Journal of Surgical Dermatology

doi: 10.18282/jsd.v7.i2.190

REVIEW ARTICLE

Value of auxiliary examination in diagnosis and treatment of condyloma acuminatum

Xiaojing Zhou, Zhou Chen, Wenhai Li*, Jianzhong Zhang

Department of Dermatology, Peking University People's Hospital, Beijing 100044, China

***Abstract*:** Condyloma acuminatum (CA) is a common sexually transmitted disease caused by human papillomavirus (HPV) infection, with the characteristics of strong infectivity, long incubation period and easy recurrence. Long-term infection with HPV, especially high-risk types, can also lead to tumorigenesis. Therefore, early detection and appro-priate intervention is important. This article summarizes the common clinical auxiliary examination methods of CA, and introduces the principle, operation mode, manifestations, advantages, disadvantages, and indications of each method, aiming to provide theoretical basis for clinicians to adopt these methods reasonably to diagnose and treat CA in practice.

Keywords: condyloma acuminatum; HPV infection; auxiliary examination; clinical application

*Correspondence to: Wenhai Li, Department of Dermatology, Peking University People's Hospital, Beijing 100044, China; lwh8lwh@sina.com

Received: 4th February 2023; **Accepted:** 19th March 2023; **Published Online:** 27th March 2023

Condyloma Acuminatum (CA) is a common sexually transmitted disease caused by human papillomavirus (HPV) infection, mainly with verrucous proliferative changes in skin and mucosa. It has the characteristics of strong infectivity, long incubation period and easy recurrence[1]. Clinical HPV infection consists of clinical infection (CA), subclinical human papillomavirus infection (SPI) and latent human papillomavirus infection (LPI)[2]. CA refers to HPV infections that are visible to the naked eye as a verrucous rash in the skin and mucous membrane and can be diagnosed by visual inspection or auxiliary examination, while SPI refers to microscopic HPV infections that are difficult to be detected with naked eyes and it requires ancillary tests such as the vitriol test, endoscopy and dermoscopy to detect the lesion when histopathological changes are present. LPI refers to HPV status that does not cause any clinical or histological changes and can only be detected by molecular biological methods.

All persons infected with HPV are infectious, including the vast majority of SPI and LPI[3], the latter being in the early stages of HPV infection and highly contagious. At the same time, due to the absence of a rash, it is often overlooked, becoming the main source of infection, which is the main reason for the recurrence of CA[2,3]. Although CA is a benign lesion, precancerous lesions (vulvar, anal and penile intraepithelial neoplastic lesions) or malignant lesions can coexist or develop within the wart[4,5]. HPV infection in pregnant women may lead to adverse pregnancy outcomes such as premature birth, premature rupture of membranes and intrauterine growth restriction[6]. Mothers infected with HPV can also transmit the virus to their newborns through the placenta, delivery, breastfeeding and close contact, leading to CA and laryngeal papilloma in newborns. It is therefore important to detect HPV infection early and intervene appropriately.

Of the more than 200 HPV species identified today, approximately 30–40 can infect the genital tract[7]. While more than 95% of CA is caused by HPV 6 and 11, high-

risk types, including HPV 16 and 18, are also present in CA lesions[4], and the latter is strongly associated with cervical cancer[8,9]. In addition, the regression of CA is closely related to HPV subtypes[10]. It is therefore also important to identify the type of HPV infection.

It is not difficult to diagnose and differentially diagnose typical CA through history and visualization of the lesions. However, the diagnosis, efficacy and recurrence of atypical CA lesions are difficult to determine visually and require the use of appropriate ancillary tests. Current ancillary tests for CA include acetowhitening test, ALA-PDD, dermascopy, endoscopy, cytology and histopathology, in situ hybridization, immunoblotting and polymerase chain reaction.

Acetowhitening test

Principle: abnormal keratin is produced by genital mucosal cells infected with HPV, and coagulated to whiten after encountering glacial acetic acid, while normal keratin does not react with glacial acetic acid.

Operation: after removing local secretions, apply a freshly prepared 3%–5% acetic acid solution to the lesion to be examined and to the surrounding skin mucosa, and observe it after 3–5 minutes.

