Blue nevus of the uterine cervix – a melanocytic lesion corresponding to cutaneous blue nevi

Blue nevi are benign melanocytic disorders, which commonly present cutaneous lesions and rarely arise in female genital tracts. To date, although several cases of endocervical blue nevi have been reported, their biological nature is not sufficiently clarified. The origin of melanin-loaded cells of the uterine cervical tumor has been suggested to differ from that of cutaneous tumors. Differences in reported immunohistochemical characteristics between the uterine cervical tumor and the cutaneous tumor might have exacerbated this controversy. Our present case report has become a final answer to the controversy.

A 58-year-old Japanese woman who complained of body weight loss (-4.7 kg/year) was referred to our hospital. The patient had no medical history of abnormal genital tract bleeding but a gynecological examination was performed as a part of a systemic examination. In addition to multiple uterine myomas (up to 4 cm in diameter) detected by transvaginal ultrasonography, a small endocervical polyp (5 mm in length) was found and excised promptly. Although the macroscopic observation by the gynecologist revealed no remarkable findings, examination of the histological specimen showed many pigmented spindle-shaped cells distributed in the stromal portion of the polyp (Fig. 1). Histochemical special stains verified that the intracellular pigments were melanin granules (not shown). Immunohistochemical analyses using red chromogen (Bond Polymer Refine Red Detection, Leica Biosystems, Nussloch, Germany) further revealed that the cells were positive for S100 protein, SOX10, HMB45, and MART-1 (Fig. 2). Based on the characteristic cellular morphology and immunohistochemical findings, the lesion was diagnosed as being a
blue nevus, and malignant melanoma was denied. Despite detailed medical examinations, the cause of the body weight loss was not identified.

In clinical settings, the most crucial point is to distinguish blue nevi from their malignant counterpart, desmoplastic melanoma, which can develop as a primary uterine cervical tumor. Their characteristic morphology, spindle-shape or dendritic contours and dark brown cytoplasmic pigments, serve as reliable diagnostic hallmarks. In addition, immunohistochemical findings are quite useful for the differential diagnosis. Whereas blue nevi are positive for most of the representative melanocytic markers including S100 protein, HMB45 and MART-1, desmoplastic melanomas are negative for the latter two markers. We could diagnose the present lesion as a benign blue nevus through prudent interpretation of the histological, histochemical and immunohistochemical findings, which were in agreement with descriptions in a dermatopathology textbook and most previous pathologic case reports. Surprisingly, however, the immunohistochemical features described in latest edition of a gynecopathology textbook were different from our findings and previous reports; that is, this textbook stated that endocervical blue nevi are usually negative for HMB45 and MART-1. If it is true, pathologists cannot differentiate immunohistochemically endocervical blue nevi from desmoplastic melanomas. Only two reports documented that endocervical blue nevi were negative for HMB45, but there was no report that the endocervical tumors were negative for MART-1.

Fig. 2. Immunohistochemical findings. Positive results are indicated by red color. (A) S100 protein (Dako A/S, Glostrup, Denmark). (B) SOX10 (Cell Marque Corp., Rocklin, CA). (C) HMB45 (Dako). (D) MART-1 (Nichirei Bioscience Inc, Tokyo, Japan). Melanin-loaded cells (cytoplasm or nuclei) are positive for all of those melanocyte markers. [Bond Polymer Refine Red Detection; original magnifications x150 (A,C,D) and x300 (B)]
We concluded that endocervical blue nevi are usually positive for S100 protein, SOX10, HMB45 and MART-1 and these immunohistochemical characteristics were useful for distinguishing the benign tumors from desmoplastic melanomas.

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