

# Blue Nevus of the Cervix, an Unusual Lesion – A Case Report

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## Abstract

Blue nevus is a cutaneous melanocytic lesion characterized by the proliferation of dermal dendritic melanocytes. In addition, blue nevus also has been rarely reported in various extracutaneous sites which are usually devoid of melanocytes such as oral mucosa, lymph nodes, maxillary sinus, pulmonary hilus, orbit, conjunctiva, meninges, vagina, prostate, spermatic cord, and cervix. It is suggested that these lesions may originate from either Schwann cells of the stromal nerves or from melanocytic precursors migrated from neural crest. Herein, we present a rare case of blue nevus both in the uterine cervical stroma and in the cervical polyp. Only about 100 cases have been reported so far. **Key words:** Blue nevus, cervical blue nevus, cervical polyp, melanocytes, Schwann cells.

## Introduction

Blue nevus is a well known cutaneous melanocytic lesion characterized by the proliferation of dermal dendritic melanocytes.<sup>1</sup> Rarely it has also been described in such extracutaneous sites as oral mucosa, lymph nodes, maxillary sinus, pulmonary hilus, orbit, conjunctiva, meninges, vagina, prostate, spermatic cord, and cervix.<sup>2</sup>

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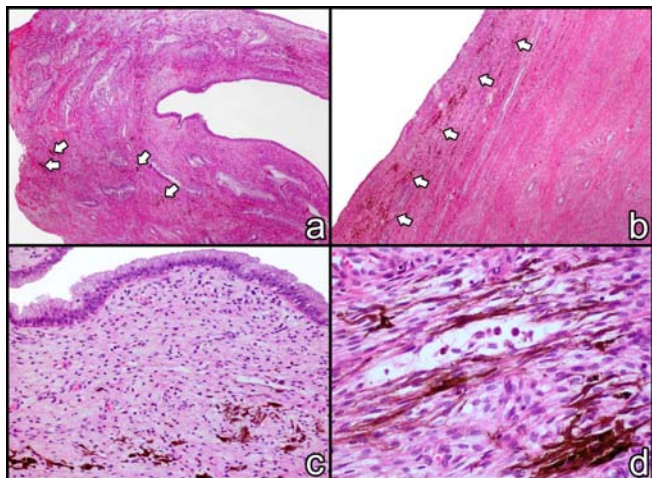
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cervix.<sup>2</sup> It is suggested that these lesions may originate either from Schwann cells of the stromal nerves or melanocytic precursors migrated from neural crest.<sup>2-6</sup> We here present a case of blue nevus both in the cervical stroma and in the endocervical polyp followed by brief discussion about its pathogenesis.

## Case Presentation

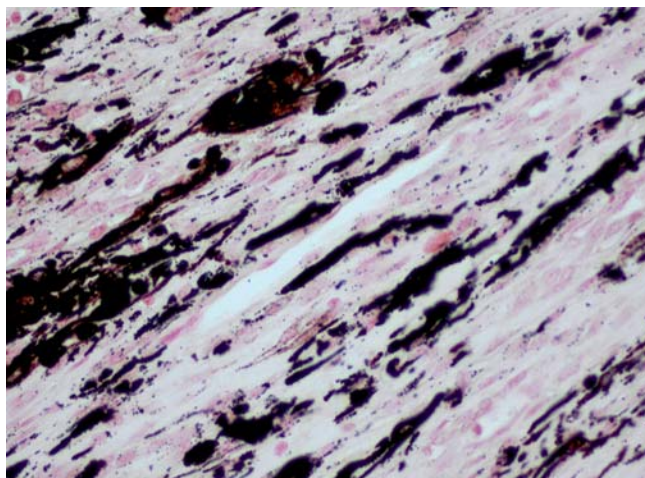
A 52-year-old woman underwent total abdominal hysterectomy and bilateral salpingoophorectomy for menometrorrhagia due to multiple leiomyomas. During macroscopic examination multiple intramural and subserosal leiomyomas were detected with diameters ranging from 0.5 cm to 10.3 cm. A 0.7x0.3x0.1 cm polypoid lesion was noted in the endocervical canal. Microscopy revealed multiple small groups of dark-brown pigmented and spindle-shaped cells in the stroma that had dendritic and bipolar cytoplasmic processes (Figure 1a). These cells had uniform, bland, round- to oval- shaped nuclei that were oriented parallel to

