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Imaging techniques for the evaluation of systemic manifestations of vasculitis [☆]

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ABSTRACT

Vasculitis create a local inflammatory process in the vessel wall, which determines the different organic manifestations according to vessel size and location. Imaging techniques play a key role in the characterization and detection of large and medium size vessel vasculitis. Imaging is able to detect the vessel wall edema and to monitor the therapeutic response. In small vessel vasculitis, imaging can indirectly analyze the organic and/or systemic manifestations, because at present, none of the imaging techniques has the necessary spatial resolution to directly visualize small vessels.

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Técnicas de imagen en la evaluación de las manifestaciones sistémicas de las vasculitis

RESUMEN

Las vasculitis provocan un proceso inflamatorio vascular que determina distintas manifestaciones orgánicas que dependen del calibre del vaso afectado y de su localización. Las técnicas de imagen desempeñan un papel importante en la caracterización y detección de las vasculitis de vasos grandes y medianos, pues son capaces de detectar el edema parietal y de monitorizar la respuesta para el tratamiento. En las vasculitis de vasos pequeños las técnicas de imagen son necesarias para estudiar las diferentes repercusiones orgánicas o sistémicas, ya que en el momento actual ninguna técnica de imagen tiene la resolución espacial suficiente para visualizarlos de forma directa

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The anatomopathological substrate of vasculitis is an inflammation of the walls of the blood vessels that can affect any size of such vessel in any organ, leading to inflammation, and necrosis.¹ Small vessel vasculitis affects arterioles, venules, and capillaries; medium sized vessel vasculitis affects visceral blood vessels and their branches, and large vessel vasculitis affect the aorta and its largest branches. Current classifications are not completely satisfactory due to the fact that the etiology and pathogenesis of most of the systemic vasculitis

is unknown and because there is considerable overlap in clinical and histological findings. The development of new diagnostic tools, such as the antineutrophil cytoplasm antibodies (ANCA), has contributed to the development of classifications adjusted to different therapeutic and prognostic strategies according to the type of vasculitis² (Table).

Imaging techniques for the study of vasculitis

Although the final diagnosis of most of the vasculitis requires histological study, different imaging techniques allow the analysis of multisystemic manifestations of vasculitis, early detection of vascular inflammatory alterations and, occasionally, monitoring of therapeutic response. Images permit the determination of organ extension and affection in small vessel vasculitis. In medium and large vessel

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Table
Classification of non infectious vasculitis

Large vessel vasculitis
Takayasu's arteritis
Giant cell arteritis
Medium vessel vasculitis
Polyarteritis nodosa
Kawasaki's disease
Primary granulomatous vasculitis of the central nervous system
Small vessel vasculitis
ANCA-associated small vessel vasculitis
Microscopic polyangiitis
Churg-Strauss syndrome
Wegener's granulomatosis
Vasculitis induced by ANCA (+) drugs
Immune complex small vessel vasculitis
Schönlein-Henoch's purpura
Cryoglobulinemic vasculitis
Lupus vasculitis
Rheumatoid vasculitis
Sjogren's syndrome associated vasculitis
Hypocomplementemic urticarial vasculitis
Behçet's syndrome
Goodpasture's syndrome
Serum sickness-associated vasculitis
Drug-induced immune complex vasculitis
Infection immune complex vasculitis
Primary antiphospholipid syndrome
Paraneoplastic small vessel vasculitis
Vasculitis induced by lymphoproliferation neoplasia
Vasculitis induced by myeloproliferation neoplasia
Vasculitis induced by carcinomas
Vasculitis associated to inflammatory intestinal disease
Miscellaneous
Buerger's disease
Cogan's syndrome

* Modified from Jennette et al.²
ANCA indicates antineutrophil cytoplasm antibodies.

vasculitis, it allows us to determine the characteristic vessel wall edema and helps to determine the precise diagnosis. In some cases even, it constitutes a part of the diagnostic criteria of polyarteritis nodosa (PAN), Kawasaki's disease, and Takayasu's arteritis.³ The main imaging techniques currently employed in the study of vasculitis are mentioned below:

