

Multicentric HPV Disease and Intra-Epithelial Neoplasia.

Usha Saraiya ● Maya Lulla ● Kanchan Sortey

Supported by a Research Grant from Medical Research Society of Sir H. N. Hospital & Research Centre, Mumbai 400 004.

Summary : A large epithelial surface of the lower female genital tract is exposed to the sexually transmitted HPV infection. The lesions frequently are multicentric.

In the Colposcopy Clinic of Sir H. N. Hospital over a 130 cases of HPV infection were seen. In all cases, routine gynaecological examination was followed by Cytology, Colposcopy and directed biopsy. We have seen 25 cases of extensive multicentric HPV disease. Analysis of symptoms indicate that leucorrhoea and warty growths were complained of by majority of the cases. Multicentric disease is far more difficult to treat than disease in a single organ. Since HPV occurs in relatively younger population, organ conservation is of utmost importance. The threat of invasive carcinoma is real, hence close observation over a prolonged period is essential. In a patient with HPV disease, a co-existing neoplasm should be looked for in the entire region. Likewise in patients with cervical or vulval neoplasia one should look for HPV and neoplasia in other areas.

Colposcope continues to be the most reliable tool in the assessment of the epithelium of lower female genital tract. CO₂ Laser is a satisfactory form of treatment as it can be applied extensively to cervix, vagina and vulva and perianal region. Since it is organ conserving, it is more acceptable to patients.

In the meantime, a search must be on for a chemotherapeutic agent specific for HPV. It is also important to emphasise on early diagnosis and control of disease while the intra -epithelial neoplastic disease is still in low grade.

Introduction

A large epithelial surface of the lower female genital tract is exposed to the sexually transmitted Human Papilloma Virus HPV infection. Current epidemiological evidence indicates that HPV is etiologically associated with the development of cervical cancer (MUNOZ et al 1992). There is an individual cell/virus interaction from the squamous epithelium starting at external os down to the skin of perianal region. Which part of the epithelium is going to respond to the virus and in what form will determine the final lesions.

It is known that the type of virus is the most important

predictor of clinical behaviour. (Reid et al 1987). Type 6 has a predilection for vulva and less for cervix; whereas type 16 has a high predilection for cervix. It is type 16, 18 which lead to rapid progression to neoplastic state, whereas type 6, 11 may remain subclinical. However, mixed viral infection is also a possibility and may lead to multicentric disease.

Material and methods

In the Colposcopic Clinic of Sir H. N. Hospital 130 cases of HPV infection were seen over a period of five years (91-95). In all cases, gynaecological examination was followed by Cytology, Colposcopy and directed biopsy.

In a few cases, serology for HIV and HSV₂ were done. Cases were treated with CO₂ Laser whenever indicated in the same Institute.

25 cases of extensive multicentric HPV disease were diagnosed. Out of these 5 were pregnant and so could not be evaluated. The balance 20 were fully evaluated with examination under anaesthesia, fractional curettage and multiple punch biopsies. Treatment by CO₂ laser was carried out subsequently after the biopsy reports were available.

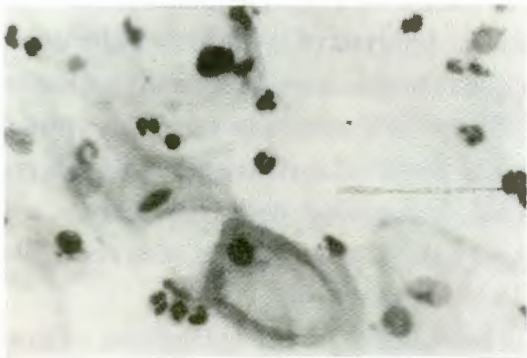


Fig 1

Diagnosis was established on Cytology by the presence of Koilocytes (fig. 1) and dyskeratocytes. The presence of dysplastic cells was carefully noted in some of the cases (fig. 2) Biopsy confirmed the histological appearance of koilocytotic changes (fig .3).

