

A morphological and immunohistochemical study of plasma cell proliferative lesions

Kaik Boo PEH MBBS, MPath and Suat Cheng PEH MBBS, MRCPATH

Department of Pathology, Faculty of Medicine, University of Malaya, Kuala Lumpur

Abstract

Monoclonal plasma cell proliferative diseases such as multiple myeloma and plasmacytoma can involve extramedullary sites at the time of first presentation, or subsequently in the course of the disease. Under such circumstances, they can mimic primary or metastatic carcinomas, neuroendocrine or neuroectodermal tumours and lymphomas, and the pathologist often has to resort to immunohistochemistry as an aid to diagnosis. We studied the morphology and immunohistochemical properties of 10 cases of previously confirmed monoclonal plasma cell proliferative lesions retrieved from the files of the Department of Pathology, University of Malaya. Serial 4µ thick paraffin sections were stained with H&E, the Unna-Pappenheim technique for nucleic acid and a panel of antibodies using a standard immunoperoxidase technique.

Light chain restriction was demonstrable in most of the cases. Seven (70%) showed kappa and 2 (20%) lambda light chain restriction. The remaining case was not stainable with most of the antibodies in the panel. The majority (80%) of cases showed accompanying IgG heavy chain in the cytoplasm, while 1 case had IgA. Seven (70%) showed membrane positivity with antibody to epithelial membrane antigen (EMA) and 7 (70%) cytoplasmic positivity with antibody to vimentin. This study enhances our awareness that neoplastic plasma cells can be positive for EMA and vimentin, and cautions us from misinterpreting these lesions as carcinomas or sarcomas. Notwithstanding that, immunohistochemical staining for kappa and lambda light chains can be helpful in differentiating monoclonal plasma cell proliferations from polyclonal ones.

Key words: Plasma cell, plasmacytoma, myeloma, EMA, LCA, immunohistochemistry

INTRODUCTION

Neoplastic plasma cell proliferative diseases such as multiple myeloma and plasmacytoma are known to involve the soft tissue and other extramedullary sites at the initial presentation or subsequently in the course of the disease.^{1,2,3} Often, the tissue diagnosis of these lesions poses no difficulty as the plasmacytic nature is readily recognised. Occasionally, where the differentiation is less obvious, they can be mistaken for metastatic carcinomas, sarcomas, neuroendocrine tumours, and malignant lymphomas.^{4,5,6,7} This is particularly true if the pathologist depends on a limited range of common antibodies in immunostaining or is unaware of the immunohistochemical profile of these lesions.

The present study was undertaken to elucidate the morphology and immunohistochemical profile of multiple myeloma and plasmacytoma, with the aim that the findings may aid the pathologist in diagnosing difficult lesions suspected to be of plasmacytic origin.

MATERIALS AND METHODS

Ten surgical specimens (biopsies and resected tumours) of clinically and histologically confirmed lesions of multiple myeloma and plasmacytoma were retrieved from the archives of the Department of Pathology, University of Malaya. They consisted of formalin-fixed and paraffin-embedded material. Serial 4µ thick sections were stained with H&E, methyl green-pyronin using the Unna-Pappenheim technique and a panel of common antibodies (Table 1) using the standard immunoperoxidase technique.^{8,9}

The cellular morphology of the cases was assessed on the basis of the H&E section and was graded as well, moderately or poorly differentiated (anaplastic), according to the degree of resemblance to mature plasma cells, the nuclear morphology and the proportion of the predominant cell type.^{10,11,12}

TABLE 1: Antibody panel for immunohistochemical staining

Antibody	Dilution	Source
<i>Polyclonal</i>		
kappa	1/10,000	Dakopatts
lambda	1/10,000	Dakopatts
IgG	1/4,000	Dakopatts
IgA	1/800	Dakopatts
IgM	1/5000	Dakopatts
Keratin	1/1600	Dakopatts
NSE	1/200	Dakopatts
<i>Monoclonal</i>		
EMA	1/50	Dakopatts
Vimentin	1/50	Dakopatts
LCA (CD45)	1/50	Dakopatts
L26 (CD20)	1/100	Dakopatts

Key : NSE = Neuron-specific enolase
 EMA = Epithelial membrane antigen
 LCA = Leucocyte common antigen

