

CASE REPORT

Simple vaginal trachelectomy as a fertility-sparing treatment to manage high-grade dyskaryosis following multiple large loop excision of the transformation zone

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SUMMARY

A 34-year-old nullipara, wishing to start a family, presented to colposcopy clinic. Her most recent cervical cytology result showed high-grade dyskaryosis. Having undergone four large loop excisions of the transformation zone during the past 6 years, this woman had no remaining vaginal cervix. In order to excise presumed high-grade cervical intraepithelial neoplasia while mitigating obstetric risk, she underwent a simple vaginal trachelectomy and isthmic cerclage. 6 months later, the patient had a negative test of cure. 7 months following surgery she became pregnant naturally. At 29 weeks she had antenatal sepsis of unknown cause, which was treated with intravenous antibiotics. She delivered by caesarean section at 37 weeks and now has a healthy child. This report will discuss the obstetric impact of colposcopic treatment, and simple vaginal trachelectomy as a fertility-sparing treatment option for women who have had multiple loop excision procedures to treat premalignant lesions.

BACKGROUND

The National Health Service cervical screening programme has recently adopted a human papilloma virus (HPV) triaging approach to account for the pathological role of HPV in cervical cancer; women with borderline cytology are now triaged to colposcopy clinic if they test positive for high-risk HPV (HR HPV). At colposcopy, women may have a biopsy to determine the need for further treatment, or undergo 'see and treat' management with large loop excision of the transformation zone (LLETZ). LLETZ is associated with a high chance of cure, but in cases of persistent HR HPV and abnormal cytology, repeat procedures may be necessary. HPV triaging increases the sensitivity of post-treatment detection of persistent disease. If the transformation zone is not visible—which is more likely following previous cervical excision—LLETZ may be used diagnostically to exclude an occult lesion.¹ This leads to the possibility that more LLETZ procedures are now being performed for diagnostic purposes at an earlier juncture. Depth of cervical excision is correlated with the risk of preterm labour; this may prove problematic for the ageing demographic of patients wishing to retain fertility.² Strategies for reducing the obstetric risk to the cervical screening population therefore need to be considered.

This case highlights important learning points regarding minimising obstetric consequences for complex patients presenting to colposcopy clinic. The successful treatment of the woman in this case also demonstrates that simple vaginal trachelectomy (SVT) is a fertility-sparing treatment option in cases where a repeat treatment is needed, but where no vaginal cervix remains.

The PubMed and the Cochrane databases were searched in full up to 5 May 2016, using the Medical Subject Headings term 'trachelectomy', without limits, and all abstracts containing keywords were reviewed.

Recent studies have observed that the morbidity and obstetric impact of SVT is certainly no greater than the well-studied and defined risks documented for radical vaginal trachelectomy (RVT) in early cervical malignancy.^{3–7} However, no reports discuss the role of SVT in the management of cervical intraepithelial neoplasia (CIN), nor of its potential obstetric advantages over RVT.

CASE PRESENTATION

An asymptomatic nulliparous 34-year-old woman, with a 6-year history of repeatedly abnormal smear test results, presented to colposcopy clinic. Her most recent cytology result showed moderate dyskaryosis. This woman had been reviewed six-monthly at colposcopy clinic since first presenting at the age of 28 years, and had undergone four LLETZ procedures, summarised in [table 1](#). She wished to imminently begin a family with her long-term partner.

She had no relevant medical or family history and had never smoked.

At colposcopic examination, the patient's cervix was flush with vault, with no visible CIN lesion. The transformation zone could not be visualised and there was no evidence of vaginal intraepithelial neoplasia.

INVESTIGATIONS

No further biopsy was attempted, as the transformation zone was not visible and there was no visible lesion. The patient's cytology was confirmed to be high grade during review at the colposcopy multidisciplinary team meeting. A HR HPV test 8 months prior to this had been positive, and was not repeated because the presence of high-grade dyskaryosis on cytological testing was unequivocal; the cytopathologist strongly recommended a



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Table 1 Summary of the four LLETZ procedures undergone by the patient

