cord-stromal markers, inhibin, calretinin, and CD56, with only focal staining with calretinin and CD56 in 2 cases each; these 3 markers stained the luteinized cells, which may be a reaction to the proliferation of spindled and ovoid cells.[2–6] Thus, we could not provide immunohistochemical evidence that the ovarian lesion in luteinized thecoma associated with sclerosing peritonitis exhibited stromal differentiation. In that study, the peritoneal lesions exhibited variable staining with cytokeratins and hormone receptors.[2]

In recent years, 2 new markers of ovarian sex cord-stromal lesions have come to the fore, steroidogenic factor-1 (SF-1) and FOXL2.[7–11] These are considered to be relatively sensitive and specific markers of sex cord-stromal neoplasms and also stain non-neoplastic ovarian stroma. They are nuclear markers, in contrast to inhibin, calretinin, and CD56, which result in cytoplasmic staining; in general, nuclear markers tend to be more robust and easier to interpret than cytoplasmic markers. To further investigate the lineage of the ovarian lesion in luteinized thecoma associated with sclerosing peritonitis, we stained 11 cases with SF-1 (monoclonal antibody; 1:100; R and D systems, Abingdon, UK) and FOXL2 (polyclonal antibody; 1:25; Imgenex, San Diego, CA).

With both markers, cases were classified as positive if there was staining of any of the nuclei of the nonluteinized cells. Positive cases were classified as focal (< 50% nuclei positive) or diffuse (≥ 50% nuclei positive). The results of the immunohistochemical analysis are shown in Table 1. The nonluteinized spindled and ovoid cells were convincingly positive with SF-1 and FOXL2 in all but 1 case each (the single cases that were negative with SF-1 and FOXL2 were different cases) (Fig. 1). In general, staining was more diffuse with FOXL2 as compared with SF-1. The luteinized cells were always positive with both markers.

Our results indicate that the nonluteinized spindled and ovoid cells of the ovarian lesion of luteinized thecoma associated with sclerosing peritonitis are commonly positive with the sex cord-stromal markers SF-1 and FOXL2. Although it could be argued that the full specificity of these markers with regard to mesenchymal lesions has not been fully evaluated, our results provide evidence that this lesion is of ovarian stromal origin, although this does not shed light on whether this is a neoplastic process or a non-neoplastic reactive proliferation.

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Conflicts of Interest and Source of Funding: The authors have disclosed that they have no significant relationships with, or financial interest in, any commercial companies pertaining to this article.

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Extracavitary KSHV-positive Solid Lymphoma

A Large B-cell Lymphoma Within the Spectrum of Primary Effusion Lymphoma

To the Editor:

We read with great interest the article by Pan et al,[1] which appeared in the issue of August 2012 of the *The American Journal of Surgical Pathology*. The authors investigated the clinicopathologic features of 9 cases of Kaposi sarcoma–associated herpesvirus (KSHV)-associated large B-cell lymphomas without lymphomatous effusions in any body cavities. These lymphomas were originally termed "extracavitary KSHV-positive solid lymphoma."[2,3] Pan et al[1] also reviewed additional 43 cases of extracavitary KSHV-positive solid lymphomas and compared them with 84 cases of classic

TABLE 1. Extracavitary KSHV-positive Solid Lymphomas: Immunohistochemical Expression of 11 Secreted Proteins That Were Shared by, or Specifically Found in, PEL Secretomes

Protein (Short Name)	Case 1 (ID# 261111) (%)	Case 2 (ID# 288980) (%)	Case 3 (ID# 141125) (%)	Case 4 (ID#12715) (%)
Ezrin (EZR)*	90 S	90 S	90 S	90 S
Moesin (MOES)*	90 S	90 S	90 S	90 S
High-mobility group box 1 (HMGB1)*	90 S	90 M	90 S	90 S
Galectin 1 (LEG1)*	90 S	90 S	90 S	90 S
Stathmin 1 (STMN1)*	90 S	90 WM	90 M	90 M
Granzyme A (GRAA)†	70 S	10 M	10 M	10 S
S100 calcium-binding protein A6 (S10A6)†	90 S	90 S	90 S	90 S
Protein arginine methyltransferases 1 (ANM1/PRMT1)†	90 S	90 S	90 S	90 S
Glutathione S-transferase κ 1 (GSTK1)†	90 S	90 M	30 M	90 S
Catalase (CATA)†	10 W	70 W	60 W	90 S
Poly(rC)-binding protein 2 (PCBP2)†	90 S	90 M	90 S	90 S

Cases 2 and 3 were included among the KSHV solid lymphomas reviewed by Pan et al[1] as case no. 13[3] and 5,[6] respectively.

