Cervical Intraepithelial Neoplasia Managed With Classical Homeopathy: A Case Report

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October 18, 2021

Abstract

We present the case of 33-year-old woman diagnosed with low to high grade squamous intraepithelial neoplasia that benefited with individualized classical homeopathy. The outcomes were resolution of the pre-malignant condition and the HPV infection, preventing the use of invasive procedures that were otherwise deemed necessary.

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Running title: Cervical intraepithelial neoplasia, a homeopathic case report.

Abstract:

We present the case of 33-year-old woman diagnosed with low to high grade squamous intraepithelial neoplasia that benefited with individualized classical homeopathy. The outcomes were resolution of the pre-malignant condition and the HPV infection, preventing the use of invasive procedures that were otherwise deemed necessary.

Keywords : Cervical Intraepithelial Neoplasia, uterine cervical neoplasm, homeopathy, Low- High Grade Squamous Intraepithelial Lesions.

Key Clinical Message: Individualized classical homeopathy needs to be investigated for its relevance in treatment of cervical intraepithelial neoplasia with high risk of human papilloma virus infection, as the benefit was demonstrated in the case presented here.

Abbreviations:

CIN – Cervical intraepithelial neoplasia

HPV – Human Papillomavirus

hr HPV – high risk human papillomavirus

DNA – Deoxyribonucleic acid

ASC – Atypical Squamous Cells

ASC-US – Atypical Squamous Cells of Undetermined Significance

ASC-H – Atypical Squamous Cells - cannot exclude HSIL

LSIL – Low-grade Squamous Intraepithelial Lesion

HSIL – High-grade Squamous Intraepithelial Lesion

WHO – World Health Organisation

Pap test – Papanicolaou test

LLETZ – Large Loop Excision of the Transformation Zone

INTRODUCTION:

Cervical cancer is the fourth most common malignancy of the female reproductive system with over half a million women diagnosed, and over 300,000 deaths attributed to it globally each year^{1,2}. The important risk factors in the genesis of cervical cancer are early coitarche, infection with high-risk HPV (hr HPV), other sexually transmitted infections, age > 30 years, multiparity, multiple sexual partners and compromised host defense^{3,4}. There are over 40 types of hr HPV identified as inhabiting the female genital tract that can potentially cause cervical cancer^{5,6}. Cervical cancer has a long precancerous period, during which it may be detected and even effectively treated⁶.

The Bethesda system classifies a continuum of cytological abnormalities of the premalignant lesion in the Pap smear test. This nomenclature has replaced the earlier term Cervical Intraepithelial Neoplasia (CIN I, II and III, progressively riskier for developing cancer) with Squamous Intraepithelial Neoplasia (SIL), categorizing them into (a) Atypical Squamous Cells (ASC)-indicator of HPV infection, (b) Low grade Squamous Intraepithelial Lesion (LSIL) – cervical cells show changes that are mildly abnormal (c) High grade Squamous Intraepithelial Lesion (HSIL) cervical cells with severe changes. The ASC category is further divided into Atypical squamous cells of undetermined significance (ASC-US) and Atypical squamous cells – cannot exclude HSIL (ASC-H)⁶⁻⁸.

HPV vaccinations, local ablative methods like cryotherapy and cold coagulation, excisional methods such as large loop excision of the transformation zone (LLETZ), cone excision and hysterectomy are the approaches followed by conventional medicine as prevention and treatment modalities, but they seem to have unfavorable effect especially on the further reproductive outcomes, even when treated with conserving fertility as the goal⁹. This is of significance as the average age of women undergoing these treatments coincides with the average age of first child globally⁹.

Previous case reports of homeopathy in cancer cases have provided evidence for beneficial outcomes from classical homeopathy¹⁰. Here, we present a case of LSIL treated with homeopathy. The approach not only helped the pre-invasive disease but also improved the comorbidities.

METHODS:

Case report:

Case presentation: A 33-year-old Indian woman, presented to the homeopath after being diagnosed with LSIL-HSIL.

History of presenting complaints: On 26/08/2019, she underwent a PAP smear test which revealed ASC-US cytology (Fig. 1). Further when screened for HPV DNA, the patient tested positive for HPV (18, 52) high risk type on 03/09/2019 (Fig. 1).

Age/Sex : 32Y5M9D/F	
Sample Dt. 26/08/2019 13:23	Result Dt. 28/08/2019 16:47
CYTOTOLOGY - LIQUID BASED	
CYTOTOLOGY NO	[REDACTED]
SPECIMEN	Cervical PAP Smear.
CLINICAL DETAILS	Cervix normal, LMP- 9/08/2019.
GROSSING	Received LBC container labeled with patient s name and number. One Thin prep smear prepared and stained by PAP stain.
MICROSCOPIC	Satisfactory smear showing mixed pattern of superficial and intermediate squamous cells. Transformation zone component is present.
DIAGNOSIS	Cervical smear, thin prep cytology: - Atypical squamous cells of undetermined significance, ASCUS (Bethesda System).