Patient's age	Screening indication for performing LLETZ	Purpose of LLETZ	Histopathology of loop excision
28	Cytology: high-grade dyskaryosis (moderate) Colposcopic impression: visible transformation zone and circumferential, medium-sized lesion Biopsy: high-grade CIN 2 HPV status: unknown	Therapeutic	High-grade CIN 3 Depth LLETZ: 5 mm Completeness: clear resection margins
30	Cytology: high-grade dyskaryosis (moderate) HPV status: (unknown) Colposcopic impression: equivocal transformation zone, no visible lesion in cervix or vagina Biopsy: no biopsy taken—see and treat	Diagnostic	No CIN present Depth LLETZ: 4 mm Inflammatory changes suggestive but not diagnostic of HPV
33	Cytology: high-grade dyskaryosis (moderate) HPV status: high-risk HPV Colposcopic impression: equivocal transformation zone, no visible lesion cervix or vagina Biopsy: no biopsy taken—see and treat Discussed by colposcopy MDT	Diagnostic	No CIN present Depth LLETZ: 5 mm
33	Cytology: high-grade dyskaryosis (severe) HPV status: high-risk HPV Colposcopic impression: equivocal transformation zone, no visible lesion Biopsy: biopsy taken—inadequate specimen size Discussed by colposcopy MDT	Diagnostic	High-grade CIN 2 Depth LLETZ: 11 mm Completeness: unclear resection margins

CIN, cervical intraepithelial neoplasia; HPV, human papilloma virus; LLETZ, large loop excision of the transformation zone; MDT, multidisciplinary team.

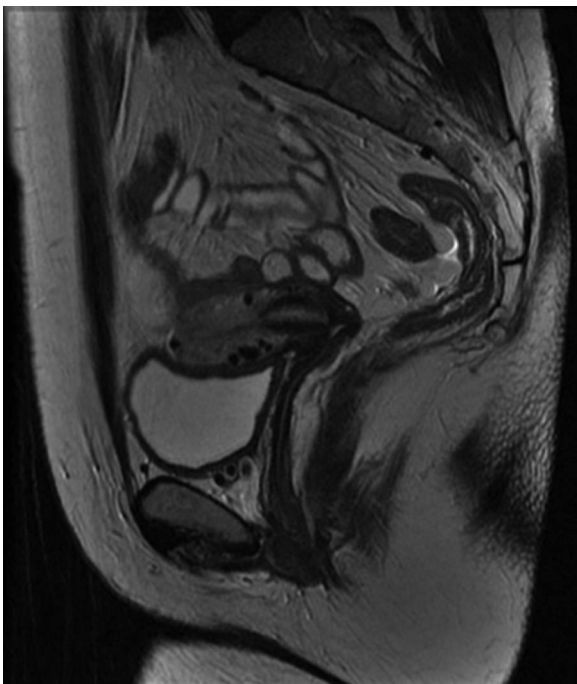


Figure 1 MRI of the pelvis, showing minimal cervix tissue remaining.

further excision. The patient was examined under general anaesthetic and had MRI of her pelvis (figure 1), to define anatomy and exclude an infiltrative lesion.

The MRI showed no vaginal cervix remaining, with 1.5 cm of cervical residuum superior to the vagina, with no evidence of malignancy.

TREATMENT

At examination under anaesthetic, further LLETZ or cold knife cone biopsy was deemed surgically unsafe, due to the risk of damaging surrounding anatomical structures. These risks outweighed the low likelihood of success in returning cytology to

normal, given the outcome of the previous LLETZ. However, persistent high-grade dyskaryosis suggested the presence of CIN above the level visible. The team and patient agreed that the risk of untreated CIN III, or the possibility of occult malignancy, was too great to continue cytological surveillance without treatment.

When there is no vaginal cervix and no vaginal disease, it is common practice to offer a hysterectomy to diagnose and treat residual CIN with a high expectation of cure.⁸ In this case, hysterectomy was unsuitable, given this individual's desire to retain fertility.

The patient had a growing desire to find a more definitive treatment that would alleviate the anxiety caused by repeated recall and LLETZ, and allow her to begin a family, with reduced obstetric risk. The recommended option was SVT and cerclage, made on the rationale that less invasive treatments had been exhausted, the patient had high risk of CIN and the significant risk of preterm labour due to her previous LLETZ (total depth 25 mm).² Based on a limited evidence base extrapolated from cancer treatment, SVT and cerclage appeared to offer an expedient way of treating underlying CIN, while mitigating the current and subsequent increased risk of preterm labour. It was decided that RVT (involving additional parametrectomy) represented overtreatment, with an unnecessary potential increase in morbidity, because the suspicion of frank cancer was low and the MRI reassuring against a macroscopic tumour that would require wider resection margin. The decision to simultaneously perform cerclage was an alternative to inserting an abdominal cerclage during pregnancy, which has greater operative risk.⁹