Colposcopic criteria included acetowhite epithelium, abnormal transformation zone and vascular patterns like punctation and mosaic (fig .4)

Observation

Analysis of symptoms indicate that leucorrhoea and pruritus was complained of by majority of cases. Presence of exophytic growths on the vulva of varying duration was complained of by 8 out of 25 cases. Others had various gynaecological complaints. In some cases cervical erosion was cauterised repeatedly. We had six interesting cases where the diagnosis and management were a challenge.

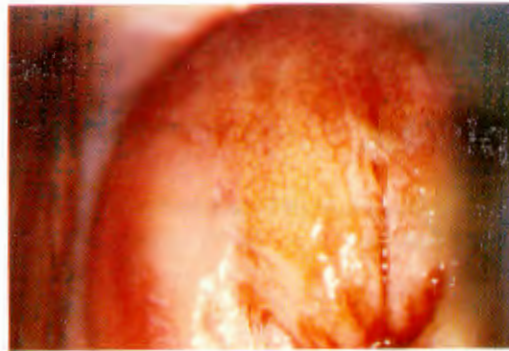


Fig 2

	Cervix	Vagina	Vulva	Serology	
Babita	CIN _{III}	Invasive	Invasive	HIV +ve HSV +ve for 5 years	Lesion static
Leela	CIN _{II}	HPV	VIN _{II}	-	Regressed with CO ₂ Laser.
Laxmi	Inv CA	VIN _{II}	HPV +ve	-	Wertheim/ Radiation
Asha	CIN _{III}	Invasive	HPV +ve	HSV _{II} +ve	Wertheim/ Radiation
Victoria	CIN _{III}	HPV +ve	VIN _{II}	-	Regressed with CO ₂ Laser.
Madhu	CIN _{II}	HPV +ve	VIN _{III}	HIV -ve	Uncontrolled with CO ₂ Laser responded to Interferon therapy.

Case 1: Mrs B was a commercial sex worker. She reported with abnormal bleeding, foul smelling discharge and extensive growths on the vulva. On investigations she was found to have tubercular endometritis, carcinoma in situ of the cervix, extensive vaginal condylomatosis, and invasive carcinoma at the base of a condyloma on the vulva. Although she was HIV negative initially, she and her husband became HIV +ve while under observation. She was treated with CO₂ Laser therapy. Partial vulvectomy was done. The Inguinal glands were biopsied and found to be negative. Anti TB treatment was started. The lesions are static for the last 3 years. She continues to be in indifferent health.

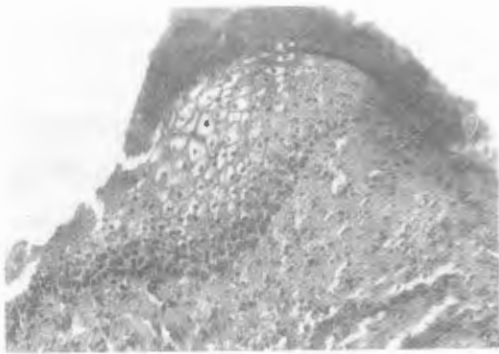


Fig 3

Case No. 2 : Mrs. L. She reported with multiple black lesions on the vulva. She was detected to have CIN_{II} of the cervix, extensive HPV of the vagina and VIN_{II} of vulva. she was negative for HIV & HSV_{II}. The lesions regressed completely with CO₂ Laser.

Case No. 3: Mrs. L. She had stage IB invasive cancer of the cervix, vaginal lesions of condyloma revealed VIN_{II}, vulval condylomas were benign. She underwent a Wertheim's

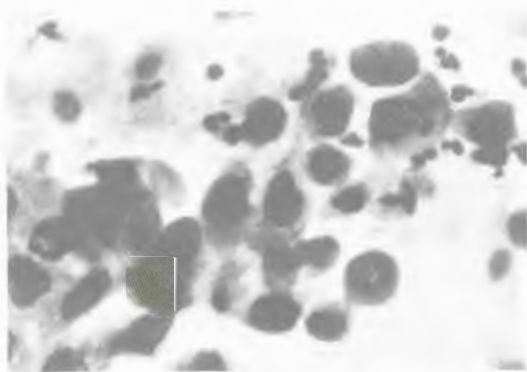


Fig 4

Hysterectomy followed by Radiation therapy.

