Correlation between radiological assessment and histopathological diagnosis in retroperitoneal tumors: Analysis of 291 consecutive patients at a tertiary reference sarcoma center

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Abstract

Objectives: Aim of study was to assess the correlation between computed tomography scan (CT) findings and histopathology.

Material and methods: Data were collected on consecutive patients with suspected retroperitoneal sarcoma (RPS) referred to a tertiary sarcoma center. Patients underwent contrast enhanced multi-detector CT scans. Radiological features of lesions were classified according to the presence of a fatty (Group A) mass, or non-fatty (Group B) mass, both subdivided according to homogeneity and intralesional high-contrasted appearance. Radiological classification was compared with histopathological diagnosis. Sensitivity, specificity, positive/negative predictive value (PPV, NPV) were analyzed.

Results: Of 291 patients, 103/291 (35.4%) masses were classified in Group A and 188/291 (64.6%) in Group B. Diagnosis of mesenchymal tumor was obtained in 231/291 cases (79%) and non-mesenchymal tumor in 60/291 (21%). Sensitivity and specificity of Group A for liposarcoma were 76.7% and 92.0%; PPV and NPV were 86.4% and 85.6%. Sensitivity of Group B for a mesenchymal tumor was 55.4% and specificity was 0%; PPV and NPV were 68.1% and 0%.

Conclusions: None of radiological criteria were sufficient to anticipate a specific diagnosis, with the only exception of well differentiated liposarcoma and angiomyolipoma. In a series of suspected RPS, 21% of the lesions were finally non-mesenchymal tumors.

Keywords: Soft tissue sarcoma; Retroperitoneal sarcoma; Diagnosis; Liposarcoma; Surgery

Introduction

Retroperitoneal soft tissue sarcomas (RPS) are rare tumors with non-specific modes of presentation. The annual incidence is 0.3—0.4 cases per 100,000 inhabitants and peak incidence occurs during the fifth decade of life. RPS are often detected as an incidental finding during radiological assessment for another clinical problem, although some cases present as a palpable clinical mass. The presence of an isolated retroperitoneal mass on imaging may be caused by a number of differential diagnoses and diagnostic certainty can be difficult based on imaging criteria alone. Differently, the more common solid retroperitoneal malignancies,
arising from the renal/urinary tract and exocrine pancreas, have characteristic diagnostic features on imaging,\textsuperscript{4,5} but less common tumors are more difficult to exclude.

The presence of a retroperitoneal mass is frequently detected by abdominal ultrasound (US), but the use of Multi-Detector Computed Tomography (MDCT) or Magnetic Resonance Imaging (MRI), are necessary to characterize and fully assess the lesion.\textsuperscript{6,7} Current published data available on the radiological assessment of RPS have focused mainly on liposarcoma.\textsuperscript{8–16} Radiological assessment of the lesion includes axial size, fat content, margin status, involvement of major vessels, and the presence of septations. Accurate radiological assessment can help to distinguish cases of suspected RPS, but identification of subtypes is challenging. In well-differentiated liposarcoma, the absence of an area of focal nodular/water density has been suggested as diagnostic of the subtype and pre-operative biopsy omitted.\textsuperscript{15} Nonetheless, histopathological assessment is currently required to establish the subtype of RPS and determine management.\textsuperscript{17,18} There are no published data on the capability of radiological assessment to predict histopathological subtype of suspected RPS identified on contrast-enhanced CT scan.

The aim of this study was to assess the correlation between contrast-enhanced MDCT findings and histopathological diagnosis, with specific focus on predictive capability, in a series of consecutive patients presenting with solid retroperitoneal masses at a tertiary reference sarcoma center.

Materials and methods

Data was collected from a prospectively maintained database on consecutive patients with an isolated retroperitoneal mass (suspected to be RPS) primarily referred to a tertiary sarcoma center between 2005 and 2012. Patients with radiological diagnoses of primary renal malignancies or pancreatic masses were excluded from analysis.

In all cases, histopathological diagnosis was confirmed by two expert pathologists. Tumor specimen was obtained either by percutaneous biopsy performed by radiologist as initial diagnostic step, or as surgical resection specimen for those who were operated on.