OUTCOME AND FOLLOW-UP

The SVT was completed without incident. In brief, the vagina was circumscribed lateral to the residual cervix, and the pouch of Douglas opened with the uterosacral ligaments, descending uterine vessels and transection of the cervix occurring at the level of the isthmus. A 5 mm Mersilene tape was inserted as a continuous cerclage over a 4 mm dilator with the knot positioned posteriorly, and the vagina reanastomosed to the uterus

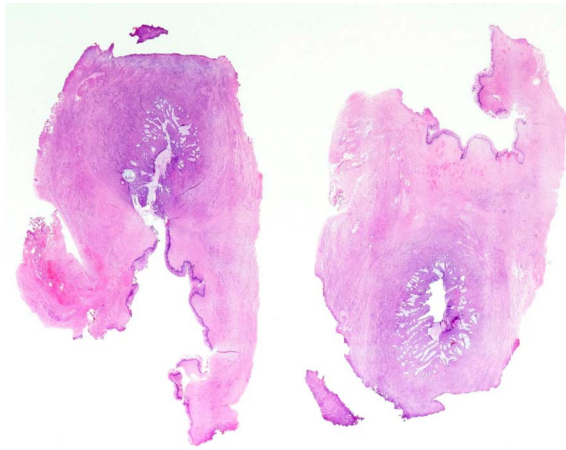


Figure 2 H+E section illustrating the cross-sectional and sagittal profile of the final specimen, and a short vaginal cuff.

via Sturmdorf sutures. The final specimen showed no CIN (figure 2). The patient was advised to wait for a minimum of 3 months before trying for pregnancy, though informed of guidelines recommending pregnancy delay for 6 months after surgery to enable adequate healing.¹⁰ At 6 months, the patient had suffered no dyspareunia and no dysmenorrhoea, passed a test of cure with no evidence of dyskaryosis or HR HPV, and had been returning to routine cervical screening every 3 years. Seven months postoperatively, she conceived naturally. A consultant obstetrician reviewed her at 9 weeks gestation and a plan was made, in the absence of other risk factors, for a consultant review at 34 weeks and for an elective caesarean section at 37 weeks, with steroid cover. The use of progesterone pessaries was discussed and the patient elected not to use these. At 29 weeks, she presented with sepsis of unknown origin, which was effectively treated with intravenous antibiotics. She received a steroid course and magnesium sulfate, although threatened preterm labour did not ultimately occur. A growth scan at this point was normal. The baby was delivered by planned lower-segment caesarean section at 37 weeks. The patient is currently in good health, with a healthy 18-month-old child.

DISCUSSION

This patient's case provides a learning opportunity to evaluate the current evidence base supporting management planning for heavily pretreated women with persistently abnormal cytology, where colposcopy is uninformative and fertility is desired.

The accepted minimum depth of LLETZ is 7 mm, or 4–5 mm beyond the affected area.¹¹ The first three treatments for this woman were relatively shallow (4–5 mm). This could have been a cause of treatment failure, although more shallow excisions in diagnostic procedures may be appropriate in order to avoid a priori deeper excisions. Evidence shows that it is depth of excision rather than number of treatments that correlates with obstetric risk, and so subsequent LLETZ treatment does not present unjustified risk.²

A complete multidisciplinary review of this patient's samples revealed no reporting errors, but multidisciplinary review was only undertaken before starting her third treatment, and it could be argued that this should occur earlier in these cases, to reduce the risk of acting on overcalled samples.¹² While repeating HR HPV testing at the time of management would likely have been positive, thus supporting the decision to treat,¹³ the

implications of a negative result would have been unclear. False negatives may occur in <1% of cases,¹⁴ but even a true negative in this clinical context would have failed to reassure the patient and address her anxieties. Therefore, HR HPV testing in similar situations should be individualised, and remains outside of the ABC benchmarking standards.¹⁵

A review of the current literature supporting the use of SVT in this context was undertaken, which produced no results. The entire evidence base, regarding the evolving role for simple trachelectomy, studies SVT as an alternative treatment option to RVT in early stage carcinoma. Multiple reviews and retrospective studies offer widespread agreement that for selected cervical tumours (<2 cm in size, with no lymphovascular space invasion) there is low risk (0.6–3%) of parametrial involvement, with SVT offering a potentially equivalent oncological outcome.^{16–19} However, a Cochrane review by Kokka *et al*²⁰ suggested that no conclusions regarding effectiveness and safety could be confidently reached due to the absence of randomised trials. In the context of carefully assessed cervical premalignancy where parametrial and vaginal margins are not relevant, the authors would extrapolate that SVT represents a safe alternative to simple hysterectomy, in the same way that RVT offers a safe alternative to radical hysterectomy for small 1b1 cervical tumours. The only guidelines the authors are aware of that discuss the role of trachelectomy in the context of treating CIN are by the Pan Birmingham Cancer Network.¹⁰ These advocate that cases of persistent CIN and absent vaginal cervix as a result of previous treatments may provide an indication for SVT as a fertility-sparing treatment.