[REDACTED]		REPORTED ON: 05/09/2019 17:46
		Report Status: Final
Tests	Results	Biological Reference Range Units
MOLECULAR DIAGNOSTICS		
HUMAN PAPILLOMA VIRUS (HPV) BY REALTIME MULTIPLEX PCR		
HPV DNA	POSITIVE	
METHOD : REAL TIME PCR		
GENOTYPE	18, 52, (HIGH RISK) ARE DETECTED.	
METHOD : REAL TIME PCR		
Specimen: LBC		
Interpretation(s)		
RESULT	REMARKS	
Positive	Sample provided contains HPV DNA	
Indeterminate	Presence of inhibitors in the sample	
Negative	Sample provided does not contain HPV DNA or number of viral DNA copies are below the detection limit of assay	
Note		
This test amplifies DNA of 14 High Risk (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 & 68) HPV types associated with cervical cancer and its precursor lesions and 2 Low Risk (6, 11) HPV types associated with genital warts, which rarely develop into cancer.		
Comments		
Over 118, Papilloma viruses have been identified belonging to the family Papillomaviridae. HPV related cervical cancer constitutes about 12% of malignancies worldwide. Persistent infection with oncogenic types of HPV followed by HPV DNA integration into the cellular genome is a required precursor in the pathway leading to cervical neoplasia. HPV types have been categorized as High risk, Intermediate risk & Low risk. A large number of women who are High risk HPV DNA positive, do not develop cervical cancer or precursor lesions like CIN-2/3. HPV infects epithelial tissues throughout the body including skin, larynx and anogenital tissues.		

Fig 1. Pap smear test report of 26/08/2019 and HPV DNA test report of 03/09/2019.

On 18/09/2019, cervical biopsy revealed a low grade squamous intraepithelial lesion with focal high grade squamous intraepithelial lesion CIN I- CIN II (Fig. 2) indicating that the condition had progressed. On 10/05/2020, cervical Pap smear test showed low grade intraepithelial lesion CIN I (Fig.2).

Age/Sex : 32Y6M10/F	
Sample Dt. 18/09/2019 17:44	Result Dt. 25/09/2019 17:49
BIOPSY : LEVEL IV	
HISTOPATH NO	[REDACTED]
SPECIMEN	Cervix, biopsy.
CLINICAL DETAILS	HPV Positive for 18 and 52, PAP Smear DC 1064/19-ASCUS.
GROSSING	Received in formalin, labeled with patient s name and number, consists of two mucosal pieces of tissue measuring 0.5 cm each. Specimen is entirely submitted in one cassette.
DIAGNOSIS	<p>Squamous and columnar mucosa, clinically from "Cervix", biopsy:</p> <ul style="list-style-type: none"> - Ecto and endocervical mucosa with low to possible focal high grade squamous intraepithelial lesion (CIN I-II) (see comment). - Extensive immature squamous metaplasia and chronic inflammation. - No evidence of invasive malignancy identified. <p>Comment: Multiple levels have been evaluated (Up to L6), to reveal ecto-endocervical mucosa with perinuclear haloing, mild variation in nuclear size and irregularity of nuclear membrane compatible with low grade squamous intraepithelial lesion (CIN I). Extensive immature squamous metaplasia with focal area showing loss of polarity, mild nuclear enlargement and hyperchromasia, suspicious for focal high grade squamous intraepithelial lesion (CIN II). Immunohistochemistry stains for P16 and Ki67 can be performed for further evaluation. Recommend clinicopathological correlation and follow up.</p>

Age/Sex : 33Y1M23D/F	
CYTOLOGY - LIQUID BASED	
Collected Date : 10/05/2020 22:48	Received Dt. 10/05/2020 23:02
	Reported Dt. 13/05/2020 15:27
CYTOLOGY NO	[REDACTED]
SPECIMEN	Cervical PAP Smear.
CLINICAL DETAILS	Cervix normal, previous (DC 20/13- LSIL), mild cervical dysplasia, LMP- 24/04/2020.
GROSSING	Received LBC container labeled with patient s name and number. One Thin prep smear prepared and stained by PAP stain.
MICROSCOPIC	Satisfactory smear showing mixed pattern of superficial and intermediate squamous cells. Transformation zone component is present.
DIAGNOSIS	<p>Cervical smear, thin prep cytology:</p> <p>Squamous cell abnormality:</p> <ul style="list-style-type: none"> - Low grade squamous intraepithelial lesion, LSIL (Bethesda System).