Manifestations: uniform and consistent white changes with clear borders were appeared at the site of HPV infection and were positive. For SPI, it became white under vinegar white[3] and the lesions can be classified as the following three categories with the help of a magnifying glass[10]: (1) microscopic warts without a tip; (2) tiny papillary elevations; (3) ring-like lesions with a normal appearance.

Advantages: useful in the diagnosis of clinically suspected CA and SPI and can show the extent of the infection[11]; simple to perform, economical and easy to obtain reagents, easy to disseminate.

Disadvantages: poor specificity. False positives can occur in the presence of localized chronic inflammatory conditions such as *Candida* infection, genital trauma, epidermal keratosis, precancerous lesions or non-specific inflammatory conditions[12,13]. A small proportion of the more typical clinically positive CA and HPV test lesions are negative for acetowhitening test[13], which may be related to the type of wart and the degree of local moistness of the lesion[14]. It cannot be used for the evaluation of cavernous lesions such as those in the urinary tract and anus, and is unable to detect LPI. It is highly subjective.

Indications: primary screening for suspected HPV infected lesions, not as a confirmatory test[4,11]. It may indicate the extent of treatment and may be used for follow-up.

5-aminolevulinic acid-photodynamic diagnosis

Principle: after administration of large amounts of exogenous 5-aminolevulinic acid (ALA), tumor cells or proliferating cells (including HPV-infected cells) preferentially and selectively take up ALA, which undergoes a series of enzymatic reactions to produce a large amount of protoporphyrin IX (PpIX) in the mitochondria and accumulates in the diseased cells[3,15]. PpIX emits a brick-red fluorescence under UV light at a wavelength of around 410 nm, which can be used to identify the site of HPV infection and to screen for SPI and LPI[3,16,17]. The intensity of the fluorescence is thought to correlate with the time of application, with the optimal time being 2 h[3,17].

Operation: clean the area to be tested with saline, apply freshly prepared 20% ALA solution/gel/cream to the lesion and the surrounding skin/mucosa within 2 cm, seal the area from light for 2 h and then irradiate with a Wood lamp or LED lamp of the appropriate wavelength in a dark room.

Manifestations: clearly demarcated brick red fluorescence under the Wood lamp was positive[3,16].

Advantages: non-invasive test with good reproducibility; high sensitivity, displaying not only SPI but also LPI[3]. ALA is relatively highly selective and specific, thus allowing better localization and diagnosis of the site of HPV infection.

Disadvantages: the use of this method is limited in women with vulvar mucosa, urethral mucosa and areas of significant inflammation, as mucous membranes, local inflammation and maceration (due to increased ALA uptake and PpIX production as a result of skin mucosal disruption) can show faint brick-red fluorescence with poorly defined boundaries, leading to false positives. There have also been reports of HPV positivity but negative fluorescence in the lesion area[3,17]. It is costly, time-consuming and cumbersome and requires a light-free environment.

Indications: aiding in the diagnosis of suspected CA, SPI and LPI in the drier areas of the vulva; showing the location and extent of lesions and guiding treatment; used for follow-up, especially for patients undergoing ALA-PDT treatment.

Dermascopy

Principle: the dermascopy magnifies the viewing area and eliminates the effect of reflected light on naked eyes,

doi:10.18282/jsd.v7.i2.190

allowing the observation of fine morphological structures not visible to naked eyes, such as the lower epidermis, superficial dermal junction and dermal papillae, effectively aiding the clinician in diagnosis[18]. The magnification of the dermascopy ranges from ×6 to × 50, with ×10 being the most common (sub-microscopic structures such as pigment networks and capillary loops that cannot be seen with the naked eye can be identified with 10 times magnification). The techniques used to eliminate reflected light from the surface can be divided into classical dermascopy, which uses liquids with different refractive indices to moisten the skin surface, and polarized light microscopy, which uses the principle of cross-polarized light to eliminate reflected light without the need for liquid moistening or even contact with the skin[19]. The classical dermascopy requires contact with the skin, which can cause compression of the lesion and affect the observation judgement. The polarized light dermascopy avoids this problem and also avoids cross-contamination due to direct contact with the skin when performing examinations for infectious diseases such as CA[20].

