

LETTERS TO THE EDITORS

242

Persistence of Cytologic Abnormality After Treatment of Bacterial, Parasitic and Fungal Infections in Older Women with Low Grade Squamous Intraepithelial Lesion

Jayashree Joshi, M.D., Ph.D., Mohd Zubair Affandi, M.Sc., Ph.D., Prayag Amin, B.Sc., Rama Vaidya, M.D., Ph.D., and Reeta Shah, M.D.
Vile Parle West and Sion, Mumbai, India



Volume 54

May-June

2010

Number 3

To,
The Editors,

It is generally observed that Low or High Grade Squamous Intraepithelial Lesion (LGSIL or HGSIL) may undergo regression in more than 30 % (1/3 rd) of cases ^{1,2} . In a large prospective study by Moscicki et al ³ it was observed that 90 % of cases with LGSIL in the younger age group ie 13 to 22 years of age, show regression on long term follow up.

We wish to report the effect of treatment of bacterial, parasitic and fungal treatment on Pap smears from women with a report of LGSIL. We have outpatient women's health clinics and cervical cancer screening program for women. Those with high grade SIL (HGSIL) or suspected cancer are referred to nearby hospitals. A research grant which involved studying the effect of pharmacological treatment of associated genital infections in women with Low Grade Cervical Intraepithelial Lesions (except viral infections) allowed us to screen women from low socioeconomic groups free of cost. Since majority of women developing cancer or Cervical Intraepithelial Neoplasia (CIN) are above 30 years of age in our population, free Pap tests were offered to this group. About 1/4rth women belong to the better socioeconomic group and they are required to pay for the Pap test. There is no universal government or insurance based screening program. The study has been approved by an independent Ethics Committee.

A total of 660 cases were screened by Papanicolaou smears from April 2007 to October 2007. More than 80% of cases were above the age of 30 years. Out of these there were 3 cases of cervical Squamous Cell Carcinoma (SCC), 7 cases of High Grade Squamous Intraepithelial Lesion (HGSIL), and 22 cases of Low High Grade Squamous Intraepithelial Lesion (LGSIL), mostly from underprivileged group. All abnormal Pap

smears, showed evidence of local infections^{4,5}. None of the women admitted premarital or extramarital relations. Only two women with HGSIL reported that their husbands were polygamous.

This report is restricted to the 15 cases of LGSIL who returned for a repeat smear within a period of 8 months after treatment of infections. Since local genital infections act as co-factors for the development of squamous carcinoma of the cervix we were interested in finding out the immediate effect of treatment of infections on cytological pattern.

Out of fifteen women with treated LGSIL, eight cases showed cytological manifestations of bacterial, parasitic and fungal infections (Table1). Koilocytosis indicating infection by Human Papilloma Virus was associated in 13 / 15 cases. The

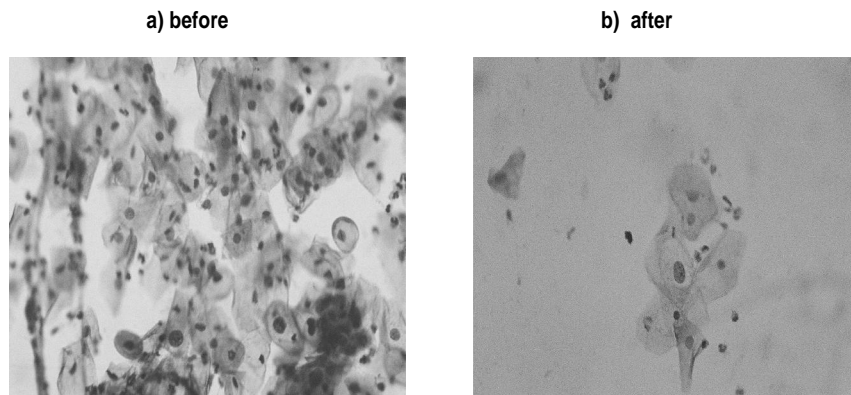
Table 1. Age, Gravidity, menstrual status, initial Pap smear and colposcopy, and follow up Pap smear after treatment of infections in 15 cases of LGSIL

