Müllerian-Type Gland Inclusions in Pelvic Lymph Nodes Mimicking Metastasis: A Case Report and Review of the Literature

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INTRODUCTION

The presence of exogenous cells in lymph nodes are generally diagnostic of metastasis. An exception to this rule are the benign inclusions, either glandular or nonglandular, with the glandular being more common, of a Müllerian origin (endosalpingiosis) (1–5). Endosalpingiosis-type inclusions are observed within pelvic and periaortic lymph nodes, exclusively in women, with or without concomitant disease of the female genital tract (1). Rare cases have been described in men (6). Although intranodal endosalpingiosis is a well-recognized entity, it may be confused with a metastatic carcinoma, especially in patients with known primary malignancies. It is thus important to be aware that benign intranodal inclusions may occur, and mimic metastasis. However, to our knowledge no such lesions have previously appeared in the Korean literature. This paper presents a case of endosalpingiosis in the pelvic lymph nodes of a 50-year-old woman, with a review of the relevant literature.

CASE REPORT

A 50-year-old woman was admitted, with a known endometrial carcinoma, to the department of Gynecologic Oncology Service at our hospital. One month prior to her admission, she was diagnosed as having an endometrial adenocarcinoma on an endometrial curettage at another institution. There was no other significant past medical or surgical histories. The general examination was unremarkable. Following a preoperative MRI of the pelvis, which demonstrated an ill-defined hypointense mass at the endocervical canal, possibly representing cervical involvement of an endometrial malignancy, the patient under-
went a hysterectomy and selective bilateral pelvic and periaortic lymphadenectomies.

Histologically, multiple sections of the uterus revealed extensive adenomyosis, with no residual tumor. Both ovaries showed no malignancy, but exhibited endosalpingiosis. Most of the regional lymph nodes showed reactive changes, but with no metastatic tumor, with the exception of the left external, and common, iliac lymph nodes, where glandular structures were found. These glands were distributed at the periphery of the lymph nodes, and were lined by a single layer of cuboidal to columnar endosalpingiotoxic epithelium (Fig. 1). Ciliated cells were occasionally present. The nuclei were regular, basally oriented or pseudostratified, and large, round to oval, with occasional small nucleoli (Fig. 2). Mitoses were absent. There was no evidence of inflammatory, or fibrous, reactions or endometrial-type stroma, around the inclusions.

The patient tolerated the procedure well, made an uncomplicated postoperative recovery, and was discharged on the seventh postoperative day.

**DISCUSSION**

Intranodal inclusions of exogenous cells generally give rise to a strong possibility of metastasis. However, benign inclusions may occur, and should not be mistaken for metastasis at the time of primary staging and diagnosis, or at a second-look exploration. The included structures may be either glandular or nonglandular.

Several types of epithelial differentiation have been described: squamous, renal tubular, colonic and Müllerian. The Müllerian-type of inclusions are much more common, ranging from 5 to 41%, based on lymph nodes sampled in women (1). The glands are lined by an admixture of ciliated, secretory and intercalated cells, with (endometriosis) or without (endosalpingiosis) associated stroma (7). These inclusions may cause a diagnostic problem, with regard to whether they are benign and incidental, or if they are related to the tumor metastasis in patients with gynecological malignancies (8). The increased frequency of these lymph node inclusions, sampled for primary ovarian malignancies, suggested they were more likely the bland-appearing forms of metastatic tumor (9). However, much of the recent literature considers these inclusions as benign, incidental lesions. Features favoring benignity include: a capsular or interfollicular location of the glands, different types of lining cells, including ciliated forms, a lack of significant cellular atypia and mitoses, periglandular basement membranes and the absence of stromal desmoplasia (1,7).

The histogenesis of Müllerian inclusions is unclear. Although, metaplasia of the embryonic rests of the coelomic epithelium is the most widely accepted mechanism (1,3,4). Other theories have been postulated, including peritoneal implantation of sloughed tubal epithelium, lymphatic dissemination of tubal mucosa and surgical implantation (10–12). However, it is our belief that surgical implantation is the least likely, because intranodal inclusions are often seen in patients with no previous surgical history.

Malignancies found within the intranodal glandular inclusions have been reported (13–15). There was a well-documented case of an ovarian, serous borderline tumor, with pelvic lymph nodes, showing an admixture of benign endosalpingeal gland inclusions and neoplastic tissue, which were identical to the ovarian tumor (13). Whether the neoplastic epithelium found in the lymph nodes represented true metastasis, or a synchronous malignant transformation of the metastatic Müllerian epithelium, is uncertain. If it was a true metastasis, occult microinvasion should be considered as a possible source of the metastasis. In their case, however, there was a lack of stromal microinvasion, or destructive invasion, in the multiple sections from the ovaries. This, along with the juxtaposition of the benign endosalpingeal epithelium to the neoplastic serous epithelium, strongly suggested the possibility of the synchronous development of a primary serous borderline tumor from a preexisting endosalpingiosis of the lymph nodes. This was supported by other investigators, who described, not only transitional forms from endosalpingiosis to evolution of papillary serous borderline tumor in lymph nodes (14), but also a papillary serous cystadenocarcinoma, arising in inclusion cysts in pelvic and inguinal lymph nodes, with no other synchronous tumor identified (15). Due to the small number of such cases in the literature, and a lack of follow-up data, the mode of nodal spread, the role of Müllerian inclusions, as an independent source for tumor development, and their prognosis, remain to be determined.

The much less common nonglandular (nonepithelial) inclusions that have been described were nevus cells, mesothelial
cells, decidual and leiomyomatosis (1). Nevus cells are observed in cervicoaxillary lymph nodes, but rarely in inguinal lymph nodes, whereas mesothelial inclusions most commonly involve the mediastinal lymph nodes, followed by abdominal lymph nodes. In most intranodal mesothelial inclusion cases, there is hyperplasia, with inflammation of the associated serosal membranes, thus, its distinction from mesothelioma may be difficult. Benign inclusions, however, consists of cytologically bland-looking cells, not impinging on the nodal structure. The mesothelial cells found in the lymph nodes are thought to be transported to the draining lymph nodes through the lymphatic system, which may be facilitated by the inflammatory process.

This is the first case reported in the Korean literature of benign, Milllerian-type, glandular inclusions in the pelvic lymph nodes of a patient with an endometrial adenocarcinoma. Awareness of these inclusions is essential, in that they simulate metastatic adenocarcinomas, potentially resulting in unnecessary therapy, or in the decision to withhold therapy. Furthermore, pelvic and aortic lymphadenectomies may be warranted for these lesions, since neoplastic transformation of preexisting, metaplastic, tubal-type epithelium is strongly suggested.

REFERENCES