All patients underwent contrast-enhanced thoraco-abdominal MDCT scanning. Studies which were not performed at the referring institution were reviewed and scans were repeated if unavailable or difficult to interpret due to image quality. The protocol for MDCT imaging was as follows: scans were performed with a 16 and 128 detectors CT scanner (Somatom Sensation 16 and SOMATOM Definition Flash; Siemens Healthcare, Forchheim, Germany). Scans obtained with a collimation 16 × 0.75 mm for Sensation and 128 × 0.6 mm for Definition Flash were reconstructed to a 5 mm slice thickness. The peak tube voltage was 120 kVp and the tube current was automatically adjusted by CAREDose4D. For all patients, 120 ml of IV contrast medium (Iopamidol 370, Bracco, Milan, Italy) was injected at a rate of 3 ml/s. Although the studies had multiphase scans, only the venous phase images (80 s scan delay) were reviewed for the purpose of present study. The MDCT images of all patients in the series were reviewed retrospectively using soft tissue window settings on PACS workstations (Syngo imaging, Siemens) by 2 senior radiologists, who have dedicated experience in soft tissue tumors. At the time of imaging review, these radiologists were blinded to the final histopathological diagnosis and assessment of images was performed using a new classification proposed here.

On the basis of previous multidisciplinary experience, a classification system was devised for the assessment of isolated retroperitoneal masses suspected to be sarcomatous in origin. Firstly, retroperitoneal tumors were categorized into two main groups, according to the presence (Group A - fatty lesions) or absence (Group B - non-fatty lesions) of a hypodense fatty component, identified as forming a significant part of the mass and concordant with the subcutaneous adipose tissue. Each group was subdivided and four categories were identified and defined according to characteristic features. Group A lesions were classified according to the homogeneity of the mass and the presence of intralesional high-contrasted images:

- Group A1: homogeneous mass with complete fat attenuation throughout the lesion, plus thin septa;
- Group A2: heterogeneous fatty mass characterized by ground-glass opacities more dense than fat but less dense than muscle, plus thick intralesional septa, without intralesional vessels;
- Group A3: heterogeneous mass with ground-glass opacities more dense than fat but less dense than muscle, plus thick septa, and with intralesional vessels;
- Group A4: heterogeneous fatty mass with solid nodules present within the lesion.

Group B lesions were subdivided into four groups, according to homogeneity pattern and contrast-enhancement appearance. Contrast-enhancement was considered high if the density in the venous phase was comparable to major vessels, and moderate if comparable to muscle tissue. The following subcategories were identified:

- Group B1: homogeneous mass with high contrast-enhancement;
- Group B2: homogeneous mass with moderate contrast-enhancement;
- Group B3: heterogeneous mass with high contrast-enhancement;
- Group B4: heterogeneous mass with moderate contrast-enhancement.

The radiological classification was compared with final histopathological diagnosis. Single histopathological types were grouped into mesenchymal tumors and non-mesenchymal tumors. Mesenchymal tumors included
adipocytic tumors, as well as benign and malignant histotypes (namely, myelolipoma, angiomyolipoma, well differentiated liposarcoma, and dedifferentiated liposarcoma).

Correlation between radiological assessment and histopathological subtype was analyzed, and sensitivity/specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated where applicable.

When both preoperative biopsy and final diagnosis on surgical specimen were available, accuracy of biopsy was analyzed (number of correct biopsies/all biopsies).

Results

291 patients with a median age at diagnosis of 58.5 years (range 16–81; Interquartile range [IQR] 47–68) affected by primary retroperitoneal mass were eligible for inclusion. Gender distribution was equal (152 men and 139 women). The novel classification identified 103/291 (35.4%) masses in Group A (fatty group) and 188/291 (64.6%) in Group B (non-fatty group). The median tumor size, measured as the largest diameter on cross-sectional or coronal MDCT image, was 15 cm (range 4–75; IQR 10–21). Radiological subgroup classifications and histopathological diagnoses are listed in Table 1.

Radiological assessment

In Group A, 7/103 cases (6.8%) were classified as A1, 31 (30.1%) as A2, 10 (9.7%) as A3, and 55 (53.4%) as A4 (Fig. 1). In Group B, 15/188 cases (8.0%) were classified as B1, 19 (10.1%) as B2, 127 (67.6%) as B3 and 27 (14.4%) as B4 (Fig. 2).

Group A (Fatty lesions)

Fatty appearance of the tumor on MDCT imaging correlated highly with adipocytic tumors on pathological evaluation (102/103, 99.0%). Mesenchymal adipocytic tumors in Group A were identified with a sensitivity of 79.1% and a specificity of 99.4%. The PPV and NPV of these tumors were 99.0% and 85.6%. Overall, in group A, 13/103 (12.6%) were finally found to have a diagnosis of a benign tumor (myelolipoma, angiomyolipoma).

