Imaging in Idiopathic Retroperitoneal Fibrosis: What are the Options for Diagnostic, Disease Assessment and Follow-Up?

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Abstract

The purpose of this paper is to review current imaging techniques used for diagnostic, disease monitoring and follow-up of idiopathic retroperitoneal fibrosis (IRF), as to provide the reader with up to date information that can be useful in clinical practice.

We conducted a PubMed search for original articles, literature reviews and series reports published in English in the past 16 years regarding IRF, mainly focusing on imagistic study of the disease and selected 52 articles which we found most relevant.

Today, CT and MRI seem to be the wise choice and the right combination of imaging techniques, with reasonable accessibility of the method and widespread use in clinical practice, but we reviewed all imagistic methods that might be of use, in order to provide the reader with an overview of current information regarding this topic.

Keywords: idiopathic retroperitoneal fibrosis, imaging, diagnostic, follow-up, CT, MRI, scintigraphy, IVU, PET, PET/CT. PET/MRI, HASTE.

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Introduction

Idiopathic retroperitoneal fibrosis (IRF) is a chronic disease consisting of inflammatory retroperitoneal tissue, usually found around the aortic bifurcation with various degrees of extension to envelop one or both ureters, with obstruction and a grade of renal impairment, or to other abdominal organs, which was first described by J. K. Ormond in 1948. It is a rare disease with estimated prevalence of 1.38/100,000/year, which affects male up to 3 times more often than females, in their 5th to 6th decade of life.

Among all cases of retroperitoneal fibrosis, IRF accounts for about two thirds, whereas one third is secondary to drugs, other cancers, radiotherapy or surgery. IRF is a benign fibro-inflammatory disease of unknown aetiology linked to the aortic atheromatosis, but its autoimmune nature is highly suspected due to its pro-inflammatory status (high inflammatory markers such as ESR and CRP, autoantibody presence or association to other autoimmune diseases), and recent association with the vast spectrum of IgG4 related diseases, but none of these are specific to IRF. Clinical manifestations are also non-specific with a predominance of dull abdominal or lumbar pain, nausea, malaise, weight loss or constipation, which seems to be the most common findings. Up to 60% of IRF cases present a degree of renal impairment at presentation.

Diagnosis relies upon a high clinical suspicion, neither symptomatology nor laboratory findings being specific. Imaging plays a key role but unfortunately cannot distinguish between benign and malignant forms of retroperitoneal fibrosis. Therefore positive diagnosis can be established only through biopsy.

The purpose of our paper is to review imaging methods that could be useful in the diagnosis, treatment monitoring and follow-up of IRF. Today high resolution imaging provided by CT and MRI are considered the main imagistic tools for IRF assessment. However, we chose to review all the methods that could be useful in everyday clinical practice.

Ultrasonography

Ultrasonography (US), as an extension to clinical exam, is widely used as a first line diagnostic tool, because it is accessible, harmless and omnipresent in today medical practice. Although US cannot assess the function of the kidneys, it is very useful in assessing uni or bilateral hydronephrosis, renal atrophy or proximal dilated ureters, which are common findings in IRF. Sometimes it can even assess the presence and the localisation of the fibrous plaque, which usually appears iso- or hipoecoic. Doppler mode is useful to delineate great abdominal vessels trough IRF plaque, but it cannot distinguish benign from malignant tissue. US have lots of limitations with low sensitivity in IRF diagnosis, especially regarding subtle details of the plaque and moreover, it’s been demonstrated that only 25% of IRF diagnosed with CT-scan show US abnormality.

Plain abdominal film

Plain abdominal film may show the disappearance of the psoas shadow due to the fibro-inflammatory tissue spreading around the major vessels, but this is a highly variable finding. Thus, it is not considered useful anymore in assessment of IRF. It could play a role in appreciating bowel distension or in some situations, articular or bone changes from other diseases associated with IRF.

Intravenous urography

Intravenous urography (IVU) lost a lot of ground as a diagnostic tool, perhaps because it uses a nephrotoxic contrast agent, given that in the majority of IRF patients show a grade of uraemia at first presentation, but mainly because IVU was slow replaced by CT-scan which offers far superior anatomic detail, which are not limited to the lumen of the urinary tract, even on native examination. It has been demonstrated that CT-scan with contrast enhancement, is superior to IVU even in terms of opacification of mid ureter and pielocaliceal system.