the surface epithelium (Figure 1a-c). These cells were also present in the cervical stroma adjacent to the endocervical polyp (Figure 1b-c). There was no pigmentation in the endocervical epithelium or proliferation of basal melanocytes. This pigmented lesion was not appreciated on initial macroscopic examination and the specimen was reexamined. In the endocervical canal multiple brownish dot-like lesions ranging from 0.2 cm to 0.4 cm in diameter were noted to comprise an area about 2 cm in diameter totally. Cervix uteri was entirely sampled and evaluated microscopically. No additional findings or malignancy was detected.



**Figure 1:** Small groups of dark-brown pigmented cells (arrows) in the stroma of the cervical polyp (H&E x40) (a), and adjacent endocervical stroma (H&E x40, H&E x200, respectively) (b-c). Higher magnification of the spindle-shaped cells containing brown pigment with dendritic and bipolar cytoplasmic processes (H&E x400) (d).

Histochemically, the pigment was positive for Masson-Fontana (Figure 2) and negative for Prussian blue. Then, the lesion was diagnosed as blue nevus.



**Figure 2:** Masson Fontana positivity of the pigment showing melanin (x400).

## Discussion

Blue nevus of the endocervix was initially defined in 1959.<sup>7,8</sup> It is an extremely rare lesion and so far only about 100 cases have been reported in the world.<sup>7,9</sup> Patel and Bhagavan reported 3 cases of blue nevus in 2500 hysterectomy specimens (1, 6). Uehara et al. demonstrated that serial sections could increase the incidence of it (10). Similar to our case, cervical blue nevus is usually incidentally detected in cases operated for leiomyomas, dysfunctional uterine bleeding and adenomyosis, etc.

In general, they are blue-gray colored macular lesions about 0.1-0.4 cm in diameter. Thus, these lesions are often missed during macroscopic examination. They are localised most frequently in the posterior wall of the endocervix.<sup>2, 6, 7</sup> They may sometimes occur in endocervical polyps and may be multiple as in our case.<sup>11, 12</sup>

The differential diagnosis of blue nevus of the cervix includes cervical endometriosis, hemangioma, focal hemosiderin deposits particularly during colposcopic and macroscopic examinations. Also, pigmented lesions such as melanosis, lentiginous melanocytic lesions, cellular blue nevus, and malignant melanoma are considered histopathologically in the differential diagnosis of cervical blue nevus.<sup>3,7</sup>

Histopathologically, blue nevus is usually confined to the stroma of the cervix. The histologic features are similar to the common blue nevus of the skin. Microscopically, melanophages and irregular clusters of slender, elongated, wavy and dendritic-shaped cells containing melanin are observed in the superficial subepithelial stroma of the endocervix. These cells are usually located parallel to the surface epithelium.<sup>7</sup> Cytological atypia or high mitotic activity are absent. Histochemically, the cells of the blue nevus are positive for Masson-Fontana that demonstrates melanin pigment. Our case was positive for Masson-Fontana. Immunohistochemically Melan-A, S-100 and HMB-45 are used to show the melanocytic origin. However, it should be noted that there are some cases of endocervical blue nevus reported in the literature that showed negativity for HMB-45.<sup>2</sup> HMB-45 is suggested to show positivity in immature melanosomes in the literature.<sup>2</sup> Thus, the presence of mature melanosomes more than immature melanosomes in the blue nevus may provide an explanation to the negativity for HMB-45.<sup>2</sup>