The most common pathological subtype was liposarcoma (89/103) with sensitivity of 76.7% and specificity of 92.0%. The PPV and NPV were 86.4% and 85.6%. All the 7 masses classified as A1 radiologically were diagnosed as WD liposarcomas. Among the 31 masses classified as A2, 28 were WD liposarcoma and 3 were found to be myelolipomas. All the 10 masses classified radiologically as A3 were finally found to be angiomyolipomas. Among the 55 patients classified as A4, 43 were DD liposarcomas, 11 WD liposarcomas and 1 case was diagnosed as a perivascular epithelioid cell tumor (PEComa). When considering the MDCT features of solid nodules within a fatty mass (subgroup A4) as a discriminant between liposarcoma subtypes, this feature was predictive of DD liposarcoma with a sensitivity of 100.0%, specificity of 80.0%, PPV of 78.2% and NPV of 100.0%.

Table 1

<table>
<thead>
<tr>
<th>Fatty lesions</th>
<th>Non-fatty lesions</th>
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<tbody>
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<td>A2</td>
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<tr>
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<tr>
<td>Adipocytic tumors</td>
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<td>Others</td>
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<tr>
<td>Total Series</td>
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</tbody>
</table>

A1–A4 and B1–B4: see text in Materials and methods section; CE: contrast-enhancement; IVC: inferior vena cava; GIST: gastrointestinal stromal tumor; MPNST: malignant peripheral nerve sheath tumor
**Group B (Non-fatty lesions)**

The presence of a non-fatty lesion on MDCT imaging correlated with a pathological diagnosis of mesenchymal tumor in 128/188 cases (68.1%), while 60/188 cases (31.9%) had a diagnosis of other malignant neoplasm. The sensitivity of diagnosing a mesenchymal tumor in Group B was 55.4% and specificity was 0%, with a PPV and NPV of 68.1% and 0%.

It was not possible to discriminate between single mesenchymal histologies in the Group B subcategories, nor between mesenchymal or non-mesenchymal tumors. The probability of identifying a mesenchymal tumor in each subcategory (1-4) was 3/15 (20.0%), 12/19 (63.1%), 99/127 (77.9%), and 14/27 (51.9%), respectively. There were 3 patients who were classified as having B1 masses, but whose final pathological diagnoses were WD liposarcoma, desmoid-type fibromatosis and schwannoma. Among the 12 masses classified as B2, the final diagnoses were divided between WD liposarcoma, schwannoma, malignant peripheral nerve sheath tumor (MPNST) and other sarcomas. The subcategory of B3 provided the most challenging radiological images with virtually any diagnosis possible (except for myelolipoma and angiomyolipoma) among the 99 patients in this subgroup. Finally, among the 14 masses classified as B4, the histopathological diagnoses were WD/DD liposarcoma, inferior vena cava (IVC) leiomyosarcoma, desmoid-type fibromatosis, MPNST or other sarcomas. The presence of homogeneity and the contrast-enhancement pattern did not discriminate between the pathological diagnoses (Table 1).

It was noted that all the leiomyosarcomas (37, including those arising from the IVC) as well as all the 18 solitary fibrous tumors (SFT) were classified in group B3, with only 1 exception. Conversely, if the MDCT features of a heterogeneous mass with high contrast enhancement (subgroup B3) are considered as a predictor of leiomyosarcoma or SFT, it had a sensitivity of 98.2% and specificity of 38.9%, with a PPV and NPV 55.6% and 96.6%.

Overall, in group B, 10/128 patients (7.8%) were found to have a diagnosis of a benign tumor (schwannoma), with the majority being categorized in Group B2 and demonstrating homogeneity and moderate contrast enhancement. The predictive role of CT features in distinguishing between single non-mesenchymal tumors was not an aim of present study, and therefore it has not been further investigated.