IVU describes the classical triad comprised of upper ureter dilation, ureteral medialisation and lower lumbar ureteral narrowing, due to extrinsic compression from the fibrous plaque, with frequent hydronephrosis and delay in renal excretion.

Data gathered over time shows that things are little bit different because in a significant proportions of patients, ureteral anatomical position is not modified as they can be entrapped by IRF in their anatomical position. Moreover Saldino et al. showed that ureteral medialisation can be present in 20% of healthy individuals.

Another argument in favour of CT-scan is the large number of other pathology that can mimic one or more of the IVU triad elements, of which the most significant are other malignant diseases that may have the same localisation and may not have an impact on the inner wall of the urinary tract.
Retrograde pyelography

Retrograde pyelography (RP) is still a widely used imaging method for routine endourologic procedures. It can be useful when there is no renal function and classic IVU cannot obtain a satisfactory opacification of urinary tract, but, as for IVU, it can only provide details about the lumen of the ureter22,29. It is interesting to note that even in an extensive extrinsic fibrosis, the ureteral catheter for RP can be easily passed through the affected area which adds to the theory that IRF obstruction is most likely due to ureteral peristaltic disturbance, than mechanical obstruction16,27.

Computed tomography

CT-scan, without, but more important, with contrast enhancement offers today a standard for evaluation of the retroperitoneal space, hence for the assessment of IRF. CT can provide accurate information regarding localization, extent and anatomical relations with neighbouring structures of the fibrous plaque16. Usually, IRF appears as a confluent mass with clear margins, but irregular contour, firstly at the aortic bifurcation at L4-L5 level and usually spreads in a cranial and lateral fashion, encasing the aorta and the inferior vena cava (IVC) and often one or both ureters, with a variable degree of medialisation leading to obstruction and hydronephrosis, but also in a caudal manner, encasing the common iliac arteries at their origins(Fig. 1,2)5,24,30.

Lateral extension of IRF plaque does not usually go beyond lateral psoas margin24, and usually does not dislodge the aorta from posterior paraspinal plane17,22,31. Posterior aortic dislodging is an important sign of malignancy, most likely of lymphoma or neoplastic adenopathy, but with low sensibility and specificity17,20,31. The fibrous plaque may extend anteriorly, affecting duodenum, pancreas or even the spleen16, as cranially it may reach the mediastinum32, and caudally it may extend distally to the sacrate promontorium, in the “true” pelvis, mimicking gynaecological tumours33, creating very difficult diagnosis situation when it doesn’t affect the classic periaortic region. Exceptionally, IRF atypical localisation was described in perirenal space34.

Regarding the medialisation of ureters, we have to reiterate Saldino et al.,28 that showed nearly 4 decades ago, that it can be an imagistic feature of approximately 20% of healthy individuals. This observation should not lead us to completely ignore this sign that is frequently reported in the literature (Fig. 2).

Fig. 1 CT-scan in a 72 male patient with IRF.

a: Coronal reconstruction; white arrows point to the fibrous plaque which encase the aorta and common iliac arteries
b: Sagittal reconstruction; white arrows show the fibrous mass that encase the aorta anteriorly without any posterior extension or dislodgement from the spine.

Source: photo archive of the Center for Urology and Renal Transplantation, Fundeni Clinical Institute, Bucharest, Romania
Personal image processing using RadiAnt™ DICOM viewer 3.2.3 64-bit, evaluation version; http://www.radiantviewer.com/

Fig. 2 CT-scan of a 49 years old male patient with IRF, where bilateral JJ stenting was performed to relieve obstruction of the renal units

a: Coronal reconstruction; white arrows point to the ureters that are encased in the fibrous mass and show a moderate medialisation at the level of the aortic bifurcation
b: CT-topogram; white arrows that shows bilateral ureteral trajectory; both ureters are “drawn” in the retroperitoneal mass.
c: Axial reconstruction; black arrow points to the fibrous tissue enveloping major iliac arteries; white arrows point to the ureters that are encased in the mass.