Fig 2. Biopsy report of 18/09/2019 and Pap smear report of 10/05/2020.

Conventional treatment advice: Patient was advised to undergo conization.

Due to fear of the adverse consequences that cervical conization might have on her future fertility and obstetric outcome, patient chose to approach homeopathy for a non-invasive therapeutic intervention.

Homeopathic consultation: The initial anamnesis of the case took place on 18/05/2020. Along with the said diagnosis, patient had PCOS, menstrual cycles every 35-36 days; nodular, facial acne and hair fall. Patient was very anxious about her health.

Past medical history: Bronchial asthma with breathing difficulty in humid climate and atopic dermatitis on flexor surface of joints in childhood, treated conventionally.

Family history: Father had hypertension, bronchial asthma and eczema. There was a history of bronchial asthma and eczema in his siblings. The mother was healthy.

Obstetrics and gynecological history: Menarche at 11 years. Nullipara. Menstrual cycle every 33-36 days.

Flow is scanty to normal.

Diagnosis: Low-High grade squamous intraepithelial lesion CIN I-CIN II (ICD 10 - R87.612) ¹¹

Homeopathic intervention:

After thorough case taking, Pulsatilla nigricans 200CH was prescribed in diluted form for 1 month (one tablespoon per day). The remedy was selected on the basis of principles of classical homeopathy, which includes an integral picture of the physical and mental/emotional suffering.

RESULTS:

The patient underwent homeopathic therapy for a period of approximately 4 months, during which a simultaneous amelioration of comorbidities such as irregular menstrual cycles, acne and eczema were observed along with the resolution of Low-High grade squamous intraepithelial lesion.

Follow up :

The follow up of the case with cytological and symptomatic observations are presented in table 1.

Table 1: Follow up of the case

Date	Detailed symptoms/observations	Gynecological/ Cytological findings	Homeopathic prescription:
22 nd June 2020	Patient is still anxious about her condition. Facial acne got worse. Dry eczematous rashes on fingers started appearing, which was an old complaint during childhood. Patient was advised to not intervene in any way with the skin manifestation.	Cervical erosion, CIN I –CIN II HPV 18,52	Silicea 200 CH was given in diluted form, one tablespoon every day for 1 month.
22 nd July 2020	Folliculitis over abdomen appeared and resolved in 3 days. Acne is better, scar marks seen. Hair fall has reduced. Dry eczema over finger has reduced. Menstrual cycles are regular.	Size of cervical erosion has reduced.	Calcarea carbonica 200CH was given in diluted form, one tablespoon for 1 month.
3 rd September 2020	Patient developed boils over back. Sleep is very refreshing now. No acne noted. Anxiety about health – completely better. Dry eczema on hands persists with a decreased intensity.	No cervical erosion noted. Cervix looks healthy.	Calcarea carbonica 200CH was given in diluted form for 1 month.

26 th October 2020	Eczema has resolved. No acne. Menstrual cycles are regular, no menorrhagia noted.	Negative for intraepithelial lesion and malignancy. (Fig. 3) HPV-DNA tested negative in November. (Fig. 3)	Homeopathic prescription stopped.
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Outcome: The last pap smear performed on 26/10/2020 showed no signs of intraepithelial lesions, and the test for viral DNA done on 7/11/2020 detected no HPV DNA (Fig 3).

CYTOLOGY - LIQUID BASED

Collected Date : 26/10/2020 15:57 Received Dt. 26/10/2020 16:19 Reported Dt. 29/10/2020 16:3

CYTOLOGY NO [REDACTED]

SPECIMEN Cervical PAP smear.

CLINICAL DETAILS Minimal erosion at posterior lip of cervix, chessy vaginal discharge, previous (DC 20/13 and DC 20/341- LSIL and colposcopy biopsy in 2019- CIN I-II), mild cervical dysplasia, LMP- 01/10/2020

GROSSING Received LBC container labled with patient s name and number. One Thin prep smear prepared stained by PAP stain.

MICROSCOPIC Satisfactory smear showing mixed pattern of superficial and intermediate squamous cells. Transformation zone component is present.

DIAGNOSIS Cervical smear, thin prep cytology:
- Negative for intraepithelial lesion or malignancy (Bethesda System).