Immunohistochemical staining studies of the 11 selected proteins on KSHV-negative neoplasms have also been performed. KSHV-negative neoplasms included plasma cell myeloma (4 cases) and plasmablastic lymphoma (2 cases). All proteins except for GRAA and CATA were expressed in the 2 plasmablastic lymphomas tested. Moreover, all proteins except for STMN1, GRAA, GSTK1, and CATA were expressed in the 4 plasma cell myelomas tested. In the positive cases, most tumor cells were stained, and the intensity was high.

*Proteins shared by all PEL cell lines tested.

†Proteins specifically secreted by PEL cell lines when compared with secretomes of cell lines derived from solid tumors and leukemias.

M indicates moderate staining intensity; S, strong staining intensity; W, weak staining intensity.

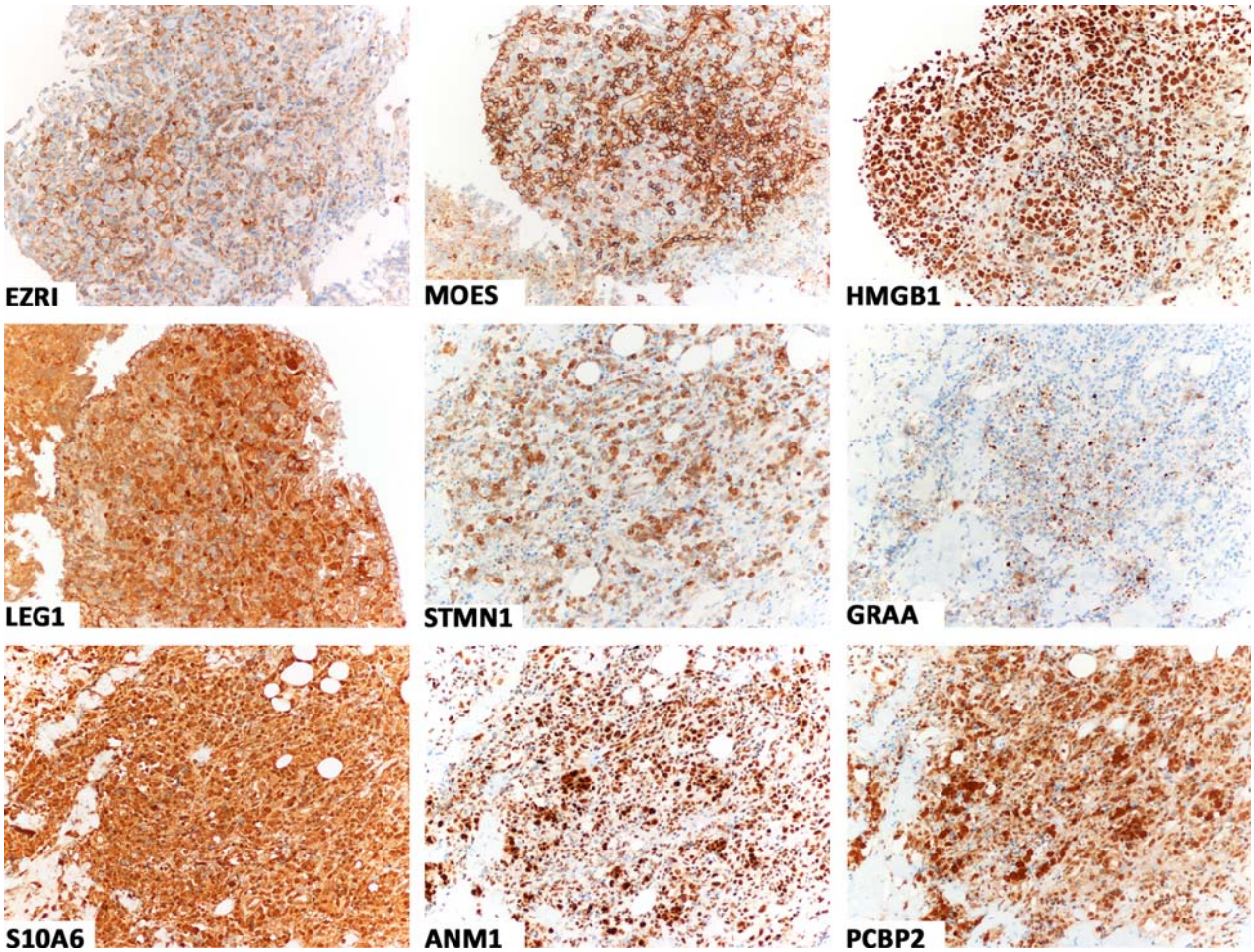

FIGURE 1. Immunostains showing tumor cell positivity for ezrin (EZRI), moesin (MOES), high-mobility group box 1 (HMGB1), galectin 1 (LEG1), and stathmin 1 (STMN1) in case 3, and granzyme A (GRAA), S100 calcium-binding protein A6 (S10A6), protein arginine methyltransferases 1 (ANM1), and poly(rC)-binding protein 2 (PCBP2) in case 2. Almost all tumor cells were stained; the intensity of staining was usually strong (immunoperoxidase, hematoxylin counterstain).

primary effusion lymphoma (PEL)[4] from the literature. The authors found different clinical presentations and some variations in immunophenotype between extracavitary KSHV-positive solid lymphomas and classic PEL and concluded that it is still uncertain whether it is justifiable to separate them as 2 distinct entities.[1] Nevertheless, they recommended the diagnostic term "KSHV-associated large B-cell lymphoma (KSHV-LBL)" to replace many different names previously used.[1]

Previously, we found that the expression of a subset of genes, identified by gene expression profiling, distinguished PEL tumor cells from other HIV-related and unrelated large cell lymphomas.[5] Importantly, the expression of this subset of genes was also found, by real time polymerase chain reaction and immunohistochemistry, in KSHV-positive solid lymphomas and was similar to that identified in PEL but distinct from other HIV-related and unrelated large cell lymphomas.[3] Combined results suggested that KSHV-positive solid lymphoma may represent part of the spectrum of classic PEL.