- **Echography and Doppler echography:** widely accessible and with the best spatial resolution, it allows for the study of abdominal parenchymal and soft tissue affection. It is also the best technique for the study of large peripheral vessels because it not only detects stenosis but also early inflammatory alterations of large vessel vasculitis.⁴ Its limitations are mainly related to interobserver variations and a limited field of study
- **Computerized tomography (CT):** permits the study of almost any organ or system affection. It is the study of choice for lung alterations. Since the advent of multislice CT (MCCT), it is possible to obtain post contrast angiographic images with a high resolution of almost any part of the vascular system, including the coronary vessels. It can also detect vessel wall alterations.⁵ Its main limitation lies in the use of radiation and nephrotoxic contrast
- **Magnetic resonance (MR):** it is the technique with the greatest resolution regarding contrast and tissue characterization. It allows for the study of the different aspects of vasculitis

manifestations in almost any territory except lung parenchymal alterations. It is the best technique to detect and monitor vascular edema in medium and large vessels.⁶ It also allows performing high spatial or temporal resolution angiographic studies, studying the vessel wall and quantifying flow. It is the technique of choice for central nervous system (CNS) alterations secondary to vasculitis. Its main limitations reside in the visualization of submillimetric vascular segments, in the detection of vascular calcifications and because of the use of gadolinium chelation, which have recently been associated to the development of systemic nephrogenic fibrosis in patients with moderate to severe kidney failure⁷

- **Angiography:** digital subtraction angiography (DSA) has traditionally been chosen for the imaging diagnosis of vasculitis. It has been progressively substituted by axial acquisition imaging techniques because it only permits the study of the vessel lumen and not the wall, it cannot detect the origin of stenosis, can be difficult to perform if there are large segments of stenosis, represents a risk for ischemic complications and uses high amounts of contrast and radiation.⁶ It currently is still commonly used for the diagnosis of CNS vasculitis and to perform invasive procedures (stenting or angioplasty)
- **Positron emission tomography (PET):** has shown its role in large vessel vasculitis, although the experience using it is still limited.⁷ It is used to differentiate between vasculitis and atherosclerosis with a high degree of specificity.⁷ The lack of spatial resolution of PET has improved with the use of PET-CT

Vascular manifestations

Imaging techniques play a fundamental role in the diagnosing and monitoring of large vessel vasculitis. Takayasu's arteritis mainly affects young women, in the zone of the thoracic and abdominal aorta as well as its branches and pulmonary arteries. They typically present occlusion or proximal stenosis of subclavian and common carotid arteries. Up to 33% of patients for aortic aneurysms, which rarely rupture (Figure, A).⁶ Conventional angiography is frequently normal in early forms (non-pulseless phase), and diagnosis is not usually reached until stenosis occurs (occlusive phase).⁸ Inflammatory affection on the wall of the affected vessels is an early sign that can be detected using echography, CT, MR, and PET.³ For the analysis of the aorta it is preferable to use angiographic techniques with CT or MR (which is the most sensitive technique for the detection of edema) (Figure, B). PET has demonstrated sensitivity similar to MR for the detection of the disease, detecting more affected segments than the latter.¹⁰ Giant cell arteritis is another form of granulomatous vasculitis that mainly affects cranial branches of the aortic arch, mainly the temporal artery. In the evaluation of the temporal artery, Doppler echography has shown to have a sensitivity nearing 85% or 90% and specificity over 95%, something comparable or superior to biopsy of the temporal artery.^{3,4} MR can also evaluate temporal and occipital vessels with results similar to echography.¹¹ Aortic and supraaortic vessel affection can be performed by echography, CT, MR, or PET in a way similar to Takayasu's arteritis.³

Typical angiographic findings of medium sized vessel vasculitis include areas of dilation and stenosis. Although any vascular territory can be affected, mesenteric and renal arteries tend to be more frequently affected. Aneurysms and thrombi tend to occur in vascular bifurcations. DSA is the study of choice for PAN, which can produce multiple microaneurysms in the renal arteries and visceral branches of the aorta in 50% of cases, with stenosis being the most frequent.¹² Small vessel vasculitis mainly affects postcapillary venules and skin arterioles, and different modalities of angiography do not tend to be very useful in their detection because of the small vessel size.



Figure. Fifty-nine-year-old woman with Takayasu's arteritis. A) MIP sagittal reconstruction of a 3D angiographic sequence after contrast of the thoracoabdominal aorta. It shows an aneurysm of the distal descending aorta. Stenosis and tubular morphology of the descending thoracic and abdominal aorta and stenosis of the outlet of the left subclavian artery, celiac trunk, and superior mesenteric artery is shown. B) Axial STIR black blood image showing an aneurysm of the distal thoracic aorta with vessel wall edema that appears as signal hyperintensity.