Operation: aim the dermascopy lens at the rash to be examined, adjust the light source and magnification and observe the image when it is clear (in the case of the classical dermascopy, surface infiltration is required on request).

Manifestations: CA appears microscopically as pink, dark red or milky white papillae or flat protrusions[20], which are characterized by a combination of morphological and vascular features. The morphological patterns of the lesions are non-specific, mosaic, globular and finger-like. The lesions tend to show a mixed pattern, with the finger-like and globular patterns being the most common[21]. Vascular features include glomerular, punctate, arcuate, dendritic, circumferential, hairpin-like and polymorphic vessels[18,21]. CA lesions are often rich in vascular components and may be associated with multiple vascular patterns[18], although some lesions are not vascular[21]. It has been suggested that the morphological pattern and vascular characteristics of dermoscopic lesions reflect the different periods of genital warts[22]: flat lesions tend to have a mosaic pattern, while elevated lesions tend to show a globular and finger-like pattern. Hairpin-like vessels are more often seen in finger-like lesions, glomeruloid/dotted vessels are more often seen in globular and mosaic lesions, and vessels are often absent in non-specific patterns[21].

Advantages: the dermascopy can improve the sensitivity and accuracy of diagnosis without compromising diagnostic specificity[18]. The dermascopy has a polarized light, which makes wart morphology and vascular structures clearer when magnified by the dermascopy, helping to identify warts that are not easily identified by naked eyes and improving diagnostic yield[20]. It can provide efficient and accurate evidence in differential diagnosis[18,23], thus reducing unnecessary biopsies. It can serve as a dynamic observation and assessment of efficacy in the follow-up of treatment[23]. Compared to pathological biopsy, it is non-invasive, simple, time-consuming and economical, while CA patients can visualize their condition from the report and have better patient compliance[18]. As a non-invasive diagnostic modality, a dermascopy is not only reproducible, rapid, simple to perform, highly sensitive, specific and accurate, but also can reduce patient anxiety and misdiagnosis leading to over-treatment and injury, pain and expense. It has, therefore, high clinical application value and is worth promoting[23].

Disadvantages: the vascular morphology of CA is less specific under the dermascopy, that the diagnosis of CA through the dermascopy requires observing both morphological and vascular features combining with the medical history[20]. The lesions deep in the lumen cannot be directly observed[18]. It can be influenced by somewhat subjective factors[18,24]. It is less specific than pathological examination.

Indications: diagnosis and differential diagnosis of small warts, atypical warts and SPI that cannot be well determined by naked eyes[20,23,25]; defining the boundaries of warts to determine the extent of treatment[24]; determining the efficacy of treatment[18,24]; the dermascopy can be used for follow-up and routine investigations, photographing and recording the lesions to facilitate comparison of the efficacy of treatment before and after treatment, as well as to facilitate communication and learning between doctors[18,25].

Endoscope: Colposcopy, colorectal colonoscopy, urethroscopy

Principle: the endoscope is an optical inspection instrument consisting of a cold light source lens, light source illumination, fiber optic lead, image transmission system, screen display system, etc. It allows access to the natural cavities of the body and can magnify images. For CA in the cavity (e.g. vaginal, urethral and rectal mucosa), the scope and morphology of the CA in the cavity can be directly displayed with the aid of the endoscope. The optical fibers of some endoscopes can deliver laser beams to cauterize superfluous organisms or tumors and close bleeding vessels, which is of great clinical value for diagnosis, guidance of treatment and follow-up.

doi:10.18282/jsd.v7.i2.190

Among the endoscopes, colposcopy is used to visualize the vaginal mucosa and cervical epithelium, urethrocystoscope is used for the treatment of urethral CA, and colorectal colonoscopy is used to visualize lesions in the anus and rectum.

Operation: insert the endoscope inserted into the cavity to observe the morphology and extent of the rash; adjust the light source, magnification and focal length so that the lesion is clearly visible on the screen; carry out biopsies when the lesion is identified and take photographic images when suspicious lesions are found. This must be done in the appropriate department.

