

Through the microscope: The correct diagnosis to decide a suitable therapy

It is a real honor and privilege for me to introduce the section “Through the microscope”, in this issue of the journal.

The relationship between tumor morphology and the clinical behavior of tumors has been known for more than a century, and the study of such clinicopathological correlations could be traced to the teachings of Rudolf Virchow and the scientific beginnings of microscopic pathology. The German pathologist, von Hansemann first opined that the biological and clinical behavior of tumors could be predicted from their microscopic characteristics.^[1]

The final histopathology report of tumor specimen must be concise, clear, and relevant to patient management; and it has to be qualified by assessment of prognostic indicators such as tumor grade, extent of spread, relationship to primary excision margins, and lymphovascular spread. Further, the diagnosis should be refined as much as possible using the available novel immunohistochemical or molecular techniques so that patients may be recruited to suitable treatment protocols.^[2]

In this issue of the journal, we are fortunate to have three interesting articles pertaining to three different organs namely central nervous system (CNS), ovary, and salivary gland.

Patnayak *et al.*,^[3] retrospectively evaluated 40 secondary CNS tumors with histopathological examination followed by workup with an array of relevant immunohistochemical markers in addition to radiological modalities and clinical profile. Majority of the cases were found to be in the 4th and 5th decade presenting mostly with symptoms of raised intracranial pressure and majority having single lesions in the cerebral hemisphere followed by cerebellum. Adenocarcinoma accounted for the maximum number of cases ($n = 25$, 62.5%) with lungs being the most common primary site and noticeably there was a significant number of secondary tumors due to unknown primary. The authors correctly focused on the practical issues like difficulty in identifying the primary by histologic appearance only, nonavailability of some of the organ specific immunohistochemical markers, and lastly the huge expenditure of using all the markers especially in the unknown primary cases and in metastases with undifferentiated morphology. A long term follow-up study

with survival analysis and assessment of the Karnofsky performance status should be carried out to predict the prognosis and choose the suitable therapeutic protocol.

The tremendous advances in understanding the molecular pathways that mediate brain colonization and the discovery of new molecular compounds have led to an increase of interest in preclinical and clinical investigations in the field of brain metastasis. Molecular subtyping of tumors and treatment with specifically targeted therapy is a rapidly developing area in oncology.^[4,5] Hence, organizing well-designed clinical trials and finding novel targets and secondary resistance mechanisms are essential.

Kriplani, *et al.*,^[6] have attempted to evaluate the role of immunohistochemistry in differentiating primary ovarian carcinoma from secondary tumors of the ovary using a panel of six markers. They found CK7 to be the most useful marker for the same. The authors have correctly addressed a very practical problem. In practice, assigning the primary diagnosis to be mucinous carcinoma of the ovary without considering clinical information, is analogous to diagnosing a bone tumor without any knowledge of the radiological findings, or a cytopathological specimen without knowing the anatomic site.^[7] The distinction of primary and metastatic ovarian neoplasms is further complicated by the occurrence of synchronous or metachronous independent ovarian and nonovarian neoplasms having similar histologic features.^[8]

Immunohistochemistry is an important aid in the classification of poorly differentiated neoplasms, and it is essential for the diagnosis and classification of metastatic tumors that involve the ovary. A panel of immunostains needs to be evaluated because some primary ovarian neoplasms fail to stain for CK7 and a proportion of metastatic carcinomas in the ovary are CK7-positive. CK20 immunostaining, which is positive in most adenocarcinomas of the large and small intestines, helps to differentiate primary female genital tract adenocarcinomas from adenocarcinomas arising in other organs. However, CK20 is also positive in intestinal-type mucinous tumors of the ovary, thus requiring additional markers. Positivity of monoclonal carcinoembryonic antigen (CEA) in ovarian mucinous adenocarcinomas, CA125 expression in primary nonmucinous epithelial ovarian cancers, and WT1 expression in serous carcinoma of the ovary are also helpful in distinguishing the primary and secondary tumors of the ovary.^[9] These problems were also addressed in the study by Kriplani, *et al.*^[6]

Salivary gland tumors can demonstrate a strikingly diverse range of histomorphologic variations and architectural configurations leading to a plethora of individual tumor types and subtypes and a frequently changing terminology.

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Classification is further complicated by the presence of dedifferentiated and hybrid tumors.^[10] Laishram, *et al.*,^[11] carried out a very simple but useful retrospective observational study on patterns of salivary gland tumors in Manipur for 10 years on 78 cases. Pleomorphic adenoma was the commonest benign neoplastic lesion and mucoepidermoid carcinoma was the commonest malignant tumor in their study.

However, many molecular genetic studies are ongoing to provide important information on genetic and epigenetic alterations in salivary gland tumors, especially on implications of their tumorigenesis, differential diagnosis, and therapeutic strategies. Specific chromosomal translocations have been reported especially in pleomorphic adenomas and mucoepidermoid carcinomas.^[10]

We hope that you will find these three articles a pleasant reading and a useful resource for your knowledge. We will appreciate your participation in providing constructive suggestions and look forward to receive more such original studies for the future issues of this journal.

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