Cardiac manifestations

Cardiac manifestations in vasculitis are probably more frequent than commonly revealed in autopsy series, although their real clinical consequences are yet to be determined. The variety of

these manifestations is wide: pericarditis, myocarditis, myocardial fibrosis, ischemic disease, pulmonary hypertension, electrical alterations, and systolic or diastolic dysfunction.¹³ Vasculitis is part of the causes of non-familial dilated cardiomyopathy. Coronary affection can occur in Kawasaki and Churg-Strauss' diseases. Myocarditis is frequent in Churg-Strauss syndrome (although endomyocardial hypereosinophilic fibrosis is rare), in Kawasaki's, in Takayasu's, and in secondary vasculitis. Pericardial effusion and pericarditis are frequently associated to microscopic polyangiitis, Wegener's and, Churg-Strauss syndromes, Kawasaki's disease, and Behçet's. Valvular affection is also a relatively frequent finding of Behçet's disease.

Echocardiography is the most commonly employed technique for the evaluation of cardiac affection. MR has turned into a reference criterion of heart function and allows us to detect areas of edema, fibrosis, and non-viable myocardial tissue. MCCT is the test of choice for the diagnosis and non-invasive follow-up of typical coronary artery aneurysms in Kawasaki's disease.¹⁴

Abdominal manifestations

In the evaluation of the abdominal manifestations, MCCT has become the imaging technique of choice, allowing detecting both vascular alterations as well as parenchyma alterations simultaneously.

Gastrointestinal manifestations are typical of PAN, because mesenteric circulation is affected in 50%-70% of cases.¹ Gastrointestinal symptoms can be non-specific, although some major complications, such as hemorrhage or intestinal infarction, vary in frequency between 1% and 6%.¹⁵ The most common genitourinary affection of vasculitis is glomerulonephritis, which has a poor and non-specific imaging representation. Cases of renal hemorrhage secondary to PAN or Wegener's granulomatosis have been described.¹⁶ PAN, and with less frequency Wegener's, microscopic polyangiitis, and lupus vasculitis can all lead to spleen or liver infarctions.¹

Thoracic manifestations

Lung manifestations are more commonly associated to ANCA associated small vessel vasculitis. Clinical manifestations that most commonly suggest vasculitis and affect the respiratory system are diffuse alveolar hemorrhage (DAH), lung-kidney syndrome, nodules or lung cavitations in the chest x-ray, and deforming or ulcerating lesions in the upper airway.¹⁷ DAH is the most frequent lung manifestation of vasculitis. It is characterized by a triad of diffuse alveolar infiltrates, which are exceptionally unilateral, hemoptysis (no indispensable) and the descent in hematocrit or hemoglobin. DAH is caused both by ANCA positive vasculitis as well as other small vessel vasculitis that affect the lung.

In Wegener's syndrome, lung alterations seen in imaging tests are quite common (66% to 85%).¹⁸ The presence of nodules, cavitations, or persistent lung infiltrates is part of the diagnostic criteria. In high resolution CT, nodules or masses are seen in up to 90% of cases, bronchial thickening in 73%, bronchiectasia in 13% of cases, and parched consolidations and in ground glass in 23% of cases.¹⁹ Ground glass infiltrates and cavitated nodules represent active lesions, while septal affection and bronchiectasia represent chronic alterations.¹⁸ In Churg-Strauss, the presence of migratory lung infiltrates is part of the diagnostic criteria. Small nodules can be seen in the lungs in up to 63% of cases, ground glass infiltrates in 53% of cases, consolidations in 42%, tree branch opacities in 37%, and interlobular septal thickening in 42% of cases.²⁰

Microscopic polyangiitis leads to lung affection, such as DAH, in less than 30% of cases.¹⁷

Neurological manifestations

In CNS vasculitis it is important to perform an early and specific diagnosis because its etiology is variable and its treatment and further prognosis depend on its origin. In CNS affection, the diagnosis can be reached through blood analysis or biopsy of distant anatomical zones.²¹ However, in those forms that exclusively affect the CNS, the diagnosis is complicated and based on imaging techniques and biopsies of the leptomeningeal tissue. Clinical manifestation and images of CNS vasculitis present a great degree of overlap with other entities.²² MR is considered a great tool for surveying the presence of CNS vasculitis.^{21,22} MR tends to be frequently negative. However, in a variable number of cases typical angiographic alterations compatible with vasculitis have been described with normal MR findings.²³ Typical vasculitis MR findings have also been described, even having a positive biopsy and no evident angiographic findings. Angiography does not have the sufficient spatial resolution to detect small vessel alterations and is not free of complications. Biopsies are difficult to perform and are associated to important morbidity; in addition, a negative biopsy does not exclude the presence of vasculitis, because it presents a high rate of false negatives.²⁴ Therefore, the diagnosis of CNS vasculitis does not present a clear diagnostic algorithm. In many occasions, its diagnosis is based on clinical suspicion with compatible MR or angiographic alterations.