RESULTS

In sixty percent (6/10) of cases, the neoplastic plasma cells closely resembled mature plasma cells (Fig 1a). Three cases showed moderate plasmacytic differentiation (Fig 1b). In one case, the tumour cells were so poorly differentiated that there was very little morphologic resemblance to mature plasma cells (Fig 1c). Methyl green-pyronin staining demonstrated the presence of cytoplasmic RNA in the neoplastic plasma cells of all cases (Fig 1d). Light chain restriction was also observed: 7 (70%) were kappa and 2 (20%) lambda. One case did not express either kappa or lambda cytoplasmic light chains and reacted negatively with all other antibodies except EMA

and vimentin. The lesion was, however, shown to be **monoclonal** plasma cell proliferations biochemically on the basis of the presence of **IgG** myeloma protein in the serum and Bence-Jones proteinuria. Eight (80%) cases expressed cytoplasmic **IgG** and one (10%) case showed **IgA** positivity. Seven (70%) cases showed positive binding with antibody to EMA (Fig 2a). Seven (70%) cases showed positive staining with vimentin antibody (Fig 2b), of which 5 were also EMA positive. Unequivocal EMA and vimentin **positivity** in addition to kappa light chain restriction and cytoplasmic **IgG** were demonstrated in the case with very poor differentiation (Fig 3a,b,c,d,e,f). None of the 10 cases were immunoreactive for keratin, LCA, L26 or NSE (Table 2).

DISCUSSION

The present study showed that in most cases of neoplastic plasma cell proliferative diseases, the neoplastic plasma cells bear morphologic resemblance to their benign mature **counterparts**.¹ In these cases, a correct diagnosis of either multiple myeloma or plasmacytoma could easily be made based on the clinical findings, histological appearances and the demonstration of light chain restriction in the cells. Cytoplasmic kappa light chain and **IgG** are the most common light chain and immunoglobulin class present respectively. This is in agreement with the findings of other studies.^{13,14,15,16} In addition, a high percentage of cases showed that neoplastic plasmacells express EMA (70%) and vimentin (70%), regardless of the degree of morphological differentiation. However, not all EMA positive cases are vimentin positive, and vice-versa. More importantly, the

TABLE 2: Immunohistochemical profile and morphological differentiation

Case No	Morphological differentiation	Kappa	Lambda	IgG	IgA	IgM	LCA (CD45)	L26 (CD20)	EMA	Vimentin	Keratin	NSE
1	W	-	+	+	-	-	-	-	-	++	-	-
2	I	+	-	-	+	-	-	-	+	-	-	-
3	W	+	-	+	-	-	-	-	+	++	-	-
4	W	+	-	+	-	-	-	-	+	++	-	-
5	W	+	-	+	-	-	-	-	-	+	-	-
6	I	+	-	+	-	-	-	-	-	+	-	-
7	W	-	+	+	-	-	-	-	+	-	-	-
*8	W	-	-	-	-	-	-	-	±	+	-	-
9	P	+	-	+	-	-	-	-	+	+	-	-
10	I	+	-	+	-	-	-	-	+	-	-	-

Key: - = Negative; ± = weak positive; + = positive; ++ = strong positive;
 W = Well differentiated; I = moderately differentiated; P = poorly differentiated

*This case showed negative immunostaining with all antibodies except **vimentin and EMA** (weak staining), but was confirmed to be monoclonal proliferation clinically and biochemically

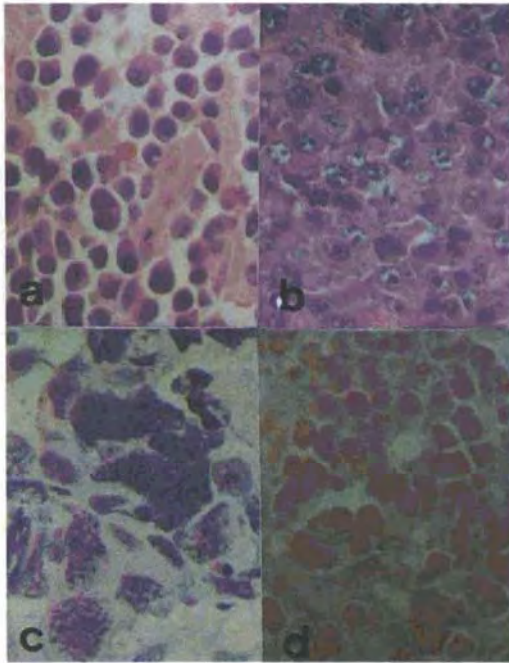


FIG. 1: (a) Well-differentiated plasmacytoma. H&E X100. (b) Moderately-differentiated neoplastic plasma cells. H&E X100. (c) Poorly-differentiated (anaplastic) neoplastic plasma cells. H&E X100. (d) Methyl green-pyronin positivity in neoplastic plasma cells. Unna-Pappenheim X100

negative reactions with antibodies to leukocyte common antigen (CD45) and L26 (CD20) suggest that B cells tend to lose leukocyte antigens when they differentiate to plasma cells. This