No	Age Years	Gravida	Menses	Local Symptom	Pap smear Initial	Colposcopy	Treatment	Pap smear FU
1	47	3	PM	Discharge	LGSIL + Koilocytes	ACW		LGSIL + Koilocytes
2	45	8	R	Discharge	LGSIL + Koilocytes	CIN 1		LGSIL + Koilocytes
3	43	3	R	Bloody Discharge	LGSIL + BV +Koilocytes +Fungus	CIN 1		LGSIL + Koilocytes +AGUS
4	30	4	R	Discharge	LGSIL + BV	CIN 1		ASCUS
5	48	3	PM	Nil	LGSIL + TV Koilocytes	CIN 1		LGSIL + Koilocytes
6	55	3	PM	Nil	LGSIL + Koilocytes	Atrophy		LGSIL + Koilocytes
7	44	4	PM	Discharge	LGSIL +BV+ Koilocytes	Cervicitis		LGSIL + Koilocytes
8	56	3	PM	Nil	LGSIL + Koilocytes	ACW		LGSIL + Koilocytes
9	67	5	PM	Nil	LGSIL+BV+ Koilocytes	ACW		LGSIL + Koilocytes +AGUS
10	45	4	IR	Discharge	LGSIL + Koilocytes	ACW		Atypia
11	55	2	PM	Nil	LGSIL + Koilocytes	CIN 1		LGSIL + Koilocytes
12	45	3	R	Nil	LGSIL+BV	Cervicitis		Atypia
13	32	3	IR	Nil	LGSIL + Koilocytes	Cervicitis		LGSIL + Koilocytes
14	44	2	IR	Discharge	LGSIL + Koilocytes	Cervicitis		Atypia

15	48	3	R	Discharge	LGSIL+AGUS Koilocytes	Polyp		LGSIL + Koilocytes
----	----	---	---	-----------	--------------------------	-------	--	-----------------------

Key: R= Regular, PM= Postmenopausal, TV= Trichomonas vaginitis, BV= Bacterial vaginitis, ACW= Acetowhite areas, CIN 1= Cervical Intraepithelial Neoplasia 1, Pap smear FU= Pap smear report at follow up after treatment of infection

Figure 1. Cervical smear from a 44 year old patient with LGSIL a) before and b) after treatment with satronidazole for Bacterial vaginitis (X 400; Papanicolaou stain)



prevalence of Koilocytosis in smears in the general population in our clinics is 8 %. All had 2, 3 or 4 pregnancies. Eight women were postmenopausal whilst 7 were premenopausal. Two cases were 30 and 32 years old and the remaining were between 42 and 67 years of age. All 15 women and their husbands (N= 10 living with husbands)

were treated for bacterial , parasitic and fungal infections. Cases were treated with metronidazole or satronidazole, azithromycin and or fluconazole alongwith the partners. Women with persistent cervicitis or erosions were treated for presumptive gonorrheal infections along with their partners. All abnormal slides were screened by two cytologists. Colposcopy was negative in 10 cases and suggested CIN 1 in 5 cases.

After treatment, LGSIL regressed in less than 1/3 rd , ie 4 out of 15 cases , and even in these ASCUS or Atypia was persistent (Fig 1). Although the bacterial, parasitic and fungal infections responded to treatment, Koilocytosis persisted in all. Glandular atypia (AGUS) was observed in 1 case at initial examination and in 2 other cases at follow up.

We wish to highlight the high rate of persistence of LGSIL in our series after treatment of associated genital infections in women above 30 years with a diagnosis of LGSIL with concurrent koilocytosis. The role of multiparity also cannot be excluded. The limitation of the study is that we were not able to assess the reversibility in the younger age group. Premarital and extramarital sex , although definitely prevalent and increasing over the years, are still not too common in our conditions. Younger women therefore are not usually agreeable for Pap tests and for follow up visits. However SILs are common and so are STDs in the high risk group and we have reported this earlier ⁵.