MR studies tend to show multifocal white and grey matter lesions due to ischemia, infarction or both. These lesions are associated to vasculitis if they are present in several vascular territories, once an embolus has been ruled out, and in cases of young patients with stroke and no known cardiovascular risk factors.²¹ When studying cerebral ischemia, diffusion allows for the differentiation between vasogenic edema and cytotoxic edema. Dynamic post-contrast perfusion studies are capable of detecting hypoperfused areas without infarction, increasing the sensitivity of MR.²¹

Typical findings of vasculitis in cerebral angiography cerebral are areas of smooth or discretely irregular stenosis alternating with dilated segments. Additional signs are straightening and interruptions of the vessel lumen due to wall thickening and the presence of multiple microaneurysms.^{21–25} Angioresonance studies have shown their usefulness, but it is not capable of analyzing distal vascular segments.²⁶ The addition of post-contrast MR sequences using thin slices and preferably accompanied by fat saturation for the study of vessel wall inflammation are useful, because they appear as thickened and enhanced areas.²¹ Therefore, when faced with a clinical suspicion of cerebral vasculitis, a complete MR must be performed as an initial test. If vasculitis is not diagnosed, conventional angiography must then be performed in order to exclude inflammatory alterations of medium caliber vessels. A biopsy is useful in small vessel vasculitis and to classify vascular inflammatory changes when imaging techniques are inconclusive.

Large vessel vasculitis can exceptionally lead to stroke. Isolated primary angiitis of the CNS is a medium and small vessel vasculitis that is manifested as multiple intracranial stenosis that lead to infarction.²² Its etiopathogenesis has been related to varicella zoster virus and HIV.²¹

PAN can produce neurological alterations (25%–30% of cases) such as ischemic strokes.²⁵ Neurological affection in small vessel vasculitis is the most challenging to diagnose and a biopsy is indicated in this group of patients. Churg–Strauss syndrome produces neurological alterations in 62% of cases, usually ischemic or hemorrhagic.²¹ Wegener's syndrome has neurological alterations in less than 40% of cases. Alterations include direct extension from the paranasal sinuses to the meninges, infarctions, and pituitary thickening.²⁵

In summary, imaging techniques help to treat and characterize vasculitis and its manifestations in different organs and systems.

Current angiographic techniques do not allow us to study vascular wall alterations of small vessel vasculitis, but rather of their systemic manifestations through the use of CT and MR. In medium and large vessel vasculitis, both luminal and wall alterations can be visualized. In this sense, MR (and in the future probably PET too) is capable of detecting and monitoring post-treatment changes of vessel wall alterations, mainly in large vessel vasculitis.