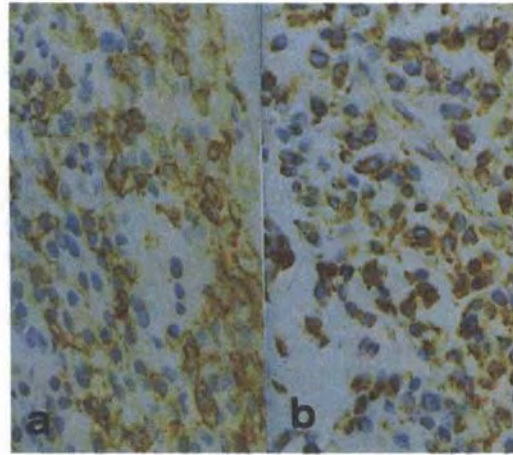


FIG. 2: (a) EMA positivity in plasmacytoma. Immunoperoxidase by ABC method X100. (b) Vimentin positivity in plasmacytoma. Immunoperoxidase by ABC method X100.

finding has diagnostic implications, especially when taken in the light that in the majority of cases, the neoplastic plasma cells can express EMA and/or vimentin positivity. Under such circumstances, less differentiated plasma cell lesions, particularly in the extramedullary sites, may be misdiagnosed as carcinomas or sarcomas. Likewise, their presence in the bone marrow may be wrongly interpreted as a metastatic malignancy. Such mistakes occur if pathologists are unaware of the immunohistochemical profile of neoplastic plasma cells, and the attempt at eluci-

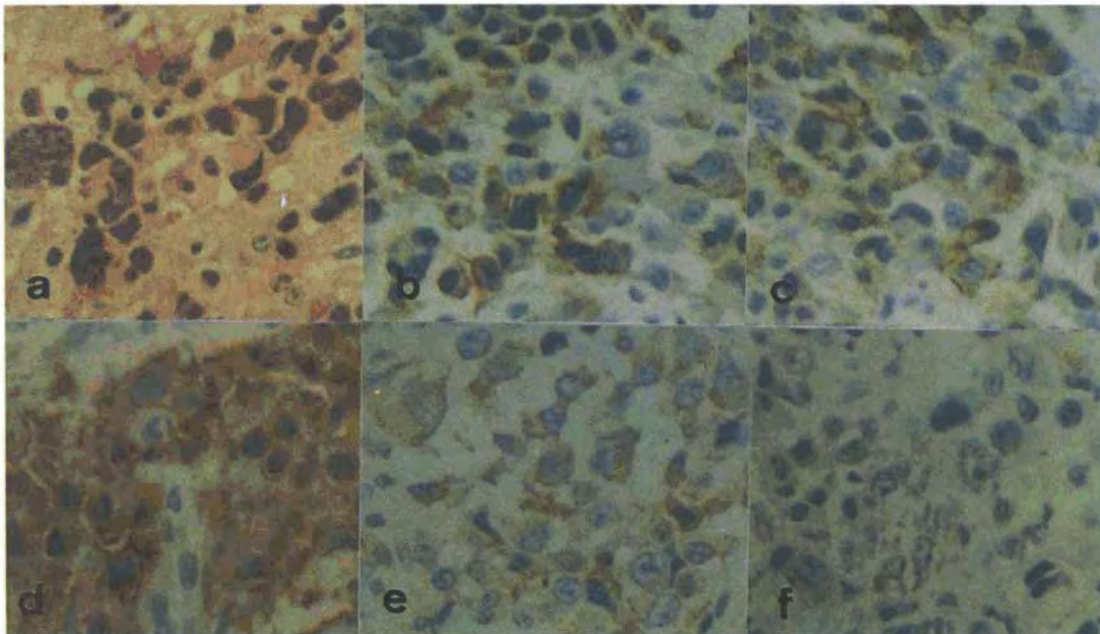


FIG. 3: A case of multiple myeloma with poorly-differentiated neoplastic cells showing (a) anaplastic cells with H&E stain, (b) vimentin positivity, (c) EMA positivity, (d) Kappa lightchain restriction, PAP technique. (e) Cytoplasmic IgG, PAP technique. (f) LCA (CD45) negativity, Immunoperoxidase by ABC method.

dation of the histogenesis of the tumour cells is based on immunohistochemical staining with a limited range of common antibodies, such as LCA, EMA and vimentin.

In conclusion, the results of this study reiterate the importance of recognising the existence of a morphological spectrum of the neoplastic plasma cells, in particular those in **extramedullary** sites, and the necessity to be aware that neoplastic plasma cells can express positive reactions with antibodies to **EMA**¹⁷ and vimentin, and can be non-reactive with antibodies to leukocyte common antigen (**CD45**) and **L26 (CD20)**. Therefore, when assessing the immunohistochemical findings of undifferentiated malignancies, the possibility of poorly differentiated plasmacytoid neoplasia must be constantly kept in mind. It is necessary to use antibodies to a range of epithelial antigens in combination with antibodies to light chains to distinguish undifferentiated carcinomas from anaplastic plasmacytic tumours.

ACKNOWLEDGEMENTS

We would like to thank Mr. Y.C. Mah for his invaluable technical assistance and acknowledge the support of Grant **CMB/UM 30205**.

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