Case No. 4 : Mrs. A. She was diagnosed to have CIN_{III} with invasive lesion in the vagina and extensive condyloma of the vulva. she was HIV negative but HSV II+ve. She was treated with Wertheim and Radiation. She was well for 5 years after which she developed a recurrence of squamous cell carcinoma.

Case No. 5 : Mrs V. She had CIN_{II} of the cervix,

extensive benign condyloma of the vagina and VIN_{II} of vulval condyloma. She was negative for HIV and HSV_{II}. She was a smoker and was advised to stop smoking. She responded well to Co₂ therapy.

Case No. 6 : Mrs. M. She had extensive condyloma of the vulva with VIN_{II}. Vagina showed extensive condyloma and cervix had CIN_{II}. She was negative for HIV & HSV_{II}. She was treated with Co₂ Laser. Although cervical and vaginal lesions responded, the vulval lesions reappeared. She had another treatment with Co₂ laser but still the lesions were larger than before. She finally responded to Interferon.

Discussion

Multicentric disease is far more difficult to treat than disease in a single organ (Campion et al 1986). Since HPV occurs in relatively younger population, organ conservation is of utmost importance. The threat of invasive carcinoma is real, hence close observation over a prolonged period is essential. (Choo et al 1980).

Although the most important single factor is the type of virus, other factors too need to be considered.

The host response to virus is important to assess. Malnourished individuals with avitaminosis and chronic debilitating disease like tuberculosis succumb easily and develop extensive lesions. The role of tobacco habit and use of contraceptive pills have proved significant in all cases of CIN. Another interesting feature is association of other similar virus like HSV_{II} and HIV also sexually transmitted. The quantity of virus entering the organ is a factor difficult to determine but may be of importance (Campion et al 1985).

Conclusion

It may be considered a guiding principle that in a patient

with HPV disease, a co-existing neoplasm should be looked for in the entire region. (Maracus 1960). Likewise in patients with cervical or vulval neoplasia one should look for HPV and neoplasia in other areas. (McCance et al 1985).

A thorough clinical examination coupled with liberal use of diagnostic aids is necessary to detect synchronous or subsequently occurring tumours. Colposcope continues to be the most reliable tool in the assessment of the epithelium of lower female genital tract.

CO₂ Laser is a satisfactory form of treatment as it can be applied extensively to cervix, vagina, vulva and perianal region. When carried out under general anaesthesia, it enables one to do multiple biopsies. Laser treatment can also be repeated for large or recurrent lesions. Since it is organ conserving, it is more acceptable to patients.

For those with uncontrolled, persistent or recurrent lesions, interferon offers a new hope. It is expensive and not freely available. Ancillary treatment with improvement

in health and hygiene contribute to well being.

Equally important is the possible persistence of carcinogenic stimulus which places these individuals at a greater risk to the development of subsequent malignancies. Hence follow up has to be prolonged and thorough.

References

1. Campion MJ, McCance DJ, Cuzick J : Lancet, 2 : 237-40 (1986).
2. Campion MJ, Clarkson P, McCance DJ : Clin Obst Gyn. 12:265-80 (1985).
3. Choo YC, Mortey GW : Obst Gyn. 56 : 365 (1980)
4. Maracus SL : Am J Obst & Gyn. 80 : 802 (1960).
5. McCance DJ, Campion MJ, Clarkson PK : Br J Obst & Gyn. 92 : 1101-105 (1985).
6. Munoz N, Bosch ZX, De Sanjose : Int J Cancer 52 : 743-49 (1992).
7. Reid R, Greenberg M, Jenson AB : Am J Obst Gyn. (1997).