References

- Ha HK, Lee SH, Rha SE, Kim JH, Byun JY, Lim HK, et al. Radiologic features of vasculitis involving the gastrointestinal tract. *Radiographics*. 2000;20:779–94.
- Jennette JC, Falk RJ, Andrassy K, Bacon PA, Churg J, Gross WL, et al. Nomenclature of systemic vasculitis. *Arthritis Rheum*. 1994;37:187–92.
- Schmidt WA, Wagner AD. Role of imaging in diagnosis of and differentiation between vasculitides. *Future Rheumatol*. 2006;1:627–34.
- Karassa FB, Matsagas MI, Schmidt WA, Ioannidis JP. Meta-analysis: Test performance of ultrasonography for giant-cell arteritis. *Ann Intern Med*. 2005;142:359–69.
- Kim SY, Park JH, Chung JW, Kim HC, Lee W, So YH, et al. Follow-up CT evaluation of the mural changes in active Takayasu arteritis. *Korean J Radiol*. 2007;8:286–94.
- Gotway MB, Araoz PA, Macedo TA, Stanson AW, Higgins CB, Ring EJ, et al. Imaging findings in Takayasu's arteritis. *Am J Roentgenol*. 2005;184:1945–50.
- Sadowski EA, Bennett LK, Chan MR, Wentland AL, Garrett AL, Garrett RW, et al. Nephrogenic systemic fibrosis: Risk factors and incidence estimation. *Radiology*. 2007;243:148–57.
- Walter MA. Fluorodeoxyglucose PET in large vessel vasculitis. *Radiol Clin North Am*. 2007;45:735–44.
- Sueyoshi E, Sakamoto I, Uetani M. MRI of Takayasu's arteritis: Typical appearances and complications. *Am J Roentgenol*. 2006;187:569–759.
- Meller J, Grabbe E, Becker W, Vosschenrich R. Value of F-18 FDG hybrid camera PET and MRI in early Takayasu aortitis. *Eur Radiol*. 2003;13:400–5.
- Bley TA, Uhl M, Carew J, Markl M, Schmidt D, Peter HH, et al. Diagnostic value of high-resolution MR imaging in giant cell arteritis. *Am J Neuroradiol*. 2007;28:1722–7.
- Stanson AW, Friese JL, Johnson CM, McKusick MA, Breen JF, Sabater EA, et al. Polyarteritis nodosa: Spectrum of angiographic findings. *Radiographics*. 2001;21:151–9.
- Knockaert DC. Cardiac involvement in systemic inflammatory diseases. *Eur Heart J*. 2007;28:1797–804.
- Peng Y, Zeng J, Du Z, Sun G, Guo H. Usefulness of 64-slice MDCT for follow-up of young children with coronary artery aneurysm due to Kawasaki disease: Initial experience. *Eur J Radiol*. 2007;26 (Epub).
- Jee KN, Ha HK, Lee JJ, Kim JK, Sung KB, Cho KS, et al. Radiologic findings of abdominal polyarteritis nodosa. *Am J Roentgenol*. 2000;174:1675–9.
- Daskalopoulos G, Karyotis I, Heretis I, Anezinis P, Mavromanolakis E, Delakas D. Spontaneous perirenal hemorrhage: A 10-year experience at our institution. *Int Urol Nephrol*. 2004;36:15–9.
- Frankel SK, Cosgrove GP, Fischer A, Meehan RT, Brown KK. Update in the diagnosis and management of pulmonary vasculitis. *Chest*. 2006;129:452–65.
- Lee KS, Kim TS, Fujimoto K, Moriya H, Watanabe H, Tateishi U, et al. Thoracic manifestation of Wegener's granulomatosis: CT findings in 30 patients. *Eur Radiol*. 2003;13:43–51.
- Lohrmann C, Uhl M, Schaefer O, Ghanem N, Kotter E, Langer M. Serial high-resolution computed tomography imaging in patients with Wegener granulomatosis: Differentiation between active inflammatory and chronic fibrotic lesions. *Acta Radiol*. 2005;46:484–91.
- Kim YK, Lee KS, Chung MP, Han J, Chong S, Chung MJ, et al. Pulmonary involvement in Churg–Strauss syndrome: An analysis of CT, clinical, and pathologic findings. *Eur Radiol*. 2007;17:3157–65.
- Küker W. Cerebral vasculitis: Imaging signs revisited. *Neuroradiology*. 2007;49:471–9.
- Aviv RI, Benseler SM, Silverman ED, Tyrrell PN, Deveber G, Tsang LM, et al. MR imaging and angiography of primary CNS vasculitis of childhood. *Am J Neuroradiol*. 2006;27:192–9.

23. Wassrman BA, Stone JH, Hellmann DB, Pomper MG. Realibility of normal findings on MR imaging for excluding the diagnosis of vasculitis of the CNS. *AJR.* 2000;177:455-9.
24. Harris KG, Tran DD, Sickels WJ, Cornell SH, Yuh WT. Diagnosing intracranial vasculitis: The role of MR and angiography. *Am J Neuroradiol.* 1994;15:317-30.
25. Moritani T, Hiwatashi A, Shrier DA, Wang HZ, Numaguchi Y, Westesson PLCNS. Vasculitis and vasculopathy: Efficacy and usefulness of diffusion-weighted echoplanar MR imaging. *Clin Imaging.* 2004;28:261-70.
26. Demaerel P, de Ruyter N, Maes F, Velghe B, Wilms G. Magnetic resonance angiography in suspected cerebral vasculitis. *Eur Radiol.* 2004;14:1005-12.