Single-organ vasculitis of the cervix accompanying human papillomavirus infection

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Abstract: Single-organ vasculitis (SOV) has rarely been reported to involve the female genital tract but mostly the uterine cervix. A 39-year-old woman was diagnosed to have a high-grade cervical intraepithelial lesion and was treated by large loop excision of the transformation zone. Histopathological evaluation of the excised specimen confirmed the diagnosis of cervical intraepithelial neoplasia grade III accompanied by human papillomavirus infection. The excised second specimen showed the evidence of vasculitis of medium-sized vessels of the cervix, which is a quite rare form of SOV. It seems to be important to be aware of the localized form of polyarteritis nodosa limited to the female genital tract to prevent unnecessary immunosuppressive therapies.

Keywords: cervical intraepithelial neoplasia, single-organ vasculitis, human papillomavirus, polyarteritis nodosa, uterine cervix

Introduction

Single-organ vasculitis (SOV), previously entitled as “limited/localized/isolated,” is a form of vasculitis restricted to a single organ or organ system [1]. This form of vasculitis has rarely been reported to involve the female genital tract but mostly the uterine cervix, which might present histopathologically similar lesions with polyarteritis nodosa (PAN), giant cell arteritis, or Wegener granulomatosis [2]. Here, we present a case of asymptomatic SOV of the uterine cervix with PAN-like lesions, in the presence of cervical intraepithelial neoplasia grade III (CIN 3) and accompanying human papillomavirus (HPV) infection, in view of the previous literature.

Case Report

A 39-year-old, G2P2, woman was admitted to the university outpatient department with the complaints of pelvic pain and intermittent vaginal bleeding. She had chronic renal failure for several years due to familial Mediterranean fever. Her gynecological examination was routine, but cervical smear was reported as low-grade squamous intraepithelial lesion. Colposcopy was performed and histopathological evaluation of the directed punch biopsy and endocervical curettage showed the evidence of CIN 3. She was treated by large loop excision of the transformation zone (LLETZ). Histopathological evaluation of the LLETZ specimen confirmed the diagnosis. In addition, HPV positivity was reported, revealed by immunohistochemical evaluation and endocervical glandular invasion. Since the surgical margins of the specimen were reported to be positive for the lesion (CIN 3), a second cone excision was performed for about 1 month after the first intervention. The second specimen was free of cervical intraepithelial neoplasia, but transmural inflammation and fibrinoid necrosis of medium-sized or small arteries (Figs 1 and 2) and necrotizing vasculitis compatible with PAN were reported. The patient was referred to the relevant departments to rule out the presence of systemic vasculitis. Complementary laboratory tests, including antinuclear antibodies (ANA), rheumatoid factor (RF), Venereal Disease Research...
Laboratory (VDRL) test, hepatitis B surface antigen (HBsAg), hepatitis C virus antibodies, cryoglobulins, perinuclear and cytoplasmic antineutrophil cytoplasmic antibodies (ANCA), and HIV, were all negative. No further treatment was planned and the patient was discharged uneventfully. No systemic manifestations were noted during a follow-up of 24 months.

Discussion

PAN is a medium-vessel vasculitis, mainly classified as systemic (classical) or SOV [3, 4], which can involve single or multiple foci [5]. The SOV form is usually an incidental finding and there are a few reports in the literature concerning the limited form of vasculitis in the female genital tract. A 23-year retrospective survey concluding about gynecological vasculitis in surgical samples of hysterectomies or cervical amputations reported the incidence of vasculitis of the female genital tract as 0.04% (46/120,000 cases) [6]. Cervix was the most frequently involved part of the female genital tract, since 30 out of 46 lesions were found in cervical specimens. The authors proposed that inflammation or precancerous lesions might be the precipitating factors for progression of SOV.

Infectious agents including viruses (parvovirus B19, cytomegalovirus, varicella-zoster, hepatitis B virus, and Epstein–Barr virus) have been associated with different vasculitis such as giant cell arteritis, PAN, Kawasaki’s disease, Henoch–Schonlein purpura, and Behcet’s disease.
disease. The correlation between infectious agents and vasculitis has been proposed to be by two mechanisms either by direct infection of vascular wall or by indirect immunologic pathways such as hypersensitivity reactions [7]. Comorbidity of HPV infection in cases with cervical SOV has been reported previously [5]. Herein, the case we report also has premalignant cervical lesion accompanied by HPV infection with the incidental diagnosis of SOV. The possible underlying mechanisms of comorbidity infection and vasculitis might be just high prevalence of HPV infection in the female genital tract or an unknown causality between immunological pathways induced by the virus, which needs to be clarified. However, since this form is quite rare, an etiological relationship has not been revealed yet. In addition, since inflammation has been suggested to be one of the possible precipitating factors for SOV, the inflammation induced by surgical intervention might be another explanation for the vasculitis. However, the exposure interval and degree of inflammation that result with vasculitis should also be elucidated with further research.

The histopathological findings of systemic and localized types of vasculitis are indistinguishable. However, even when the systemic disease affects only one organ, abnormalities in other systems or laboratory parameters are expected [5]. Since PAN is a potentially life-threatening disease, it is mandatory to evaluate such patients with SOV of female genital organs for systemic involvement [2] and a 6-month follow-up period with no progression to systemic disease has been suggested as a cutoff to clarify whether the disease is local or systemic [8]. A retrospective report [4] comparing the characteristics of patients with classical or limited PAN denoted that the SOV group were mostly young females with more relapses compared to classical PAN. However, none of the cases with SOV progressed to generalized disease possibly due to different pathogenesis of two forms [4]. A literature review from Hoppé et al. [9] also reported that among 118 cases diagnosed to have SOV of the cervix, 99.1% did not progress to systemic disease and excision of the lesion seemed to be curative. The presented case also did not reveal the involvement of other organs and was free of disease in the 2-year follow-up period.

In conclusion, the presented case supports the previous reports about SOV of the uterine cervix, which conclude PAN-like SOV as a limited lesion rather than a part of a systemic vasculitis. Although there is not enough evidence to confirm whether there is a correlation between HPV infection of the cervix and SOV of the uterine cervix, this deserves to be clarified with further research.

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