is poor and current recommendations from the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR)[50,51], are based mainly on observational or retrospective studies, while randomized clinical trials have been published only for tocilizumab and abatacept.

Steroids represents the mainstay of therapy[50,51]. Virtually all patients respond to adequate glucocorticoid doses (40-60 mg/die of prednisone-equivalents). Lower doses might be required for milder cases, while severe complications such as myocarditis or vital organ ischemia might require pulse intravenous therapy. Once remission has been obtained, steroids are usually tapered down to the minimum dose effective for preventing disease relapses. There is no trial evaluating the best tapering scheme[52], and we usually reduce the steroid dose of about 5 mg/die of prednisone equivalents every other week until the dose of 20 mg/die, then 2.5 mg/die every other week until 10 mg/die, followed by 2.5 mg/die every 4 weeks until discontinuation or flare[8]. Disease relapses occurs in about 60-80% of subjects on steroid monotherapy[52]. Accordingly, it is generally accepted that all patients with active TA should be offered a combination of steroids and one steroid-sparing agent. Subjects with burn-out disease may not benefit for any immunological therapy.

Low-dose methotrexate (e.g. 15-25 mg/week) is the most widely used steroid-sparing agent for maintaining TA remission[53]. Other conventional synthetic DMARDs that have been used are azathioprine, mofetil mycophenolate and leflunomide[50,52,54]. Some centres use cyclophosphamide, mainly through the intravenous route, for severe disease complications (e.g. myocarditis), but pulse steroid aishighly effective and it is unclear if cyclophosphamide-containing regimens confer actual advantages.

Disease flares or grumbling activity may occur in about a third of subjects treated for five years with a combination with steroids and conventional synthetic DMARDs[55]. Tumour-necrosis factor (TNF) blockers have been used for these subjects with good results[50,56-58]. Observational studies suggest that all TNF blockers might be effective, despite some concerns about the efficacy of etanercept in other granulomatous conditions[59]. Most available data refers to infliximab and adalimumab[56]. Interleukin-6 blockage with tocilizumab may be another valid alternative for patients refractory to traditional combinatory therapies[60]. However, a small randomized clinical trial on 36 patients with relapsing TA showed a difference in the primary outcome (time to relapse) only in the per protocol analysis and not in the intention-to-treat analysis[61]. An important drawback of tocilizumab for TA is that disease response might not parallel that of systemic inflammation[56,62], implying the central role of imaging in the follow-up of these patients. Other agents have been studied for refractory TA: a randomized controlled trial with abatacept failed to identify an improvement in the relapse-free survival in the treatment arm[63]. Preliminary obser-

vational studies with B-cell depletion by rituximab and with the anti-IL12/IL23 agent ustekinumab are limited by the small number of enrolled subjects. Experience with JAK inhibitors such as tofacitinib has been reported recently[64-68]. In an observational prospective trial, tofacitinib was associated with lower relapse rate and significant steroid sparing as compared to methotrexate[68].

INTERVENTIONAL AND SURGICAL

Considering that TA prognosis is mainly related to organ ischemias and aneurysms, interventional procedures – either endovascular or surgical- have been proposed to restore normal blood flow and avoid further complications. However, procedures in TA patients are limited by worse outcomes than those performed for other arterial disorder such as atherosclerosis[8,69-74]. Technical difficulties are increased, because of potential difficulties in crossing long stenoses in thickened and stiff arteries by guidewires, in arterial dilatation without causing dissection upon endovascular, and in identifying proximal or distal arterial segments suitable for a vascular anastomosis. Late complications are one of the main concerns in these patients, and include restenosis or peri-anastomotic aneurysms[8,73]. It is believed that inflamed arteries are at higher risk of undergoing post-procedural remodelling and it has been shown that performing vascular procedures during disease remission and the use of post-procedural immunosuppressive therapies improves the long-terms outcomes[75-78]. The role of bare-metal as well as of drug-eluting stents remains to be defined, due to concerns about long-term patency[73].