**Histopathological assessment**

Preoperative histopathological diagnosis was obtained by percutaneous biopsy in all cases and confirmed by
histopathological examination of the surgical specimen in 204 patients (the remaining 87 patients did not undergo surgery according to diagnosis of metastatic disease, lymphoma, germ cell tumor, etc.). One hundred patients were biopsied at our center, while 104 had been biopsied before referral. There were no biopsy-related complications recorded in the series and no biopsy track seeding was evident during follow-up. A final histopathological diagnosis of mesenchymal tumor was obtained in 231/291 cases (79.4%), and non-mesenchymal tumor in 60/291 (20.6%). Among the mesenchymal tumors, 129/231 (55.8%) were adipocytic tumors: 50 well-differentiated (WD) liposarcoma (21.6%), 66 dedifferentiated (DD) liposarcoma (28.6%), 10 angiomyolipoma (4.3%), and 3 myelolipoma (1.3%). Non-adipocytic tumors were diagnosed in 85/231 cases (36.8%): 10 benign schwannoma (4.3%), 6 desmoid-type fibromatosis (2.6%), and 1 gastrointestinal stromal tumor (GIST) (0.4%). Among the non-mesenchymal tumors, final diagnosis was metastatic carcinoma in 32/60 cases (53.3%), lymphoma in 19 (31.7%), germ cell tumor in 5 (8.3%) and other tumors in 4 cases (6.7%; see Table 1).

An analysis of accuracy and predictive value of preoperative biopsy was performed in the subgroup of 100 patients in whom both preoperative and final histology were available for retrospective review.

A biopsy of liposarcoma on biopsy had an overall accuracy of 86.0% (43/50).

The diagnosis of DD liposarcoma on biopsy had a PPV of 90.5%, with an accuracy of 57.1% (20/35).

In the remaining 15 cases, 8 had a diagnosis on biopsy of WD liposarcoma, 5 of sarcoma NOS, 1 of liposarcoma NOS, and 1 of leiomyosarcoma.

The diagnosis of WD liposarcoma on biopsy had a PPV of 59.1%, while the NPV was 97.4%, with an accuracy of 86.7% (13/15).

Discussion

In this series of 291 consecutive patients referred for a suspected RPS, a final pathological diagnosis of mesenchymal tumor was confirmed in 79% of cases (231/291). In the remaining 21% the final diagnosis was primarily that of metastatic carcinoma, lymphoma, and germ cell tumor.

The use of the classification system for a solitary retroperitoneal mass was useful in identifying a group of lesions (group A) that were predictive for liposarcoma histotypes (specificity 92.0%, and PPV 86.4%).

In group A, 12.6% of cases were diagnosed as benign conditions on histopathology and both myelolipoma and angiomyolipoma demonstrated specific radiological
features (subgroups A2 and A3). While angiomyolipoma showed pathognomonic radiological features in 100% of cases, myelolipoma demonstrated features on MDCT scans in common with WD liposarcoma and could be only differentiated on pathological examination. There were no diagnoses of benign retroperitoneal lipoma in the overall series, but even if it were the case, the same consideration regarding the need of pathological diagnosis made for myelolipoma would similarly apply. Radiological identification of a fatty mass does not have sufficient diagnostic prediction and preoperative percutaneous biopsy should still be considered mandatory in cases of suspected RPS.

MDCT scanning has previously been assessed with regard to the identification of WD liposarcoma according to different radiological features. Lahat et al. found that focal nodular/water density images, infiltrated organs, hypervascularity and cystic necrotic areas were radiological features that can help in distinguishing WD and DD liposarcomas.15 Murphey et al. described MDCT findings of WD liposarcoma as a >75% lipomatous mass, with non-lipomatous images as containing thick septa and focal nodules <2 cm.13 In our study, the MDCT radiological features of a homogeneous mass with complete fat attenuation throughout the lesion plus thin septa, exclusively identified WD liposarcomas (Group A1, 7/7 cases). This represented only 14% of the WD liposarcoma within the series and preoperative biopsy should not be excluded based on this finding alone.

The presence of focal nodules within a fatty mass has been suggested as being a predictive finding for DD liposarcoma.13,15 This has also been confirmed in our series, but with a weak predictive value as only 43/66 of DD liposarcomas were fatty masses, and among subgroup A4 (solid nodules within a fatty mass) we found both 11 WD and 43 DD liposarcomas. Specificity of solid nodules for DD liposarcoma was 80.0%, with a PPV of 78.2%. If the knowledge of differentiation status is important for surgical planning, as it will determine the differing extent of the surgical approach in order to achieve the best long-term outcomes for the patient,19 then a biopsy should always be taken. In this study, according to MDCT findings, WD and DD liposarcomas were distributed throughout the majority of all radiological subtypes and radiological assessment was not predictive for the different subtypes. In view of our findings, radiological findings do not have high enough sensitivity or specificity to replace the use of preoperative needle biopsy.

