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Original Research Article

A study on spectrum of tumours diagnosed after immuno-histochemical analysis

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Abstract
Epithelial Membrane Antigen may be used as a supplement marker to CKs for detection of epithelial differentiation, especially in sarcomatoid carcinoma or those undifferentiated carcinomas that are negative or only focally positive for CKs. Epithelial membrane antigen is not entirely specific for carcinomas. Every eligible specimen diagnosed as undifferentiated malignant tumors, poorly differentiated malignant tumours and small round cell tumours in histopathology received for immunohistochemistry in IHC LAB, Department of pathology, SMS Medical college and Hospital, Jaipur. Total out of 92 cases, most frequent diagnosis was mesenchymal followed by epithelial, hematopoietic and germ cell tumours.
Keywords: Spectrum of tumours, immuno-histochemical analysis, histopathology

Introduction

The low-molecular-weight cytokeratins (LMW CKs), including CK8, CK18, and CK19, recognized by the antibodies CAM 5.2 or 35BH11, and a cocktail of keratins (pankeratin), recognized by the antibody AE1/ AE3, are useful screening markers for the recognition of epithelial differentiation. Absence of cytokeratin does not always exclude a carcinoma. For example, adrenal cortical carcinomas are often negative for CK, and hepatocellular carcinomas (HCCs) are often negative for pankeratin [1].

Epithelial Membrane Antigen may be used as a supplement marker to CKs for detection of epithelial differentiation, especially in sarcomatoid carcinoma or those undifferentiated carcinomas that are negative or only focally positive for CKs. Epithelial membrane antigen is not entirely specific for carcinomas. Epithelial membrane antigen expression has been seen in some normal and neoplastic hematopoietic cells, including reactive and neoplastic plasma cells, lymphocytic and histiocytic (L & H) cells in nodular lymphocyte predominant Hodgkin lymphoma, and neoplastic cells in some T-cell lymphomas; thus, most anaplastic lymphoma kinase (ALK)–positive anaplastic large cell lymphomas (75%) are EMA positive [2].

Vimentin is the sole intermediate filament characteristic of mesenchymal cells and present in virtually all sarcomas and melanomas and variably in lymphomas.

Frequent coexpression of vimentin with CK is seen in some carcinomas, for example, renal cell, endometrial, papillary and anaplastic thyroid, and ovarian serous (variably) carcinomas. The finding of vimentin/CK coexpression helps focus on certain types of epithelial tumors and helps in diagnosis of primary sites in the evaluation of metastatic tumors [3].

S100 Protein is considered as a screening marker for melanoma with more than 95% sensitivity in primary and metastatic sites. A valid positive S100 requires both nuclear and cytoplasmic staining. S100 protein, however, is also expressed in various other lesions, including peripheral nerve sheath, granular cell, cartilaginous and salivary gland tumors, chordomas, Langerhans cell histiocytosis, and occasional adenocarcinomas to varying degrees. Thus, to confirm the melanocytic nature of an S100-positive neoplasm, the tumor

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should be also positive for one or more melanocyte-specific protein (eg, HMB-45 or MART-1/Melan-A) [4].

Methodology

Study design: Laboratory based descriptive type of observational study.

Study Universe: IHC LAB, Department of pathology, SMS Medical college and Hospital, Jaipur.

Inclusion criteria

All cases of undifferentiated malignant tumours, poorly differentiated malignant tumours and small round cell tumours diagnosed by histopathology during the study period.

Exclusion criteria

1. Inflammatory pathology
2. Benign tumours
3. Specific differentiated malignant tumours

Sample size

Sample size was calculated at 95% confidence level assumed 98.65% positive cases and at 3% absolute error, minimum 60 cases of malignancy are required.

Sampling technique

Every eligible specimen diagnosed as undifferentiated malignant tumors, poorly differentiated malignant tumours and small round cell tumours in histopathology received for immunohistochemistry in IHC LAB, Department of pathology.

Study tool

Immunohistochemistry. In our study we will use CK, LCA, Vimentin, S-100 as a primary panel of antibodies. Use of secondary panel will depend on result of primary panel.

Results

Table 1: Distribution of cases according to final diagnosis

	No. of cases	Percentage
Mesenchymal	34	36.96%
Hematopoietic	26	28.26%
Epithelial	29	31.52%
Germ cell	3	3.26%
Total	92	100.00%

Total out of 92 cases, most frequent diagnosis was mesenchymal followed by epithelial, hematopoietic and germ cell tumours.

Table 2: Distribution of mesenchymal neoplasms according to sex

Mesenchymal Neoplasms	Sex (No.)	
	Male	Female
Clear Cell Sarcoma	1	-
Epithelial sarcoma	1	-

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Ewing's Sarcoma	11	10
Gastrointestinal stromal tumour	1	-
Leiomyosarcoma	-	1
Lutenized Granulosa cell tumour	-	1
Malignant mesenchymal neoplasm	1	-
Neuroblastoma	3	-
Rhabdomyosarcoma	-	2
Synovial sarcoma	-	2
Total	18	16

Table 3: Distribution of Hematopoietic neoplasms according to sex

Hematopoietic neoplasms	**Sex (No.)**	
	Male	**Female**
Burkitt's lymphoma	1	1
Classical Hodgkin's Lymphoma	2	-
Lymphoblastic lymphoma	1	1
Lymphoma	1	-
Non-Hodgkin's B cell Lymphoma	2	-
Non-Hodgkin's Lymphoma(DLBCL)	7	8
Plasmablastic neoplasm	1	-
Primary cutaneous anaplastic large T-cell lymphoma	1	-
Total	16	10

Table 4: Distribution of Epithelial neoplasms according to sex

Epithelial neoplasms	**Sex (N %)**	
	Male	**Female**
Adenocarcinoma	3	2
Malignant melanoma	2	2
Metastatic carcinoma	-	1
Nasopharyngeal carcinoma	2	2
Neuro endocrine neoplasm	3	1
Neuroendocrine carcinoma	1	1
Renal cell carcinoma	-	1
Squamous cell carcinoma	3	1
Undifferentiated carcinoma	4	-
Total	18	11

Table 5: Distribution of Germ cell tumours according to sex

Germ cell tumours	**Sex (N %)**	
	Male	**Female**
Spermatic seminoma	1	-
Metastatic Germ cell tumour	1	-
Mixed Germ cell tumour	1	-
Total	3	-

Based on above findings, Incidences are more in males than in females in all the lineages.

