Case 6

Primary malignant peripheral nerve sheath tumor of the uterine cervix

Neli Basheska, MD, PhD, Professor, Head

Department of Histopathology and Clinical Cytology, University Clinic of Radiotherapy and Oncology, Faculty of Medicine, University Ss. Cyril and Methodius, Skopje, Republic of Macedonia

Clinical History

The repeated curettements in a 57-year-old woman with a history of prolonged vaginal bleeding, revealed polypoid fragments of a sarcomatous neoplasm. Subsequently, total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. Postoperatively, the patient received six courses of chemotherapy. Twenty-three months later, a local vaginal and left parametrial recurrence occurred. During the next 24 months, the pelvic mass persisted, causing excessive vaginal bleedings and necessitating numerous procedures of radiotherapy and chemotherapy. Eventually, 48 months following surgery lung metastases were confirmed and the patient died of respiratory failure nine months after.

Pathological Findings

The cervix was enlarged, markedly distorted by 5.5 x 2.5 x 2.5 cm neoplasm involving predominantly the anterior wall of the cervical canal. Microscopically, the tumor had a variable sarcomatous appearance, predominantly composed of cellular fascicles of spindle cells with hyperchromatic nuclei and eosinophilic cytoplasm. There were also hypocellular areas frequently with prominent myxoid stroma. Cytological atypia varied within the tumor, whereas mitoses were readily identified. The neoplasm penetrated deeply into the fibromuscular wall of the uterine cervix, infiltrating proximally the lower uterine segment and the myometrium of the distal part of the anterior wall of the uterine corpus. Beneath the mucosa the malignant spindle cells tended to infiltrate but not destroy the native endocervical glands. Immunohistochemical examination demonstrated that many of the tumor cells showed diffuse strong positive staining for S100 and vimentin, as well as S100A4, Wilms tumor 1 protein, and p16, and only focal positivity for CD56 and NSE. Tumor cells were negative for cytokeratin, EMA, CD57, GFAP, NFP, alpha-SMA, desmin, caldesmon, CD10, CD34, CD117, CD99, HMB-45, Melan-A, as well as estrogen and progesterone hormone receptors, while the proliferative index determined by Ki-67 was 15-20%.

Diagnosis: ***Primary malignant peripheral nerve sheath tumor (MPNST) of the uterine cervix***

Discussion

Primary malignant nerve sheath tumor (MPNST) of the uterine cervix is an extremely rare neoplasm. An extensive review of the literature shows only fifteen cases of MPNST at this location occurring in patients ranging in age from 22 to 73 (mean, 46) years, usually presenting with irregular bleeding. The majority of the tumors typically formed mass lesions or cervical polyps measuring from 1.2 to 8 cm (mean, 4.3 cm). Although up to 50% of MPNSTs arise in patients with neurofibromatosis type 1 (NF-1), so far no patient with MPNST of the uterine cervix has been reported to have NF-1. Nevertheless, one patient with endocervical fibroblastic MPNST had a history of unilateral acoustic schwannoma, benign nerve sheath tumor of the leg and dermatofibrosarcoma protuberans of the lumbar spine region raising a possibility of a unique manifestation of neurofibromatosis or possibly a previously undescribed syndrome.

The tumors were composed of mitotically active spindle cells, arranged in herring-bone, nodular or storiform fascicles pattern, often with alternating hypercellular and hypocellular areas. Hypocellular areas may be myxoid, fibrous or edematous. Morphological variations that have been reported include epithelioid areas in at least 2 cases and melanin pigmentation in one case. Immunohistochemically, most of them (13/15) showed S100 expression. The recently described endocervical fibroblastic MPNST shows diffuse of S100 expression in addition to CD34 expression suggesting that this tumor may be related to an anatomically restricted CD34-positive progenitor cell population.