Source: photo archive of the Center for Urology and Renal Transplantation, Fundeni Clinical Institute, Bucharest, Romania
Personal image processing using RadiAnt™ DICOM viewer 3.2.3 64-bit, evaluation version; http://www.radiantviewer.com/

Technically, IRF tissue has similar attenuation to the psoas muscle on non-contrast enhancement CT17. After contrast agent administration, when the renal function
Editorial

is good, tissue enhancement of IRF is non-homogenous, which correlates well with the stage of the disease. In the active stage, with predominant inflammation, the enhancement increases with 20-60 HU after administration of contrast, whereas in the late fibrotic stage there is usually minimal or no enhancement.

This behaviour might be very useful also for imagistic assessment of good treatment response, but there is data suggesting that metabolic activity of IRF is difficult to estimate by CT-scan, especially in advanced uremic stages where contrast agent cannot be used, and then, disease evaluation can be monitored by serial determination of inflammatory biomarkers. Therefore, the main utility of CT-scan in disease monitoring is its high sensitivity for detection of dimensional change in the plaque.

Another important finding is the presence of micro-adenophatic lesions that can be distinguished by CT-scan in the proximity of the fibrous tissue in up to 25% of cases, but which are usually very small and most likely they are only the immune reaction to the plaque, without any neoplastic significance.

G. Bier et al. studied the possible benefits of using volume perfusion CT (VPCT) on IRF evaluation, regarding the assessment of microvascularization in the fibrous plaque, thus appreciating the cellular activity in the tissue, and they concluded that VPCT might be useful for IRF follow-up after medical treatment, especially when correlation with bio-inflammatory markers became weak or inexistent. Aside all afore mentioned, CT-scan of the abdomen provides important information about other abdominal organs, but not the least of blood vessels, aortic atheromatosis and eventual aortic wall defects, and also of arterial branches, being established that IRF affects renal vessels in one third of cases.

It is obvious that by means of CT it is possible to evaluate the thorax, pin-pointing eventual atypical localisation of IRF already mentioned.

All of these being said, CT-scan, as a diagnostic tool, has some disadvantages. Logically, the main limitation of the method is the intravenous iodine contrast administration for patients with significant renal impairment, which makes it less valuable in disease monitoring as mentioned above. Moreover, Brun et al., studying 23 IRF patients, discovered that approximately one third had normal CT aspect of the retroperitoneum, although the disease was proven histologically.

Last but not least, we have to mention that CT-scan exposes the individual to ionizing radiation. A large study on this topic by Smith-Bindman et al. showed that the median radiation dose on a multiphase CT-scan of the abdomen and pelvic regions is of 31mSv (IQR 21-43 mSv), which translates to a median adjusted risk of 4 radiation-induced cancers/1000 patients during their lifetime and exposes especially young females to a form of malignancy induce by CT, as for a 20 year old female patient, this risk might be as high as 1:80. This risk decreases substantially with age.

MRI

MRI is another excellent imagistic asset, which allows high resolution imaging of the retroperitoneal space, being superior to CT-scan by means of soft tissue contrast, without the necessity of iodine contrast agent and without radiation exposure. Localization and extension of fibro-inflammatory process can be very well defined by MRI, because the signal intensity and relaxation time for T1 and T2 weighted sequences are different between IRF, surrounding fat and psoas muscle (Fig. 3).

IRF shows hypo-signal in T1-weighted MRI, whereas T2-weighted signal may have considerable variation, determined by the degree of active tissue inflammation, with hyper-signal in the active phase, with oedema and rich cellularity, and low signal in late fibrous phase.

This observation is useful for diagnosis, but also for follow-up and for assessing treatment response, by considering the decrease of the inflammatory component, hence T2 signal intensity, as a favourable response, features that are similar after gadolinium contrast enhancement administration. It has been noted...
that, after gadolinium administration, there is a marked increase in fibro-inflammatory tissue signal especially for untreated IRF.

For MRI study of IRF, HASTE protocol (Half Fourier Acquisition Single Shot Turbo Spin Echo) was recently applied because it offers a high fidelity image, with minimum artefact by respiratory and intestinal movement, with rapid execution time of approximately 2 minutes, which is similar to a CT-scan, but without the need of paramagnetic contrast enhancer or radiation exposure, therefore, providing a viable alternative to classical IVU or contrast enhanced CT for patients that have renal insufficiency or are allergic to iodine based contrast, but of course at a higher price.