Manifestations: typically similar to structures seen under naked eyes, single or multiple redundant growths of varying sizes, locally elevated or diffuse, moist and soft in the form of papillae, cauliflower and coronas, mostly with a tip at the root, pale red, flesh-colored or pink, brittle and easily bleeding[5,26,27]. For SPI, it presents positive response with clear borders by vinegar-white test, and there are burr-like or pinpoint protrusions on the surface, and characteristic vascular collaterals with fine punctate vessels[27,28].

Advantages: the endoscopic procedure is relatively simple, quick, less invasive and repeatable. The endoscope is connected to an electronic display device, which allows visualization of the rash in the cavity. The rash can be magnified to reveal lesions that cannot be seen with naked eyes, allowing a more accurate determination of the type and extent of the rash. Combined with the vinegar-white test, which shows the intravaginal and cervical SPI, the colposcope can be used to further improve the diagnostic accuracy of colposcopy based on the change in the pattern of vinegar-white response over time at the site of the lesion, combined with a digital calculation system[12]. A clear endoscopic view allows for guided biopsies and treatments (e.g. colposcopy combined with LEEP knife[29], endourethral electrodesection/radiography/medical local irrigation[30]), avoiding the blindness of traditional multi-point biopsies and treatments and improving detection and cure rates. The lesion can be photographed and documented.

Disadvantages: high cost and equipment requirements. Test results are subjective to the examiner. There is possibility of false positives and false negatives[31].

Indications: diagnosis of CA in the cavity and microscopic lesions not easily visible to naked eyes, detection of SPI with a vinegar-white test[27]. Biopsy, treatment and follow-up can be performed under endoscopic view. Colposcopy should be performed after initial evaluation when cervical/vaginal lesions are suspected, e.g. when lesions are found in the vagina or when the patient reports possible intravaginal lesions, or when there is increased leucorrhea, contact bleeding and gynecological examination with cervical erosion without signs of vaginal inflammation[4,27]. Urethroscopy should be performed when deep warts are found in the external urethra with symptoms of frequent urination, painful urination, hematuria, dyspareunia and urethral itching[26] or when there is a discharge from the urethra and antibiotic treatment is not effective. Patients with warts found at the anus, with anal bleeding or discharge, or with a foreign body sensation should undergo rectal palpation and proctoscopy[4]. Patients with a history of anal intercourse and having new organisms or blood by palpation are likely to be associated with CA in the anal canal.

Pathological examination

Principle: HPV can enter the epidermis through tiny wounds in the skin mucosa and colonize the basal cells. After HPV infection, the cells will undergo morphological changes, and gradually move upward and finally fall off with keratinocytes. Thus, under an optical microscope with sufficient magnification, a characteristic change in the cells of the lesion can be observed, i.e. vacuole-like cells.

Operation: clean and fix the tissue, embed it in paraffin, section and stain it with HE, and then observe it under an optical microscope.

Presentation: epidermal atypical hyperplasia (hypertrophy/basal cell hyperplasia) with hyperkeratosis and lamellar dyskeratosis. In the superficial layers of the epidermis (granular layer and upper spiny layer), the characteristic vacuolated keratinocytes (KC) are seen, characterized by large grey nuclei, in focal, lamellar or scattered patterns, and rarely by typical hollow cells characterized by cytoplasmic vacuolation and nuclear crinkling[32]. Sometimes granular material of varying sizes with thick stain, i.e. viral inclusions, can be seen in the KCs[33]. The superficial dermal vasculature is dilated and infiltrated by lymphocyte-dominated inflammatory cells. It has been found that there is no statistically significant difference in the rate of positive HPV-DNA in situ hybridization between pyknotic and suspicious pyknotic cells in SPI lesions, and it has been suggested that suspicious pyknotic cells are vacuolated cells[2,11].

Advantages: gold standard for diagnosis, timely detection of tissue anomalies and early guidance for intervention.

Disadvantages: CA occurs in specific areas such as the genital mucosa, and it is very invasive and time-consuming. Pathological examination is limited due to sampling, sectioning and experience. Atypical lesions may require multiple retrievals. When the rash is too

doi:10.18282/jsd.v7.i2.190

small, it is difficult to obtain material. LPI cannot be detected.