Discussion

In 2006 Ahmed Z, *et al*. studied, Significance of immunohistochemistry in accurate characterization of malignant tumors. A retrospective study of 20,000 consecutive surgical biopsies reported in the Section of Histopathology, AKU in 2003. Out of the 20,000 biopsies, 6534 (32.67%) were neoplastic. 4726 neoplasms (72.33%) were malignant, and 1808 (27.67%) were benign. Immunohistochemistry was performed on 29.49% of malignant tumors, and 4.97% of benign tumors. Immunos were performed on only 2.82% of routine

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squamous cell carcinomas and adenocarcinomas of various organs, and in only 1.9% of infiltrating breast carcinomas, the commonest malignant tumours in females. In contrast, immunos were performed on 97.12% of non-Hodgkin's
lymphomas, 97.94% of Hodgkin's lymphomas, 98.09% of malignant spindle cell neoplasms, 87.96% of small round blue cell tumours of childhood, 87.30% of neuroendocrine neoplasms, and 84.37% cases of malignant melanomas. In addition, immunos were performed on all cases of malignant undifferentiated neoplasms and were able to resolve the issue in over 89% of such cases. Immunos were also performed on 54.74% of metastatic tumours. Lymph nodes were the commonest organs on which immunos were performed i.e. 96.50% of lymph node tumours, followed by CNS and renal neoplasms with 33.01% and 25.92% respectively [5].

In 2011, Bashyal R studied, Role of immunohistochemistry in the diagnosis of malignant small round cell tumors. This was a retrospective study done, A total of 40 cases small round cell tumors were selected for immunostaining. Out of 40 cases of malignant small round cell tumors, there were 21 cases (52.5%) of Non-Hodgkin Lymphoma, 11 cases (27.5%) of Ewing's Sarcoma/Primitive Neuroectodermal Tumor, 1 case (2.5%) of Lymphoblastic Lymphoma, 1 case (2.5%) of Rhabdomyosarcoma, 2 cases (5%) of Low grade neuroendocrine tumor, 1 case (2.5%) of Neuroblastoma, 2 cases (5%) of Poorly differentiated Synovial Sarcoma (small cell variant), 1case (2.5%) of Malignant Melanoma (small cell variant) [6].

In 2011 pity IS studied Histopathological and immunohistochemical approach for characterization of malignant round cell tumors. Immunohistochemical staining (IHC) with (monoclonal or polyclonal) antibodies was performed on 127 cancer cases reported as malignant round cell tumors. Malignant round cell tumors were more frequently located in the respiratory tract 30 (23.6%) followed by gastrointestinal tract 25 (19.7%), lymph node 19 (14.9%), and bone/soft tissue 19 (14.9%). Among these, 75 (82.7%) cases were primary and 22 (17.3%) metastatic. Application of immunohistochemistry resulted in characterization of 112 (88.2%) cases. Non-Hodgkin lymphoma 21 (16.5%) was at the top of the diagnosed list followed by adenocarcinoma 20 (15.7%), sarcoma 17 (13.4%), and small undifferentiated carcinoma 15 (11.8%) [7].

In 2013, vasudha bhagat, *et al*. studied the role and significance of immunohistochemistry for accurate diagnosis and subtyping of undifferentiated malignant tumours as it is essential in guiding therapy and prognosis. Immunohistochemical staining (IHC) performed was based on Peroxidase Antiperoxidase (PAP) method on paraffin sections, using appropriate mono/polyclonal antibodies. Total 74 cases were studied. The histopathology and IHC reports of 74 tumours were reviewed and assigned to appropriate categories. It was possible to arrive at a diagnosis in 73 cases (98.65%) with the help of IHC. Carcinoma was the commonest diagnosis (27 cases, 36.50%) followed by lymphoma (18 cases, 24.32%), sarcoma (14 cases, 18.92%), malignant melanoma (3 cases, 4.05%) and neuroblastoma (3 cases, 4.05%) [8].

In 2016, Alka mittal *et al*. studied "clinicopathological and immunophenotypic characteristics of ewings sarcoma family of tumors: special emphasis on role of friend leukemia integration - 1(fli-1) antibody and occurrence of tumor on rare sites". They included total 58 cases of Ewing's sarcoma/PNET in their study. They found mean age of presentation was 20 years with male preponderance [9].

In 2017, Mouhamed HA studied. The Diagnostic Utility of Immunohistochemistry in Undifferentiated Ovarian Carcinoma. IHC staining performed on 20 cases of undifferentiated ovarian carcinomas. IHC staining results showed that: 2 cases were malignant mesothelioma (calretinin+, panCKA1/A3+, CK7+, EMA+, vimentin+). Two other cases were granulosa cell tumor (inhibin+, calertinin+, vimentin+). Sixteen cases were undifferentiated ovarian carcinoma (PAX8+, vimentin+, panCKA1/A3+, CK7+, EMA+) [10].

Conclusion

Out of 92 cases, most frequent diagnosis was mesenchymal followed by epithelial, hematopoietic and germ cell tumours.

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