Despite its obvious advantages it’s worth being said that MRI has certain disadvantages and risks. Aside of high costs, relatively high examination time and significant artefacts produced by movement during examination, it’s been recently discovered that contrast enhanced MRI is not so inoffensive as it was previously assumed, especially for patients with renal insufficiency. A significant association between gadolinium-based enhanced MRI and the risk of developing systemic nephrogenic fibrosis, which is a disease similar to scleroderma, mainly affecting skin, but also liver, heart, lungs or muscles, sometimes leading to complete immobilisation, has been reported. Systemic nephrogenic fibrosis has been reported almost exclusively in uremic patients, does not have any form of treatment and it seems that the only wise attitude regarding it, is it’s prevention.

Nuclear imaging

Diethylenetriaminepenta-acetic acid (DTPA) renography might aid in appreciation of ureteral obstruction and also in assessing differential renal function, with high sensitivity. Gallium scintigraphy, reveals that radionuclide uptake seems to correlate with the disease stage, being truly vivid in the acute inflammatory phase and reduced or absent in late fibrotic stage. Although latest data shows that even for the estimation of glomerular filtration rate (GFR), the determination of GFR by measuring the clearance of iodine contrast enhancer at CT-scan is superior to the classical isotopic renography, which was considered the gold standard up until now.

Positron emission tomography (PET) with the aid of $^{18}$F-deoxyglucose ($^{18}$FDG/PET) and PET/CT were also evaluated in the assessment of IRF, based on its high sensitivity in assessment of cellular metabolic activity, already widely used in oncology, knowing the avidity of neoplastic cells for radioactive glucose. This
features showed similarities for inflammatory or autoimmune lesions, hence the low specificity23.

Several reports underlined the role of PET/CT in assessing IRF, revealing hyper metabolic activity in the plaque, especially in the active phase when the degree of metabolic activity shows good correlation with IRF stages45,46,47,48,49.

Jansen et al.50 delineates the importance of PET/CT in assessing IRF stage, especially when symptoms or inflammatory status are absent, in patients where IRF or IRF recurrence is suspected. Another study by G. Piccoli et al.51 highlighted PET/CT for follow-up evaluation of IRF, as data recovered on every visit is useful to aid in therapeutic management, in terms of medical treatment optimisation or timing of the removal of urinary drainage, in order to reduce morbidity and increase quality of life in IRF patients.

Because it is a whole body exam, PET/CT offers a good overview of IRF lesions and their extension, is a good tool for assessment of multifocal disease, while also being able to identify simultaneous infectious, neoplastic or autoimmune lesions that coexist with IRF22.

All of these being said, because of reduced accessibility, owing to prohibitive price, low specificity in delineating benign from malign fibrosis and also the lack of solid prospective studies regarding its usefulness, PET/CT is yet to be validated by future research as a tool for diagnosing and follow-up of IRF16,22.

Recent study by V. Ruhlmann et al. evaluated 18FDG-PET/MRI combination, suggesting its high potential in multiparametric high resolution imaging for IRF in terms of diagnosis as well as treatment monitoring. As for PET/CT, future research is needed, for evaluating and validation of this imaging technique in IRF management22.

Conclusions

Imagistic exploration is an indispensable asset in the management of IRF, in terms of diagnostic, monitoring of disease stage and treatment response and follow-up.

Unfortunately, none of the actual techniques is able to delineate malignant lesions from all retroperitoneal fibrosis cases, therefore positive diagnostic can be achieved only by means of biopsy.

Of the all afore mentioned techniques, CT and MRI seem to be the wise choice and the right combination of imaging techniques, with reasonable accessibility of the method and widespread use in clinical practice. Care must be taken in advanced renal impairment as both techniques could add significant morbidity if not managed correctly. CT scan, which is probably the most widely used technique, should be judiciously managed, especially because of radiation exposure with the risks afore mentioned, especially since the vast majority of patients will repeat examination over the time of their lives.

PET/CT and PET/MRI are highly sensitive methods in assessment of tissue metabolic activity, but with low specificity and accessibility due to their prohibitive price, and their role in IRF management warrants future research.

References