

Case Reports

Grade 3 vulvar and anal intraepithelial neoplasia in a HIV seropositive child - therapeutic result: case report

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Summary

A case report of a HIV seropositive 8-year-old child with vulvar and anal border neoplasia, both grade 3, and the adopted therapeutic management are presented. The mother reported the history of a progressively growing verrucous lesion in the vulva since the age of three and a half years. On physical examination a pigmented and elevated lesion was observed in the whole vulvar region extending to the anal region and intergluteal sulcus. After biopsies and anatomic pathological examination, antiretroviral therapy, adequate for age, and topical application of podophyllotoxin associated with *Thuya officinalis* extract was started. Three months afterwards vaporization and CO₂ laser excision were performed in five sequential sessions, thereafter associated with topical imiquimod application. After the first two sessions of laser therapy early relapses occurred. After four weeks of imiquimod use, already a significant improvement of the lesions was observed, making the following laser therapy sessions easier. We conclude that antiretroviral therapy associated with podophyllotoxin and *Thuya* was not effective regarding regression of the lesions. Laser therapy alone led to early relapses. The local use of imiquimod associated with laser was effective in decreasing and controlling the lesions.

Key words: Human papillomavirus; HIV; VIN; AIN; Imiquimod; Laser.

Introduction

Condyloma acuminata is a disease caused by the human papillomavirus (HPV) and expressed as anogenital verrucae. It constitutes one of the most frequent transmissible sexual diseases [1].

An increasing number of anogenital verrucae in children has been observed. Its natural history in the pediatric population and the potential for neoplastic evolution has been the subject of studies [2-4].

Vulvar intraepithelial neoplasia (VIN) and anal intraepithelial neoplasia (AIN) is little described in children. In a study on 11 girls with vulvar condylomata, with a mean age of 2.3 years, one case of high-grade VIN was found [5].

Seventy percent of VIN are related to HPV, affecting young women; they are characterized by extensive lesions, associated with cervical and vaginal intraepithelial neoplasia, common in immunosuppressed patients [6].

AIN is the precursor lesion of anal squamous carcinoma. Biologically it resembles uterine cervical cancer; it is also associated with oncogenic HPV [7].

Women with HIV are at increased risk for intraepithelial and invading neoplasms of the inferior genital tract and the anal canal [8].

There are several therapeutic options for these cases. In children, no treatment has been well studied.

The impact of antiretroviral therapy on the evolution of inferior genital tract and anal intraepithelial neoplasia in patients with HIV is not fully elucidated yet.

Case report

A case of an eight-year-old HIV positive child, due to vertical transmission, without retroviral therapy is presented. She had a history of emergence of pigmented verruca in the vulva since the age of 3.5 years, which increased in the last year. On examination a dark and elevated lesion, occupying the vulvar region, extending to the per anal region, anal canal and intergluteal sulcus was seen (Figure 1). The patient was submitted to biopsy and the anatomic pathological examination revealed grade 3 VIN and AIN; PCR was positive for HPV 6 and 16. Antiretroviral therapy was started with zidovudine and indinavir and local use of podophyllotoxin and *Thuya*, without clinical response. The initial CD4 lymphocyte count was 470 cells/mm³ and the final was 580 cells/mm³. After three months of this regimen, two sessions of vaporization and CO₂ laser excision were performed. There was an early relapse. Local treatment with imiquimod three times a week was started; a significant improvement was observed after four weeks, making the three following laser therapy sessions easier. The patient maintains a small lesion at the vaginal introitus (Figure 2).

Discussion

Treatment forms for VIN and AIN may be destructive, excision or both.

Topical fluorouracil has been used in cases of recurrent lesions and immunosuppressed patients [9].

The use of imiquimod has the advantage of preserving vulvar anatomy and function. It is a modifier of the local immune response by induction of cytokines and Langerhans cell migration. It presents good results in high-grade and multifocal VIN. In a report of 15 high-grade VIN

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Fig. 1

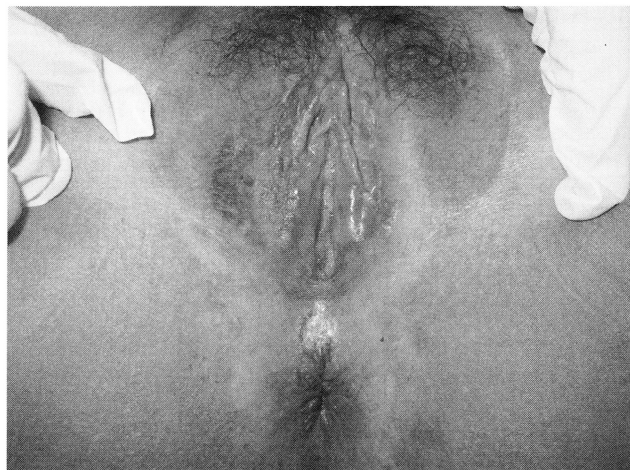


Fig. 2

Figure 1. — An 8-year-old patient with HIV + grade 3 VIN and AIN before starting the treatment.

Figure 2. — The patient after starting treatment with antiretroviral drugs, laser therapy and imiquimod.

cases a complete response was observed in 27% and a partial response in 60% [10]. There is a reduction in the surgical extension, converting vulvectomies into simple local excision. When used alone or associated with another method, it reduces relapses and prolongs the disease-free time.

As a physical treatment method, vaporization/CO₂ laser excision is preferred. The final result is excellent. Cure rates range from 76.9% to 96.8%. Complications are minimal [11].

VIN presents high recurrence rates, mainly in multifocal disease. The treatment is the same as the primary approach [12].

There is no established standard treatment for AIN; surgical excision or extensive ablation lead to considerable morbidity. The use of imiquimod for up to 16 weeks in high-grade AIN, in ten HIV positive patients promoted a two-grade regression of the neoplasia [7].

Condyloma therapy in children is similar to that of the adult; conservation of the anatomy is desirable and conservative techniques should be used. Since VIN and AIN are rare in children, it is unknown what is the best technique to be applied.

There is a case report on a 19-month-old child with extensive anal condyloma who, after the use of imiquimod for three weeks, showed an almost complete disappearance of the lesion [13].

Antiretroviral therapy has a significant impact on the natural history of HIV. However, in the control of infection with HVP, it is still controversial. Relapse and persistence rates are high, results with treatments alone are poor. Association of methods is ideal [8].

On analyzing the present case, antiretroviral therapy associated with podophyllotoxin and *Thuja* was not efficient regarding lesion regression. Laser therapy alone was followed by early relapses. Association of imiquimod was efficient regarding lesion decrease and control. Due to the fact that we are dealing with an extensive lesion in a child, surgical resection would promote a mutilation of the anatomy; therefore we opted for laser therapy. Imiquimod promoted flattening of the lesions, making laser sessions easier. We obtained a significant improvement as concerns this case. We believe that the scheme of association of methods, with the use of a local immunologic stimulator and the surgical precision of laser is the best option for rare cases as this one. The purpose of cure may not be attained due to immunosuppression but control of the disease, avoiding progression to invasive neoplasia, has been our main goal.

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