There were no specific radiological characteristics of non-fatty lesions that were able to distinguish between a mesenchymal and non-mesenchymal neoplasm, nor to some extent between benign and malignant tumors. The largest MDCT subgroup was Group B3, which identified

Figure 3. Four different histologies with similar radiologic appearance (Group B3). Panel i) dedifferentiated liposarcoma; panel ii) leiomyosarcoma; panel iii) solitary fibrous tumor; panel iv) malignant peripheral nerve sheath tumor.
non-fatty heterogeneous masses with high contrast-enhancement (127/291, 43.6%). In this subgroup, several different histopathological diagnoses were present, including sarcomas, non-mesenchymal malignancies and benign tumors (Fig. 3). This is in accordance with other reports, describing the non-fatty feature of many RPS.20–22

The clinical context still remains the cornerstone in the diagnostic process and some specific anatomical considerations will be of substantial help in recognizing specific entities. For example, direct involvement of the inferior vena cava by a B3 mass will be highly suspicious for IVC leiomyosarcoma20,21,24 (Fig. 4); the finding of a non-fatty lesion in the paraspinal region in association with neuropathic symptoms will be suggestive of a neurogenic neoplasm (even if no radiological feature was able to distinguish between benign schwannoma and MPNST in the present series)25,26; the involvement of the renal cortex by an A3 mass will confirm the renal origin of an angiomyolipoma (Fig. 4).

It could be argued that this low predictive power of MDCT features would be encompassed by MRI technology. However, to the best of our knowledge, no definite evidence of MRI superiority in distinguishing between sarcoma and non-mesenchymal tumors has been demonstrated.13,15 MRI has been described as a good tool to identify liposarcoma and in particular to differentiate between different adipocitic subtypes.8–12 Nevertheless, neither MRI nor MDCT scan have been demonstrated to predict the diagnosis of WD and DD liposarcoma when the fatty component is not visible.5,16

The use of MDCT scan as a standard staging procedure has the advantage of greater availability, faster acquisition time, and superior patient tolerance compared with MRI,27,28 and additionally allows the opportunity to screen the thorax and liver at the same time. MRI remains a valid option in selected cases, particularly if contrast-enhanced CT scan is contraindicated, or in cases of entirely pelvic lesions.

All patients in this series underwent pre-operative needle biopsy for histopathological diagnosis and the advantage of a pre-operative diagnosis of RPS diagnosis is to allow for optimal management of the lesion. Biopsy can be performed percutaneously either under CT scan or US guidance. The aim of the biopsy of a fatty mass will be both to exclude benign lesions and to distinguish WD from DD liposarcomas since the surgical approach may be different between the various conditions.29 In the subgroup of patients in which both preoperative biopsy and final surgical specimen was obtained in our institution, diagnostic accuracy of biopsy for liposarcoma was 86%. Histologic subtype accuracy was good especially for WD liposarcoma (86.7%), while it was only 57.1% for DD liposarcoma. On the contrary, a diagnosis of DD liposarcoma on the biopsy had a very high PPV.

Figure 4. Peculiar anatomic features are informative in diagnostic process. Panel i) angiomylipoma, an A3 mass with involvement of renal cortex (arrows); panel ii) inferior vena cava leiomyosarcoma, a B3 lesion arising within the vascular lumen.
Therefore, any exception to obtaining a preoperative needle biopsy should be discussed within a multidisciplinary team environment, and in practice seems to be applicable only to entirely fatty lesions, which are few in number.

Limitations

We acknowledge that this is a retrospective analysis, but believe that we have captured sufficient data in order to be able to draw our conclusions. The radiological criteria described for the different subgroups have not yet been validated and this is a limitation of the study. The limited sample size of some specific histotypes limits our analysis and the ability to draw any definitive recommendations in those subgroups.

Conclusions

In conclusion, retroperitoneal masses present with a wide spectrum of MDCT findings. None of the identified radiological criteria were sufficient to anticipate the diagnosis of a specific histological subtype. WD liposarcoma and angiomylipoma subtypes demonstrated some radiological features suggestive of a diagnosis, but without definitive conclusions being drawn. Preoperative needle biopsy remains the standard diagnostic procedure in identifying benign conditions, non-sarcomatous neoplasms, non-fatty liposarcomas and other sarcoma histotypes, and a correct histopathological diagnosis is critical in planning the most appropriate treatment options and surgical strategies.

Conflict of interest statement

The authors declare no conflict of interest for the present manuscript.

References