Indications: Biopsy is not necessary for typical CA, but is recommended when the diagnosis is uncertain and the lesions persist, when the clinical presentation is atypical (e.g. when lesions are >2.5 cm in diameter, ulceration, hemorrhage, hyperpigmentation, lesions on sclerosing lichen sclerosis, etc.[34]) or when malignancy is suspected (poor outcome after standard treatment, recalcitrant and prone to recurrence deterioration of the disease during treatment, etc.)[4,35].

HPV-DNA testing and typing

Most of the HPV nucleic acid testing and typing methods used in clinical practice are based on polymerase chain reaction (PCR), i.e. HPV genotyping based on gene amplification. In this paper, the most commonly used clinical method for HPV DNA typing, the combination of PCR and gene chip hybridization, is introduced as an example.

Principle: the HPV-specific genes (L1, E6 and E7 region genes) are amplified in a repetitive process of denaturation, denaturation and extension based on the principle of complementary DNA base pairing[36]. The amplified DNA fragments are then hybridized with a specific type of HPV probe and color developed.

Operation: wipe the surface of the suspected infected area with a brush with slight force to obtain exfoliated cells; extract the DNA of the sample cells according to the instructions of the corresponding kit, and perform PCR, hybridization, membrane washing and enzymatic coloring in sequence, and determine the results according to the coloring development.

Manifestations: specifically judging based on instructions.

Advantages: the most sensitive method for detecting HPV infection and can be used to determine early HPV infection[36]; can be used for type-specific analysis and is a good guide for follow-up; less invasive and reproducible; highly sensitive, simple and rapid.

Disadvantages: inappropriate sampling may result in false negative results and minor contamination may result in false positives. Specific HPV typing is dependent on the HPV type in the kit selected and false negative results may occur if the kit does not cover the type of HPV infected. The number of lesion cells obtained cannot be determined to quantify the HPV infection at the lesion site.

Indications: to identify HPV infection; to identify the type of viral infection, predict disease prognosis, guide treatment and follow-up; for regional HPV vaccine selection; for counselling of sexual partners.

Other methods for detecting HPV-DNA include real-time fluorescent PCR, fluorescent in situ hybridization and immunological assays, but they are not currently commonly performed in clinical practice due to the tedious nature of the technique and the laboratory conditions required.

In summary, for patients with suspected CA at the first visit, if the lesions are typical, the diagnosis can be made directly in the context of the epidemiological history or clinically in the context of the acetowhitening test. If the lesions are atypical, further HPV-DNA testing is required, and depending on the circumstances, vinegar white tests, dermascopy and endoscopy may be used to further clarify the diagnosis and to show the extent of treatment, which can also be used for outcome follow-up. For patients with CA undergoing ALA-PDT treatment, it is recommended that the extent of the lesions be visualized under a Wood light before each illumination. For lesions in the lumen, endoscopy can be used for diagnosis, treatment and follow-up as appropriate. If malignancy is suspected, or if the lesion cannot be diagnosed after the above-mentioned ancillary tests, further diagnosis is required in conjunction with biopsy pathology. It is hoped that this article will serve as a reference for clinicians to understand the significance of various adjunctive tests in the management of CA and to facilitate the rational use of these tests in medical practice.

References

1. O'Mahony C, Gomberg M, Skerlev M, Alraddadi A, de las Heras-Alonso ME, *et al.* Position statement for the diagnosis and management of anogenital warts. J Eur Acad Dermatol Venereol 2019; 33(6): 1006–1019. doi: 10.1111/jdv.15570.
2. Huang Y, Chen Y, Wang B. Advances in the study of subclinical infection of condyloma acuminatum. Journal of Dermatology and Venereology 2018; 40(6): 810–811. doi: 10.3969/j.issn.1002-1310.2018.06 016.
3. Wang HW, Wang XL, Zhang LL, Guo MX, Huang Z. Aminolevulinic acid (ALA)-assisted photodynamic diagnosis of subclinical and latent HPV infection of external genital region. Photodiagnosis Photodyn Ther 2008; 5(4): 251–255. doi: 10.1016/j.pdpdt.2008.11.004.
4. Gilson R, Nugent D, Werner RN, Ballesteros J, Ross J. 2019 IUSTI-Europe guideline for the management of anogenital warts. J Eur Acad Dermatol Venereol 2020; 34(8): 1644–1653.doi: 10.1111/jdv.16522.
5. Ljubojevic S, Skerlev M. HPV-associated diseases. Clin Dermatol 2014; 32(2): 227–234.doi: 10.1016/j.clindermatol.2013.08.007.