The histological differential diagnosis includes spindle cell neoplasms such as cellular schwannoma, primary leiomyosarcoma, endocervical stromal sarcoma, and less likely rhabdomyosarcoma, Müllerian adenosarcoma, spindle cell squamous cell carcinoma, spindle cell malignant melanoma, gastrointestinal stromal tumor and monophasic synovial sarcoma. A combination of gross and microscopic findings along with immunohistochemical studies is commonly used to diagnose a case of MNPST. In the present case, there was a strong and diffuse S100 protein reactivity which contrasts with most conventional MNPST, characterized by weak and focal S100 expression.

Although meaningful follow-up information is only present in 12 of the 16 cases, MPNSTs of the uterine cervix appear to behave better than soft-tissue MPNSTs. Thus, 6 patients were alive without disease at 1-10 years follow-up, one with advanced stage disease was alive with disease at 2 months follow-up, local recurrences were documented in 5 patients, while pulmonary metastases developed in two of them.

Acknowledgments: *Slavica Veljanoska-Petreska*, Department of Gynaecological Oncology, University Clinic of Radiotherapy and Oncology, Faculty of Medicine, University Ss. Cyril and Methodius, Skopje, Republic of Macedonia

References

1. Fadare O. Uncommon sarcomas of the uterine cervix: a review of selected entities. Diagn Pathol. 2006 Sep 18;1:30.
2. Sloan D. Diagnosis of a tumor with an unusual presentation in the pelvis. Am J Obstet Gynecol. 1988;159(4):826-7.
3. Terzakis JA, Opher E, Melamed J, Santagada E, Sloan D. Pigmented melanocytic schwannoma of the uterine cervix. Ultrastruct Pathol. 1990;14(4):357-66.
4. Junge J, Horn T, Bock J. Primary malignant schwannoma of the uterine cervix. Case report. Br J Obstet Gynaecol. 1989;96(1):111-6.
5. Keel SB, Clement PB, Prat J, Young RH. Malignant schwannoma of the uterine cervix: a study of three cases. Int J Gynecol Pathol. 1998;17(3):223-30.
6. Bernstein HB, Broman JH, Apicelli A, Kredentser DC. Primary malignant schwannoma of the uterine cervix: a case report and literature review. Gynecol Oncol. 1999;74(2):288-92.
7. Lallas TA, Mehaffey PC, Lager DJ, Van Voorhis BJ, Sorosky JI. Malignant cervical schwannoma: An unusual pelvic tumor. Gynecol Oncol. 1999;72(2):238-42.
8. Di Giovannantonio L, Bellocci R, Zappacosta R, Zappacosta B, Castrataro A, Liberatore M, Liberati M, Angelucci D. Primary malignant schwannoma of the uterine cervix: a malignant tumor with unusual behavior. A case report. Pathologica. 2005;97(1):7-9.
9. Rodriguez AO, Truskinovsky AM, Kasrazadeh M, Leiserowitz GS. Case report: Malignant peripheral nerve sheath tumor of the uterine cervix treated with radical vaginal trachelectomy. Gynecol Oncol.2006;100(1):201-4.
10. Kim NR, Chung DH, Park CY, Ha SY. Malignant peripheral nerve sheath tumor of the uterine cervix expressing both S-100 protein and HMB-45. J Obstet Gynaecol Res. 2009;35(6):1136-41.
11. Mills AM, Karamchandani JR, Vogel H, Longacre TA. Endocervical fibroblastic malignant peripheral nerve sheath tumor (neurofibrosarcoma): report of a novel entity possibly related to endocervical CD34 fibrocytes. Am J Surg Pathol. 2011;35(3):404-12.
12. Akhavan A, Moghimi M, Karimi-Zarchi M, Navabii H. Malignant peripheral nerve sheet tumor of cervix. BMJ Case Rep. 2012 May 30;2012.
13. Dong A, Zuo C, Wang Y, Zhai Z, Xu M. Enhanced CT and FDG PET/CT in primary malignant peripheral nerve sheath tumor of the uterine cervix. Clin Nucl Med. 2014;39(9):825-7.
14. Dolzhikov AA, Mukhina TS. Malignant peripheral nerve sheath tumor with perineural differentiation (malignant perineurinoma) of the cervix uteri. Arkh Patol. 2014;76(2):40-2.