In light of the importance of fertility preservation and pregnancy for this patient, the literature was reviewed regarding these outcomes following SVT. Four published studies and two conference abstracts detail the obstetric outcomes of women who have undergone SVT to treat early stage cervical malignancy, with no evidence base regarding SVT for the treatment for CIN. The two main obstetric risks identified were infertility and preterm labour. These risks are likely to be similar in SVT treatment for CIN if no fundamental physiological and anatomical differences exist between cervixes treated similarly for different conditions.^{3 5–7 21 22}

Stenosis of the neocervix is a SVT risk that may affect fertility; the magnitude of this risk is poorly defined in the literature, due to the numbers reported.^{3–7} Studies have suggested that cerclage increases the likelihood of cervical stenosis and associated post-operative dysmenorrhoea.^{3 4 23} We concluded that, across the four studies, there was no association; stenosis occurred irrespective of whether cerclage was inserted. Cervical stenosis does not necessarily result in infertility, and may be avoidable, depending on the technique employed.^{6 24} The overall calculable infertility rate of 17.9% in motivated women is only marginally higher than in the general population,^{3 6 7} and this figure may have been affected by factors not applicable to this case, such as radiotherapy treatment.

Trachelectomy removes the cervix, and so predisposes preterm labour due to the increased risk of ascending infection leading to premature rupture of membranes (PROM), approximately one-third of births following trachelectomy occur before 37 weeks gestation.^{3–7 25} Rob *et al* advocate the use of prophylactic antibiotics during pregnancy to minimise this risk, as the only case of PROM in their study occurred when antibiotic prophylaxis was ignored.⁷ Other authors do not concur; infection was not listed as a complication in the other three studies where antibiotics were not administered and, in Rob *et al*'s case, there may have been other confounding factors that predisposed to a poorer outcome.^{5–7} Regarding ascending infection, it is

now thought that cerclage can decrease preterm delivery primarily by acting as a barrier protecting against uterine infection, rather than providing structural strength.⁹

Though it is standard practice to insert a cerclage vaginally at the time of SVT or RVT, there is no agreement across the obstetric literature as to whether this might represent the optimal timing or route when compared to interval abdominal cerclage to prevent or treat obstetric complication. In two of the four studies discussed, cerclage was routinely cited, and was associated with delivery at term in 8/8 cases, although this is too small a sample to draw significant conclusions from.^{6 7}

Regarding our patient's obstetric course, a light touch was adopted in this case. There is no consensus as to the correct way to manage such pregnancies, and a full discussion of the options is beyond the scope of this report. In this high-risk group, options might include cervical imaging, regular consultant review with growth scanning and the routine prophylactic use of steroids at 34 weeks.

For women such as this patient, who already face considerably increased pregnancy risks, a current evidence base for SVT to treat CIN is absent; however, promising extrapolations from cancer treatment may be made with caveats. In the studies discussed, fertility was retained in most women; and assisted fertility was possible in some cases with postoperative stenosis. The risk of preterm labour may be offset by prophylactic antibiotics and/or cerclage, but randomised studies are essential before these preventative measures can be confidently recommended.

Learning points

- ▶ A focus on minimising the obstetric impact of colposcopic interventions is necessary and complicated cases should be reviewed by the multidisciplinary team, to prevent inappropriate overtreatment.
- ▶ On the basis that depth of large loop excision of the transformation zone is proportional to the risk of preterm labour, it is important to maintain good procedural technique balancing adequate depth while limiting the unnecessary removal of healthy tissue.
- ▶ Simple vaginal trachelectomy (SVT) in selected women with early stage cervical cancer shows promise as a safe fertility-sparing treatment. This case shows that SVT may be considered to treat repeatedly abnormal cervical cytology where excision biopsies have been exhausted, and where the synchronous insertion of a cerclage is desired.

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Competing interests None declared.

Patient consent Obtained.

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