Endometriosis of the cervix is usually red or red-blue colored lesion as a macule or a plaque that ranges from 0.2 to 2 cm in diameter. In our case, absence of endometrial stroma or glandular structure ruled out endometriosis microscopically.<sup>2</sup> Although the presence of brown pigment in the stroma may cause difficulties, focal deposition of obstetric or surgical trauma-induced hemosiderin pigment is more coarse and more refractile than the melanin pigment histopathologically. Besides, hemosiderin pigment is positive for Prussian blue histochemically.<sup>6</sup>

Melanosis of the cervix is a rare lesion that is usually associated with previous cervical trauma. It is characterized by hyperpigmentation of the basal epithelium with or without accompanying basal melanocytes histopathologically. Acan-

thosis and hyperkeratosis are often detected. In the present case melanosis was excluded by the absence of the hyperpigmentation of the epithelium.

Lentiginous melanocytic lesions arise extremely rare in the cervix that are characterized by proliferation of basal melanocytes. Benign lentigo has been reported in the cervix, however pure malignant lentigo has not been reported in the cervix up to date. In the present case the absence of the proliferation of basal melanocytes excluded the lentiginous melanocytic lesions.

Cellular blue nevus occurs rarely in the female genital tract.<sup>7, 13</sup> To the best of our knowledge there were only 2 cases of cellular blue nevi arose in myometrium and only one case that involved in the hymeneal ring, vagina and also cervix.<sup>1,2,13</sup> Cellular blue nevus is characterized by excessive proliferation of dendritic melanocytes.<sup>2,14</sup> In contrast, the dendritic melanocytes are not outstanding in common blue nevus similar to our case.

Primary malignant melanoma of the cervix is a very rare entity. To the best of our knowledge only 81 cases have been reported in the literature since 1889.<sup>15,16</sup> Malignant melanoma usually shows some features that indicate malignancy including nuclear hyperchromasia, irregular nuclear membrane, large eosinophilic nuclei, and numerous mitoses.<sup>3</sup> The present case did not demonstrate any signs of malignancy. However, the diagnosis of malignant melanoma may sometimes be difficult and may be missed when the histologic signs of malignancy are not obvious.<sup>3</sup> Lack of radial growth in small biopsies or primary/metastatic nodular malignant melanoma may cause missing of the malignancy.<sup>3,17</sup> The absence of an intraepithelial component has been reported in 14 of 43 primary malignant melanomas of the cervix that may cause underdiagnosis.<sup>18</sup> Atypical epithelioid melanocytes, at least focally, mitotic figures, and an inflammatory reaction at

the periphery should be noted as the clues to malignancy diagnosis.

Melanoma associated blue nevus and a coexistence of common blue nevus of the cervix with a vaginal malignant melanoma have been reported in the literature.<sup>3,6,19,20</sup> Although, it has not been proved precisely whether the common blue nevus of the cervix is a precursor lesion of malignant melanoma or not in the literature, extensive endocervical sampling should be performed in order to rule out malignant melanoma. In addition, screening of genital system for possible malignant melanoma should be carried out clinically. In the present case, uterine cervix was entirely sampled and evaluated after the detection of pigmented lesion in the initial samples. Then, malignant melanoma was excluded histopathologically.

The origin of blue nevus of the Mullerian tract is still debated. In the literature, there are two theories about the origin of it. One of those theories is that it may arise from melanocytic precursors migrated aberrantly during embryogenesis towards epithelium that does not usually involve melanocytes. As a support of this hypothesis, Uehara et al. detected microscopic foci (less than 1mm) of scattered stromal melanocytes by performing serial sections in 28% of 189 benign hysterectomy specimens and termed it "stromal melanocytic foci".<sup>2,9</sup> The other theory is that blue nevi may be originated from melanogenically transformed Schwann cells of stromal nerves. This hypothesis has been supported by some ultrastructural studies showing some Schwannian features.<sup>2,6,21</sup>

In summary, it should be noted that blue nevus may rarely arise in various extracutaneous sites. Herein, we have reported an endocervical blue nevus also involving the stroma of endocervical polyp. Blue nevus of the endocervix is a rare incidental lesion and the origin of it is still controversial. It is noteworthy that the differential diag-

nosis with other pigmented lesions, particularly with malignant melanoma, is crucial.

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