Supplementary Materials

Suppl 1. Imaging review, anatomic divisions and rationale.

Imaging review and determination of primary site of tumor

All CT scans were with intravenous contrast and at most 5 mm in slice thickness and reconstructed in axial and coronal planes. All MRI scans were contrast enhanced with sequences tailored to the specific anatomical region. All imaging available were then reviewed by one of the radiologists (21 years in practice). Both radiologists devised the method of designation of tumor origin *a priori* and reviewed 15 random vascular LMS cases consensus to standardize and synchronize the method of review. LMS site of origin was assigned with an increasing confidence rating of 1-5. When more than two sites of origin were suspected, all possible sites were recorded and a confidence rating of 1 was applied. Confidence rating of 2 was applied when two possible sites of origin were noted. All tumors with confidence ratings of 1 and 2 were secondarily reviewed with a 2nd abdominal/sarcoma radiologist (CM, 32 years in practice) external to the institution to reach consensus. At this second consensus review, if more than two organs/veins were suspected, the tumor origin was designated as indeterminate. If two organs/veins were suspected, both were recorded as possible sites of origin. For tumors that were involving an organ, the organ was automatically designated as the primary site, even if there was a question of venous involvement. For tumors arising from veins, the designation of the primary venous segment was as follows: If the tumor had an extraluminal invasion, the geometric center of the site of invasion was assigned as primary site. For example, if a IVC LMS was within IVC IIA and IVC IIB intraluminally, but there was an extraluminal extension involving IVC IIA, the latter was taken as primary site of tumor (because the radiologists agreed that intravascular tumors extend downstream but are likely to extend extraluminally at their primary site). For venous tumors that were exclusively intravascular, the widest axial diameter was designated as the primary site. If the widest component traversed two veins/vein segments, both were designated as co-primary sites.

155/225 (68.9%) patients with ANU-LMS met inclusion/exclusion criteria. The breakdown of the confidence rating (1, very low; 5, very high) for determination of the primary site of tumor by a single radiologist for the 155 tumors were as follows: 1, 13 (8.4%); 2, 16 (10.3%); 3, 22 (14.2%); 4, 38 (24.5%); and 5, 66 (42.5%). All 29 tumors with low confidence rating of 1 and 2 were reviewed in consensus with a second expert radiologist with 11/29 (38%) being given a higher confidence (i.e. assigned to a single anatomical site), 11/29 (38%) ascribed to 2 sites, and 7/29 (24%) considered as indeterminate (three or more possible primary sites).

Rationale for anatomical and physiological grouping of retroperitoneal veins

In prior studies documenting location of LMS, the IVC was divided into three sections (IVC I, II, and III) based on the junction of large tributaries that could easily be identified intraoperatively [4-8]. In particular, IVC I had been defined as below the renal veins, IVC II from renal to hepatic veins, and IVC III from the hepatic veins to the heart. In this study, the IVC was divided into 4 sections as follows: IVC I, below right gonadal vein or left renal vein, whichever was lower; IVC

IIA, between gonadal/renal vein and caudate lobe margin; IVC IIB, between the caudate lobe margin and hepatic veins; and IVC III, at/above hepatic veins (Fig. 2).

We altered the definition of the upper margin of IVC I to demarcate the physiologically different concentration of hormones that the IVC will experience above and below the junction of the veins draining the gonads (via the right gonadal vein or left renal vein). We divided IVC II into two segments. IVC IIA is below the liver and receives blood from both gonads and both adrenal glands, whereas IVC IIB is isolated by the liver and typically receives caudate lobe and accessory hepatic venous drainage. This division of IVC II into two separate segments was created because the liver avidly metabolizes and removes steroid hormones from the blood [12]. Therefore, portions of IVC exposed to drainage from the liver through hepatic or accessory hepatic veins (which are very common and drain into IVC IIB but not IVC IIA) result in significantly lower hormone concentrations [12]. Finally, the left renal vein was divided into two segments, medial (at and medial to the left gonadal vein), and lateral (to the left gonadal vein). Again, this division was done to account for the presumed differing concentrations of hormones produced by the gonads and adrenals draining into the more medial aspects of the left renal vein, downstream to the left gonadal vein.