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CD31 expression in plasmacytic/plasmablastic lesions

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ABSTRACT

Although CD31 has been considered one of the better, if not the best, immunohistochemical marker of endothelial cells and thereby vascular neoplasia, it is not unequivocally specific to this group of tumors. We examined CD31 staining in 34 plasmacytic lesions including 15 plasma cell myelomas, 1 extraosseous plasmacytoma, 10 plasmablastic variants of myeloma, 5 plasmablastic non-Hodgkin lymphomas, and 3 reactive plasmacytic infiltrates. All reactive plasma cellular infiltrates, 93% of plasma cell myelomas, 80% of plasmablastic variants of myelomas, and 20% of plasmablastic non-Hodgkin lymphoma cases were CD31 positive with usually diffuse and strong membranous staining. When ERG staining was performed, none were ERG positive. Plasmablastic variant of myeloma is another large cell malignancy that has the potential to be mistaken for a poorly differentiated epithelioid vascular neoplasm if CD31 is presumed to be an explicit marker of endothelial cells.

1. Introduction

CD31, also known as *platelet/endothelial cell adhesion molecule–1*, is widely known and frequently used as a sensitive and relatively specific immunohistochemical marker of endothelial cell differentiation. This 130-kd glycoprotein is found at the intercellular junctions of endothelial cells as well as on the surface of platelets and leukocytes [1]. It is involved in recruitment of leukocytes; blood vessel formation; and regulation of monocyte, neutrophil, and T-cell activation [2]. Specifically, the endothelial expression of the CD31 molecule is required for transendothelial migration of leukocytes [3].

Our interest in the expression of CD31 in plasma cells was prompted by a bone biopsy from a patient with a prior history of epithelioid hemangioendothelioma where a CD31 stain was ordered to rule out recurrent/metastatic epithelioid hemangioendothelioma. Instead of the expected negative result based on the hematoxylin and eosin (H&E) morphology, neoplastic cells were strongly positive for CD31 as well as for plasma cell markers VS38c and CD138 (syndecan), and unequivocal λ light chain restriction.

The strong and diffuse expression of CD31 by this plasma cell myeloma (PCM) prompted us to search the surgical pathology literature that revealed minimal discussion of CD31 expression in plasma cell neoplasia. Herein, we present our experience with CD31 expression in reactive plasma cells and plasmacellular neoplasms, in particular those with plasmablastic/anaplastic morphology.

2. Material and methods

We searched our files for the past 7 years for examples of PCM, plasmablastic variant of PCM (PBPCM), plasmablastic lymphoma (PBNHL), non-Hodgkin lymphoma with plasmablastic morphology, extraosseous plasmacytoma, and plasma cell neoplasms not definitively characterized. The PBPCM cases were identified using the cytomorphologic criteria defined by Greipp et al [4] and the WHO classification [5]. We also chose a few examples of nonneoplastic tissue specimens containing reactive plasma cell infiltration. Only cases with sufficient tissue for additional staining were selected. The PBNHL cases were B-cell marker–negative, CD138-positive, and EBER-positive large cell non-Hodgkin lymphomas as defined by the WHO [5]. All cases were stained with antibodies to CD31 and CD138. Additionally, selected examples of PBPCM were stained with ERG antibody using the conditions listed in Table 1. CD31 and CD138 cytoplasmic reactivity was scored as follows: percentage of positive cells (0 = negative, 1+ = 1%-25%, 2+ = 26%-75%, 3+ = >75%), intensity of positive staining (0 = negative, 1 = weak, 2 = strong), and pattern of positive staining (cytoplasmic, membranous, or both). ERG antibody was assessed for presence of nuclear staining. This study was performed with institutional review board approval.

3. Results

Thirty-four cases were examined from 32 patients. Excluding 3 examples of reactive plasmacytosis, all 29 patients having a malignant diagnosis ranged from 27 to 87 years of age with a male to female ratio of 3:1. Of these 34 cases, 15 were examples of PCM, 10 of PBPCM, 1 of extraosseous plasmacytoma, 5 of PBNHL, and 3 of reactive plasmacytic infiltrates from various anatomic sites (Table 2). All PCMs, PBPCMs, and

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Table 1
Immunohistochemistry: sources, clones, dilutions, pretreatment

Antibody	Vendor	Clone	Dilution	Instrument	Ag retrieval
CD31	Dako (Carpinteria, CA)	JC 70A	1:400	Bond	HIER, low pH
Vs38c	Dako	Vs38c	1:200	Dako	HIER, low PH
CD138	Dako	MI15	1:500	Bond	HIER, low pH

HIER, heat-induced epitope retrieval.

the single extraosseous plasmacytoma case demonstrated light chain restriction by either flow cytometry or in situ hybridization. All reactive plasma cell infiltrates (n = 3) and the vast majority of PCM (14/15, 93%) were positive for CD31. Importantly, 8 (80%) of 10 cases of PBPCM were also CD31 positive with variably intensity. Only 1 (20%) of 5 PBNHL cases was CD31 positive (weak staining with < 75% positive cells).