Given the high technical difficulties and a specific increase in late complications, interventional procedures are considered only in selected cases, where they play an ancillary role to medical therapy. The decision about undergoing interventional procedure and the choice between endovascular manoeuvre or vascular surgery should be performed only in referral centres, and depends on local expertise and on the type of vascular complication. Nowadays, indication to vascular intervention is limited to aneurysms at risk of rupture/dissection, aortic valve regurgitation and severe arterial stenosis resulting in ischemia in vital organs for which medical therapy has failed or might be too late (eg, acute-coronary syndromes and acute stroke with very severe sovra-aortic involvement). Once interventional procedures are necessary, it is advisable to induce disease remission and to continue immunosuppressive agents in the follow-up[73].

ACTIVITY ASSESSMENT

A crucial feature in the management of TA patients is the assessment of disease activity. Although a detailed discussion of the topic is beyond the scope of this review, this remains an unresolved pitfall in the field. Studies have shown that acute-phase reactants may be inaccurate in up to a half of cases and that progressive arterial involvement may occur in the absence of significant systemic inflammation[2,8]. Despite other biomarkers are being studied[79-84], none of them has entered in the clinical practice so far, nor is foreseen to enter in the close future. Further research with improved pathogenic insight is required in order to identify specific marker of selected pathogenic events.

IMAGING

Imaging represents an essential requirement for the modern management of TA. Imaging is crucial both at diagnosis and during follow-up[85]. Multiple imaging modalities are available, potentially providing complementary information. Imaging techniques can be classified according to invasiveness, the capability of provide morphological data and/or functional data on biological activity of the arterial wall, and on reproducibility and operator-dependency. At disease diagnosis, imaging has the following roles: a) assisting the diagnostic process by identifying specific signs of arteritis and excluding potential differentials; b) defining the extent and distribution of arterial involvement; c) helping to define disease activity; d) assessing the severity of arterial remodelling and helping to evaluate potential lesion requiring interventional techniques. During follow-up, imaging is intended to: a) monitor the morphology of arterial involvement (to identify new or worsening arterial lesions and b) identify signs of activity in the arterial wall.

Arterial morphology can be evaluated by digital subtraction angiography, computed tomography angiography (CTA), magnetic resonance angiography (MRA, Figure 1), and ultrasonography (US). Digital subtraction angiography has the highest spatial resolution but is invasive and does not provide information on the arterial wall. Its use is mainly limited to cases requiring endovascular procedures. CTA and MRA provide anatomical images of arterial lumen and may be used to study the arterial wall. Prospective follow-up has revealed that up to a third of lesions might undergo improvement with therapy[86]. Arterial wall characterisation by CTA and MRA might

include functional data about post-contrast enhancement, usually reflecting active inflammation or, in the case of gadolinium-containing contrast media, fibrosis (Figure 1B). Moreover, MR might characterise arterial wall oedema by T2-weighted and/or diffusion-weighted images[87]. US can provide anatomical images of arterial lumen and wall, is widely available and easy to perform. US can study the blood flow at point of involvement as well as up/downstream, allowing to define the haemodynamic impact of arterial wall lesion. Spatial resolution and accuracy depends not only on operator skills, but also on arterial districts, and its role is important especially for highly accessible arteries such as subclavian and carotid arteries[85]. Positron emission tomography (PET) provides functional images that depends on the radiotracer used for the scan, most commonly [^{18}F]-florodesoxyglucose (FDG). FDG uptake in the arterial wall is believed to reflect inflammation, although arterial diameter and the presence of arterial graft might be important confounding factors[88,89]. Concurrent therapy is another important variable[90], as steroid doses used to induce LVV remission at diagnosis may conceal pathological arterial uptake in a few days[91]. Accordingly, the role of FDG-PET in the follow-up of TA patients remains debated and accuracy for identifying active vasculitis is only moderate[92,93]. Pathological FDG uptake has been frequently observed in clinically inactive patients on treatment despite higher composite PET scores have been associated with a higher incidence of subsequent relapses[94,95]. Further research is required about the role of the uptake of FDG and of other promising radiotracers for the diagnosis and follow-up of TA[96,97].

CONCLUSIONS

Takayasu arteritis is a rare condition affecting young women with significant morbidity and potential mortality. Despite low-quality evidence, current therapies are effective in preventing the occurrence of new severe complications. Therefore, medical awareness about this condition is important to reduce diagnostic delays with significant improvement in patients' prognosis. After diagnosis, patients should be followed in referral centres to optimise follow-up and management with medical and interventional therapies.

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