In the present report, we would like to further contribute to the issue raised by Pan and colleagues by discussing new data derived from proteomic analysis of the secretome (cell conditioning media) of PEL (Gloghini et al, manuscript submitted). By applying proteomics techniques to analyze PEL secretome, we aimed at identifying putative new players in the interaction between PEL cells and microenvironmental cells and proteins that might be relevant for PEL pathogenesis. We identified secreted proteins that were shared by, or specifically found in, PEL secretomes. Among them we selected 11 proteins (Table 1) potentially related to PEL pathogenesis and cell adhesion. By immunohistochemistry we found that all these proteins were expressed in 4 cases of extracavitary KSHV-positive solid lymphomas and in several PEL cell lines and primary PEL samples tested (not shown). The profile shown in Table 1 and Figure 1 demonstrates that all the tested proteins were found to be expressed in the extracavitary KSHV-positive solid lymphomas. Almost all tumor cells were stained with a usually strong intensity. Consistent with these results, extracavitary KSHV-positive solid lymphomas show relatedness to the PEL profile in the protein expression as revealed by proteomic analysis of PEL secretome.

On the basis of previous gene expression profiling–derived observations[3,5] and the present findings, extracavitary KSHV-positive solid lymphomas can be considered as part of a continuous spectrum of classic PEL, and the diagnostic term of "extracavitary KSHV-positive solid lymphoma" may be recommended to define this tissue-based variant of PEL.

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Conflicts of Interest and Source of Funding: The authors have disclosed that they have no significant relationships with, or financial interest in, any commercial companies pertaining to this article.

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