Women with these characteristics therefore require an active follow up if invasive cancers are to be prevented. Undoubtedly the use of HPV detection techniques has made the identification of high risk cases easier in developed countries ⁶. However these are associated with larger screening costs and will require establishment of quality control for HPV DNA tests which may be more difficult to ensure than quality control of Pap smears. In India the conventional Pap smear is still the backbone of cervical cancer screening programmes⁷. The estimated number of new cervical cancer cases is 1,30,000 per year ⁸. To prevent invasive cancer it may be ideal to follow up all ASCUS or higher grade as reported by another group ⁹ but many of these may regress, and the follow up of all these women is not feasible without increased cost and infrastructure strengthening. Women above 30 years with persistent LGSIL and koilocytes may have a high risk for cervical cancer and deserve urgent attention as these are not likely to regress.

Acknowledgements: The study received a research grant from the Department of Biotechnology (DBT) , Govt of India, New Delhi.

Declaration : The authors declare no conflict of interest or financial interest with respect to the materials and findings in the study.

Jayashree Joshi, M D, Ph D*
Prayag Amin, B Sc*
Reeta Shah, MD @

MZ Affandi, M Sc, Ph D*
Rama Vaidya , MD PhD*

Corresponding author: Jayashree Joshi, MD, PhD*; e-mail: <jayash111@yahoo.co.in>

Address : * Medical Research Center, Kasturba Health Society , Jain Aradhanadham,
Desai Rd, Vile Parle West, Mumbai- 400056 (INDIA)
@ Sion Ayurveda Mahavidyalaya, Sion, Mumbai- 400022 (INDIA)

References:

1. Knight B. Project: screen South Africa. *Diagn Cytopathol.* 2005;33(5):356-8.
2. Holowaty P, Miller AB, Rohan T, To T. Natural history of dysplasia of the uterine cervix. *J Natl Cancer Inst.* 1999 ;91:252-8.
3. Moscicki AB, Shiboski S, Hills NK, Powell KJ, Jay N, Hanson EN, Miller S, Canjura-Clayton KL, Farhat S, Broering JM, Darragh TM. Regression of low-grade squamous intra-epithelial lesions in young women. *Lancet.* 2004;364:1678-83.
4. Crothers BA. The Bethesda System 2001: update on terminology and application. *Clin Obstet Gynecol* 2005; 48:98-107.
5. Joshi JV, Mali BN , Bhavé G, Wagle U. Cervical neoplasia and cytological manifestations of sexually transmitted infections in HIV seropositive prostitutes. (Letter). *Cytopathology* 1993; 4:63-64.
6. Mayrand M, Duarte- Franco E, Rodfrigues I, Walter SD, Hanley J, Ferenczy A, Ratnam S, Coutlee F, Franco E for the Canadian Cervical Cancer Screening Trial Study Group. Human Papilloma Virus DNA versus Papanicolaou Screening Tests for Cervical Cancer. *New Engl J Med* 2007; 357:1579-88.
7. Mali BN, Hazari KT, Joshi JV. Benefits of the Conventional Papanicolaou Smear. *Acta Cytologica* 2004; 48:466-467.
8. Shanta V, Krishnamurthi S, Gajalakshmi CK, Swaminathan R, Ravichandran K. Epidemiology of cancer of the cervix: global and national perspective. *J Ind Med Assoc* 2000; 98:49-52
9. Gupta S, Sodhani P, Chachra KL, Singh V, Sehgal A. Outcome of “Atypical Squamous Cells ”in a Cervical Cytology Screening Program: Implications for Follow Up in Resource Limited Settings *Diagnostic Cytopathology* 2007; 35 : 677-80.