REPORTED ON: 10/11/2020 10:56
Report Status: Final

Tests	Results	Biological Reference Range	Units
MOLECULAR DIAGNOSTICS			
HUMAN PAPILLOMA VIRUS (HPV) BY REALTIME MULTIPLEX PCR			
SPECIMEN	LBC		
HPV DNA	NOT DETECTED		
METHOD : REAL TIME PCR			
Specimen: LBC			
Interpretation(s)			
RESULT	REMARKS		
Positive	Sample provided contains HPV DNA		
Indeterminate	Presence of inhibitors in the sample		
Negative	Sample provided does not contain HPV DNA or number of viral DNA copies are below the detection limit of assay		
Note			
This test amplifies DNA of 14 High Risk (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 & 68) HPV types associated with cervical cancer and its precursor lesions and 2 Low Risk (6, 11) HPV types associated with genital warts, which rarely develop into cancer.			

Fig 3. Pap smear report of 26/10/2020 and HPV DNA test report of 07/11/2020.

Discussion:

Classical homeopathy considers the presenting pathology along with the mental/emotional disturbances experienced by the patient in association with their hereditary influences and past diseases and treatments to synthesize an integrated picture of the diseased patient. This is then used to select the remedy that is indicated for that specific picture. Thus, personalized treatment is provided to every patient. As also observed in this case, the homeopathic remedies were selected for such a totality of physical, mental and emotional suffering along with the hereditary influences, and the outcome was favorable. Homeopathy has been shown to be beneficial in various cancerous conditions, but seldom in CIN and HPV ^{10,12}. Further, in this case, we see the most pertinent favorable prognostic sign with treatment – the return of a previously suppressed skin eruption. While evidence exists for the direct association of history of atopic dermatitis with cervical cancer ¹³, the homeopathic perspective is different from this. When a patient is being treated for

what is considered deeper pathology (such as CIN in this case), the return of a more superficial pathology (in this case, atopic dermatitis) that the patient had suffered from earlier in her life and which had been suppressed at that time, is considered a sure indication of improvement in the deeper pathology ¹⁴. Here, it was corroborated by the biopsy and viral DNA analysis reports, which showed absence of CIN histology and HPV DNA after treatment. The causality assessment with Modified Naranjo Criteria for Homeopathy (MONARCH) yielded a score of 10/13, indicating strong causal relation of the effects to the treatment (Table 2).

Table 2. Modified Naranjo Criteria for Homeopathy (MONARCH) – for causality assessment.

Criteria

1. Was there an improvement in the main symptom or condition for which the homeopathic medicine was prescribed?
2. Did the clinical improvement occur within a plausible time frame relative to the drug intake?
3. Was there an initial aggravation of symptoms?
4. Did the effect encompass more than the main symptom or condition, i.e., were other symptoms ultimately improved or cured?
5. Did overall well-being improve?
- 6 (A) Direction of cure: did some symptoms improve in the opposite order of the development of symptoms of the disease?
- 6 (B) Direction of cure: did at least two of the following aspects apply to the order of improvement of symptoms: - from organic to functional, - from general to specific, - from chronic to acute?
7. Did “old symptoms” (defined as non-seasonal and non-cyclical symptoms that were previously thought to have resolved) recur?
8. Are there alternate causes (other than the medicine) that with a high probability could have caused the improvement? (In this case by pap smear and viral DNA detection)
9. Was the health improvement confirmed by any objective evidence? (In this case by pap smear and viral DNA detection)
10. Did repeat dosing, if conducted, create similar clinical improvement?

Total

The homeopathic preparations that were prescribed here are what are referred to as “polychrest remedies” in the homeopathic materia medica. This implies that these remedies have a broad systemic influence and need to be selected by the totality of pathology, mental and emotional symptomatology considered together. The mechanism of their action is unknown, although they most likely work by enhancing immune system protection, as indicated by the numerous clinical benefits.^{10,15}

Conclusions:

This case of an Indian woman diagnosed with cervical intraepithelial neoplasia with high-risk human papillomavirus infection benefited with individualized classical homeopathy. Further scientific investigations to determine the relevance of this therapy in preventing overt cervical cancer in such cases is needed.

Acknowledgement:

The authors acknowledge the help of patient in consenting for publication and Dr Aaditi Lakshman for rendering technical help.

Statement of Ethics: Written consent was obtained from the patient for publication of case details.

Conflict of Interest Statement:

The authors have no conflicts of interest to declare.

Funding Sources:

No funding was obtained for this work.

Authors’ Contributions:

OH is the primary physician who treated the patient and collected all the data, SM wrote the manuscript and obtained references and GV is the guide and guarantor of the work.

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Table Legends:

Table 1. Follow up of the case.

Table 2. Modified Naranjo Criteria For Homeopathy (MONARCH) – for causality assessment.

Figure Legends:

Fig 1. Pap smear test report of 26/08/2019 and HPV DNA test report of 03/09/2019.

Fig 2. Biopsy report of 18/09/2019 and Pap smear report of 10/05/2020.

Fig 3. Pap smear report of 26/10/2020 and HPV DNA test report of 07/11/2020.