Journal Reviews

Clinical Breast Cancer

Intraductal breast Papilloma diagnosis and treatment with vacuum-assisted core biopsy

Vacuum-assisted core biopsy in diagnosis and treatment of intraductal papillomas
Kibil W, Hodorowicz-Zaniewska D, Popiela TJ, Kulig J.
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The aim of this study was to assess the value of mammographically-guided and ultrasonographically-guided vacuum-assisted core biopsy (VACB) in the diagnosis and treatment of intraductal papillomas of breast and to answer the question whether ductal biopsy by this method allows the avoidance of surgery in these patients. The study is based on the findings from a 10 year period (2000-2010) during which a total of 1896 vacuum-assisted core biopsies were performed. Of these, 1183 biopsies were performed ultrasonographically guided and 713 mammographically guided (stereotaxic). Only 62 patients (3.2%) histopathologic examination confirmed intraductal papilloma of which 12 patients (19.4%) had atypical lesions at the initial examination. An open surgical biopsy of these 12 patients revealed invasive cancer in 2 women (false-negative rate, 16.7%; negative predictive value, 83.3%) and the biopsy from the remaining 50 patients (80.6%) revealed papilloma without atypia. All the 50 patients were later followed up to average of 5 years (range 14 months-10 years) by clinical observation and imaging examinations and did not show recurrence or malignant transformation of lesions. Hematoma developed in 3 (4.8%) patients as a complication of biopsy and surgical intervention was not required in any of the patients. In conclusion, authors' states that VACB is an efficient method for diagnosing intraductal papilloma of the breast and allows histopathologic confirmation of the lesion. Benign lesions corresponding to the clinical presentation can be managed conservatively avoiding surgery. However in all cases, histopathologic diagnosis of papilloma with atypical hyperplasia or a suspected malignant lesion on imaging, despite negative biopsy results, should always be an indication for surgical excision.

Reviewer's opinion: This study looked at the usefulness of VACB (US and Mammo guided) for the diagnosis and treatment of intraductal breast papilloma. The study even though aims to present 10 year data from a large pool of study population, however, the actual true positives were only 62 patients (3.2%) out of 1896 VACB performed. The low sample number may be in keeping with the uncommon prevalence of benign neoplasm that occurs in 2 to 3% of the population. The authors argue a case for conservative management for benign neoplasms on histology with annual surveillance with clinical, US and mammographic examinations up to 5 years without being explicit in their data as to how many image diagnosed benign lesions were completely removed with VACB. If VACB is a good technique to completely remove the lesion, why are the authors recommending an open excision biopsy for papillomas with atypical features. Alternatively, if the authors mean that VACB can help provide a diagnosis facilitating a definitive treatment later with open excision biopsy, the word 'treatment' in the context of VACB has been used interchangeably. The opinion on conservative management of papillomas without atypia seems to divided as other studies have found a higher risk of malignancy in this group. – TH

Neuro-Oncology

IDH/*MGMT*-driven molecular classification of low-grade glioma is a strong predictor for long-term survival

Leu S, von Felten S, Frank S, Vassella E, Vajtai I, Taylor E, Schulz M, Hutter G, Hench J, Schucht P, Boulay JL, Mariani L. Neuro-Oncology 2013;15(4):469-79.

Compared with the most malignant subtype of brain tumour, i.e. glioblastoma multiforme (GBM; grade IV), low-grade gliomas (LGGs; grade II) are rare and the median survival times span up to a few decades. LGGs progress in an infiltrative manner and develop into malignant tumours (grades III and IV). Grade IV tumours deriving from LGGs are designated secondary GBM and represent a small subset of GBM (~5%), compared with the more frequent primary GBM (~95%), which are considered to have developed *de novo*. Two molecular alterations characteristic of glioma have a particularly high prevalence in LGG: *MGMT* gene promoter methylation (*MGMT*met) and *IDH1*/*IDH2* mutations (*IDH*mut). Previous studies found that 41% of gliomas carried an *IDH1* mutation, whereas 2% had an *IDH2* mutation in a mutually exclusive manner. *IDH1/2* gene mutations were mostly observed in LGGs (70%–80%) and in secondary GBM (85%), compared with primary GBM (3%–7%). *TP53* mutations (*TP53*mut) mainly occur in diffuse astrocytomas, and are also associated with a younger age of onset and a shorter survival. Combined loss of heterozygosity of 1p/19q (1p19qLOH) is prevalent in oligodendrogliomas and is an indicator of longer survival. In this study, 210 adult LGGs were screened for *IDH*mut, *MGMT*met, 1p19qLOH, and nuclear *TP53* immunopositivity (*TP53*pos). Multivariate survival analyses with multiple imputation of missing data were performed in order to evaluate the impact of those biomarkers on survival. The results showed that molecular parameters were better survival predictors than histology ($P<.001$). *MGMT*met was positively associated with *IDH*mut ($P<.001$). IDHmut/MGMTmet combined status had a favourable impact on overall survival whereas *IDH*mut/*MGMT*met/*TP53*pos triple combination was a significant risk factor for malignant transformation ($P<.05$). The present study suggests that genotype better predicts prognosis than histology and therefore provides a more reliable tool for standardising future treatment strategies.

Reviewer's opinion: The impact of *IDH1*/*IDH2* mutations on survival among patients with LGG has been disputable with some studies showing no impact while others suggesting a positive correlation between *IDH* mutations and overall survival (OS). Results from this detailed retrospective study show that *IDH*mut, in combination with *MGMT*met, has a significant positive impact on long-term OS. Furthermore, a combination of biomarkers investigated in this study, along with demographic and clinical variables, provides a stronger survival predictor for LGGs than histological analysis alone. Based on their data, the authors made a statement that such markers should be routinely assessed in parallel to histopathological examination to better predict prognosis for patients with LGG. Their findings could also help standardise therapeutic strategies and identify novel targets for future therapies. – QA