doi:10.18282/jsd.v7.i2.190

6. Niyibizi J, Zanré N, Mayrand MH, Trottier H. Association between maternal human papillomavirus infection and adverse pregnancy outcomes: Systematic review and meta-Analysis. J Infect Dis 2020; 221(12): 1925–1937. doi: 10.1093/infdis/jiaa054.
7. Costa-Silva M, Fernandes I, Rodrigues AG, Lisboa C. Anogenital warts in pediatric population. An Bras Dermatol 2017; 92(5): 675–681. doi: 10.1590/abd1806-4841.201756411.
8. Ball SLR, Winder DM, Vaughan K, Hanna N, Levy J, *et al*. Analyses of human papillomavirus genotypes and viral loads in anogenital warts. J Med Virol 2011; 83(8): 1345–1350. doi: 10.1002/jmv.22111.
9. Culton DA, Morrell DS, Burkhart CN. The management of condyloma acuminata in the pediatric population. Pediatr Ann 2009; 38(7): 368–372. doi: 10.3928/00904481-20090622-05.
10. Wang X, Liang Q, Yan W, Yang F, *et al*. Analysis of relationship between the condyloma acuminatum subclinical infection outcome and human papillomavirus type. Acta Medicinae Sinica 2015; 28(3): 40–43.
11. Liu R, Hou J, Chen X, Lu X, Zhou G, *et al*. Evaluation of the acetic acid test for subclinical HPV infection in patients with condyloma acuminatum (in Chinese). Chinese Journal of Dermatology 2008; 42(5): 331–332. doi: 10.3321/j.issn:0412-4030.2008.05.017.
12. Gutiérrez-Fragoso K, Acosta-Mesa HG, Cruz-Ramírez N, Hernández-Jiménez R. Optimization of classification strategies of acetowhite temporal patterns towards improving diagnostic performance of colposcopy. Comput Math Methods Med 2017; 2017: 5989105. doi: 10.1155/2017/5989105.
13. National Center for STD control, China CDC. Clinical guidelines for the treatment of sexually transmitted diseases (extract 2). International Journal of Epidemiology and Infectious Disease 2008; 35(5): 289–294. doi: 10.3760/cma.j.issn.1673-4149.2008.05.001.
14. Jiang Y. Re-evaluate to diagnostic value of acetowhite test on condyloma acuminatum of humanity. Bulletin of Medical Research 2003; 32(7): 26–27. doi: 10.3969/j.issn.1673-548X.2003.07.014.
15. Chinese Medical Association, Chinese Association of Rehabilitation Medicine, China Association of Medical Equipment. Chinese guidelines for clinical application of aminolevulinic acid-based photodynamic therapy in dermatology (2021 edition). Chinese Journal of Dermatology 2021; 54(1): 1–9. doi: 10.35541/cjd.20200731.
16. Zhang H, Cao B, Yin G, Hao W, Zhang D, *et al*. Effect of 5-aminolaevulinic acid-photodynamic diagnosis of genital condylomata acuminata in the follow-up. Chinese Journal of AIDS & STD 2018; 24(4): 410–412. doi: 10.13419/j.cnki.aids.2018.04.25.
17. Hua R, Shi W, Mei X, Zhang W. Clinical study on the orientation and diagnosis of condylomata acuminatum with 5-aminolexodinic acid. International Journal of Dermatology and Venereology 2008; 34(3): 137–139. doi: 10.3760/cma.j.issn.1673-4173.2008.03.001.
18. Zhang Y, Jiang S, Lin H, Guo X, Zou X. Application of dermoscopy image analysis technique in diagnosing urethral condylomata acuminate. An Bras Dermatol 2018; 93(1): 67–71. doi: 10.1590/abd1806-4841.20186527.
19. Sun Q, Liu J. Atlas of dermoscopy. Beijing: People's Medical Publishing House; 2015.
20. Zhang Y, Zhou X, Guo X, Lin H. Application value of dermoscopy in the diagnosis of condyloma acuminatum . Chinese Journal of Dermatology 2017; 50(7): 493–496. doi: 10.3760/cma.j.issn.0412-4030.2017.07.006.
21. Dong H, Shu D, Campbell TM, Frühauf J, Soyer P, *et al*. Dermatoscopy of Genital Warts. J Am Acad Dermatol 2011; 64(5): 859–864. doi: 10.1016/j.jaad.2010.03.028.
22. Patar Z, Lipozenčić J. Significance of dermatoscopy in genital dermatoses. Clin Dermatol 2014; 32(2): 315–318. doi: 10.1016/j.clindermatol.2013.08.016.
23. Zeng Q, Liu P. Dermoscopy in the diagnosis and differentiation of condyloma acuminatum. Dermatology Bulletin 2019; 36(1): 141–144.
24. Shen X, Yu RX, Shen CB, Li CX, Jing Y, *et al*. Dermoscopy in China: Current status and future prospective. Chin Med J 2019; 132(17): 2096–2104. doi: 10.1097/CM 9.0000000000000396.
25. Errichetti E. Dermoscopy in monitoring and predicting therapeutic Response in general dermatology (non-tumoral dermatoses): An up-to-date overview. Dermatol Ther (Heidelb) 2020; 10(6): 1199–1214. doi: 10.1007/s13555-020-00455-y.
26. Yin G, Tang Y, Huang K, Wang J. Ureteroscope and holmium laser for the treatment of condyloma acuminate. Chinese Journal of Andrology 2009; 23(10): 48–49, 53.
27. Peng S, Peng Q, Chang L. The role of colposcopy in the diagnosis of early cervical acromegaly (in Chinese). China Practical Medicine 2010; 5(31): 126–127.
28. Liu X. Clinical experience of colposcopy in the diagnosis of cervical acromegaly (in Chinese). Journal of Clinical and Experimental Medicine 2008; 7(10): 105.
29. Tian F, Zhang Y. Clinical results of colposcopy combined with LEEP in the treatment of precancerous cervical lesions (in Chinese). Journal of Imaging Research and Medical Applications 2020; 4(4): 174–175.
30. Zhang L, Guo Q, Zheng T, Ge Y. Analysis of 14 cases of condyloma acuminata treated with holmium laser under ureteroscopy. Journal of Modern Urology 2010; 15(6): 466–467.

