Neuroendocrine tumors of cervix – clinical, morphologic, immunophenotypic, and electron microscopic features in two cases.

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Introduction

Neuroendocrine tumors of the uterine cervix are rare tumors of the gynecologic tract. The most recent Surveillance, Epidemiology and End-Results (SEER) data on neuroendocrine tumors of the uterine cervix has reported an incidence of 0.42 cases per 1,000,000 women. They are being increasingly recognized with the more routine use of immunostaining in the evaluation of histopathologic features suggesting neuroendocrine differentiation. They can present as a pure lesion or in combination with adenocarcinoma or squamous cell carcinoma. Analogous to lung neuroendocrine tumors, those of the uterine cervix are classified in four groups that are (1) carcinoid, (2) atypical carcinoid, (3) large cell neuroendocrine tumors and (4) small cell carcinoma. The first two are grouped with the neuroendocrine tumors (NETs), whereas the latter are categorized as neuroendocrine carcinomas (NECs).

We report the clinical and detailed pathologic features in two such cases. The patients were 48 and 71 years old and presented with vaginal bleeding. Both were multiparous females; both had history of hypertension and one was a prior smoker. Direct examination, and imaging studies revealed large cervical/lower uterine masses with obvious pelvic lymphadenopathy in one. The tumors ranged from 3.5 to 11.3 cm in greatest dimensions.

Recognition of NECs is important for appropriate therapy and management since these patients have worse clinical outcomes when compared with conventional cervical squamous or adenocarcinomas. Immunohistochemistry may be inconclusive in determining neuroendocrine differentiation, and should be supplemented with ultrastructural studies for confirmation and correct categorization of the carcinoma for appropriate management.

Report of two cases

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Results

Biopsies and hysterectomy specimens showed prominent neuroendocrine-type features by conventional light microscopy, with variable immunostaining results; focal adenocarcinoma features were seen in one case. One tumor showed strong, diffuse cytoplasmic p16 reaction; the other tumor showed patchy expression of p16. ER & PR were positive in Case 1, and not done on case 2 (data not shown). Transmission electron microscopy showed poorly differentiated cells with large nuclei with dispersed heterochromatin, prominent nucleoli, and occasional cytoplasmic dense-core granules. No cytoplasmic intermediate filaments were seen. Focally, luminal intercellular junctions were seen in the case with focal adenocarcinomatous features. EM pictures for case 2 are not available due to technical problems.

Conclusion

Recognition of NECs is important for appropriate therapy and management since these patients have worse clinical outcomes when compared with conventional cervical squamous or adenocarcinomas. Immunohistochemistry may be inconclusive in determining neuroendocrine differentiation, and should be supplemented with ultrastructural studies for confirmation and correct categorization of the carcinoma for appropriate management.