The percentage of CD31-stained cells in all 15 examples of PCM was identical to that of their CD138 counterparts, with > 75% positive and, in many cases, almost 100% positive cell staining. The intensity and pattern of CD31 positivity for PCM cases also mirrored those of CD138, with nearly all displaying a membranous pattern and some showing staining within the cytoplasm. We have no explanation for the single PCM case that was CD31 negative, yet CD138 positive. Seven of 8 PBPCM cases had greater than 75% CD31 positively stained cells. Nearly all PBPCM slides had a membranous-only pattern and exhibited an intense degree of CD31 positivity (Fig.). This again emulated the corresponding CD138 results. None of the PBPCM cases that were stained with ERG (another endothelial cell marker) were positive (n = 5).

4. Discussion

CD31 has been known to stain plasma cells for some time, but only a few studies in the surgical pathology literature even reference this finding. This fact is occasionally, albeit sparingly, even mentioned in textbooks [6]. Our impression, however, is that it remains well concealed from most surgical pathologists probably because most reactive and neoplastic plasma cell proliferations are readily recognized as such with the routine H&E stain. Thus, it goes without saying that it would be unusual (to say the least) to request a CD31 stain on such lesions. Lampert et al [7] showed that centrocytoid plasma cells within lymphoid follicle germinal centers did not express CD31 but that classic, more mature appearing plasma cells in germinal centers did. Based on the finding that plasma cells preferentially show CD31 expression compared with other B cells and by using magnetized CD31 antibodies to select for plasma cells in tonsil specimens, Medina et al showed by flow cytometry that using CD31 antibodies increased the yield of plasma cells obtained by a factor of 12 [8].

Plasma cells are characterized by surface expression of CD38, a transmembrane signaling receptor involved in proliferation, differentiation, and calcium mobilization [9]. Acting as a ligand for this plasma cell marker, CD31 activates an intracellular signaling cascade upon binding to it [10]. Fernandez et al [11] showed consistent expression of CD31 in plasma cells and follicle mantle B cells.

Although CD31 staining of nonneoplastic plasmacytic infiltrates is not novel, only a few earlier studies examined CD31 expression in plasma cell neoplasms. However, these previous studies often show contradictory findings [9,12]. Using a streptavidin-biotin detection system with microwave antigen retrieval, Govender et al [12]

Table 2
CD31 and CD138 expression characteristics in plasmacytic and plasmablastic lesions

Case	Age/sex	Site	Diagnosis	CD31 % cells positive/strength/pattern	CD138 % cells positive/strength/pattern
1.	50/F	Left 4th rib	PCM	3+/2/c, m	3+/2/c, m
2.	55/M	Right acetabulum	PCM	3+/2/c, m	3+/2/c, m
3.	54/M	Left femoral neck	PCM	3+/2/m	3+/2/c, m
4.	50/F	Right T12 pedicle	PCM	3+/2/m	3+/2/m
5.	48/M	Left pelvis same as pt. 30	PCM	3+/2/c	3+/2/m
6.	45/M	Right acetabulum same as pt. 7	PCM	3+/2/m	3+/2/c, m
7.	45/M	T7 body same as pt. 6	PCM	3+/2/c, m	3+/2/c, m
8.	63/M	Left distal femur	PCM	3+/2/m	3+/2/m
9.	67/F	Left scapula	PCM	3+/2/m	3+/2/c, m
10.	56/M	Left iliac bone	PCM	3+/2/m	3+/2/c, m
11.	70/F	L4 paraspinal	PCM	0/0/negative	3+/2/m
12.	67/M	Right scapula	PCM	3+/1/m	3+/2/c, m
13.	63/F	Right posterior iliac bone	PCM	3+/2/c, m	3+/1/c, m
14.	82/M	Right femur	PCM	3+/1/m	3+/2/c, m
15.	82/M	Left ischium	PBPCM	3+/2/m	3+/2/m
16.	87/M	Femur	PBPCM	3+/2/m	2+/1/m
17.	51/F	Left humerus	PBPCM	3+/2/m	3+/2/m
18.	70/M	RLL, lung	Extraosseous plasmacytoma	1+/2/m	2+/2/m
19.	43/M	Right femur	PBPCM	2+/1/m	3+/2/c, m
20.	63/M	Colon, splenic flexure	PBPCM	0/0/negative	3+/2/m
21.	61/M	Lymph node	PBPCM	3+/2/m	3+/2/m
22.	56/M	Bone marrow	PBPCM	3+/2/m	3+/2/c, m
23.	55/F	Skull	PBPCM	0/0/negative	3+/2/m
24.	47/M	Bone marrow	PBL	0//0/negative	3+/2/m
25.	47/M	Bone marrow	PBL	0/0/negative	3+/2/m
26.	52/M	Left maxillary sinus	PBL	0/0/negative	3+/2/c, m
27.	49/M	Right axillary lymph node	PBL	0/0/negative	2+/1/m
28.	27/M	Bone marrow	PBL	2+/1/m	2+/1/m
29.	47/M	Bone marrow	PBPCM	3+/2/m	3+/2/m
30.	48/M	Left scapula same as pt. 5	PCM	3+/2/c, m	3+/2/c, m
31.	19/M	Tongue	Reactive PCs	3+/2/c, m	3+/2/c, m
32.	73/F	Sphenoid sinus	Reactive PCs	3+/2/m	3+/2/m
33.	59/M	R mandible	Reactive PCs	3+/2/c	3+/2/c, m
34.	49/M	L maxilla	PBPCM	3+/2/c, m	3+/2/c, m

c, cytoplasmic; m, membranous; PBL, plasmablastic lymphoma; RLL, right lower lobe.