doi:10.18282/jsd.v7.i2.190

31. Mustafa RA, Santesso N, Khatib R, Mustafa AA, Wiercioch W, *et al*. Systematic reviews and meta-analyses of the accuracy of HPV tests, visual Inspection with acetic acid, cytology, and colposcopy. International Journal of Gynecology and Obstetrics 2016; 132(3): 259–265. doi: 10.1016/j.ijgo.2015.07.024.
32. Zhang J (translator). Dermatopathology. 2nd ed. Elston DM (editor). Tianjin: Tianjin Publishing and Media Group; 2017.
33. Condyloma acuminatum treatment guidelines (2014) (in Chinese). Chinese Journal of Dermatology 2014; 47(8): 598–599.
34. Kumar P, Bhari N, Gupta V, Ramachandran VG, Arava S, *et al*. Atypical morphology of anogenital warts is not a marker of atypical histology or of infection to the high-risk human papillomavirus genotypes. Int J Der-matol 2017; 56(10): 1017–1021. doi: 10.1111/ijd.13711.
35. Steben M, Garland SM. Genital warts. Best Pract Res Clin Obstet Gynaecol 2014; 28(7): 1063–1073. doi: 10.1016/j.bpobgyn.2014.07.002.
36. Tsakogiannis D, Gartzonika C, Levidiotou-Stefanou S, Markoulatos P. Molecular approaches for HPV genotyping and HPV-DNA physical status. Expert Rev Mol Med 2017; 19: 1–20. doi: 10.1017/erm.2017.2.

doi:10.18282/jsd.v7.i2.190