



Routine Histopathological Analysis of Non-suspicious Looking Foreskin for Adult Patients: Is It Necessary?

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Authors' contributions

This work was carried out in collaboration between all authors. Author NK designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author LK managed the analyses of the study. Author ASB managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Objective: To evaluate the routine histopathological analysis of foreskin in adult patients and determine whether histological processing is necessary in patients with non-suspicious foreskin.

Materials and Methods: All adult foreskin sent for histopathological analysis between September 2014 and February 2016 at a single institution (Leighton hospital) was included in this study. Histology was compared to macroscopic appearances. A cost analysis was performed.

Results: There were 262 specimens of foreskin sent for histopathological analysis between September 2014 and February 2016. The average age for patients was 48.5 years. Most cases showed chronic inflammation, (n=110, 42%). No cancer was identified in macroscopically non-suspicious looking foreskin. Clinically diagnosed balanitis, xerotica obliterans and suspicious looking foreskin was predictive of histological abnormality.

Conclusion: Sinister pathology was not identified in non-suspicious specimens. We recommend that foreskin of patients with a high risk for penile malignancy, and macroscopically abnormal looking foreskin should always be sent for histological analysis.

Keywords: Circumcision; histopathology; abnormal; foreskin; cancer.

1. INTRODUCTION

The incidence of adult circumcision is increasing worldwide. This increase is multifactorial. One explanation a decline in paediatric circumcision, with an increase in requests for circumcision by adult patients [1-6]. Some urologists tend to send all excised foreskin for histological analysis, yet some clinicians send only abnormal suspicious looking foreskin for histopathological assessment [7]. Analysis of abnormal looking foreskin might demonstrate balanitis xerotica obliterans, inflammatory changes, or cancer [8-11]. Previous studies have suggested a relationship between chronic inflammation from phimosis, and a subsequent risk for penile cancers. This might explain an increase in circumcisions being performed in the adult population [12]. However, the possibility of identifying an early stage of penile cancer by routine histological assessment of macroscopically non-suspicious foreskin following circumcision is not known, likely to be extremely low, expensive, and offer no clinical advantage.

Penile cancer is a rare condition, and risk factors are emerging, but include immunosuppression, occupational risk factors, age, smoking, HIV and HPV. Genetic and environmental factors influence individual risk and a patient centred approach to sending foreskin for analysis should always be employed. Circumcision was performed at least as early as the ancient Egyptian period (1300 BCE) and involves removal of the foreskin of the penis. Various surgical techniques are used, and clinical presentation largely dictates the surgical approach taken. Moreover, circumcision may be performed for clinico-pathological, religious and cosmetic reasons in adults, and therefore the population is heterogenous. In our study we solely included NHS patients undergoing circumcision as adults. We hypothesised that non-suspicious looking foreskin would not predict sinister pathology at histological examination. Indeed, abnormal appearances of foreskin, whether inflammatory, BXO or otherwise should always raise clinical suspicion for abnormal histological results. We analysed all foreskin from

a single centre in the United Kingdom and examined histological outcomes. Suspicious macroscopic appearance was correlated to histopathological assessment. We also examined the cost of sending non-suspicious looking foreskin.

2. METHODS

We retrospectively reviewed all histology results for foreskin taken from adult patients undergoing circumcision between September 2014 and February 2016 at Leighton hospital, Mid-Cheshire NHS trust.

We correlated macroscopic outcomes to histological outcomes in all patients. We provide descriptive data from our cohort, for all pathology found in the sample. All foreskin from our centre was sent for analysis within the data collection period and was reviewed by a senior consultant pathologist. A cost analysis of analysing all foreskin was also undertaken due to the nature of NHS budget requirements.

3. RESULTS

There were 262 foreskin specimens available for analysis, obtained from adult circumcisions between September 2014 and February 2016 at Leighton hospital, Mid-Cheshire NHS Trust. The most common indications (clinical diagnoses) for circumcision were recurrent balanoposthitis (71%, n=188) tight foreskin (46.5%, n=122), and suspicious of BXO (16%, n=42)

The mean age for patient was 48.5 years. One hundred and six cases (40%) showed inflammatory changes, whilst 42 (16%) had histologically confirmed lichen sclerosis. There was no cancer identified in one hundred and ten patients (42%), all of whom had non-suspicious looking foreskin. Four patients (1.5%) had suspicious looking foreskin and histopathological analysis showed SCC. In our sample, clinical BXO had a disease prevalence of 15.08% (95% CI 10.41% to 20.82%), a sensitivity of 50.00% (95% CI 31.30% to 68.70%) for histological BXO, a specificity of 88.76% (95% CI 83.00% to 93.09%), negative predictive value of 90.91%

(95% CI 87.44% to 93.49%) and accuracy of 82.91% (95% CI 76.95% to 87.87%). Clinical phimosis with a suspicion of cancer was 100% predictive of abnormal histological results in our sample for any age, with 4 cases of SCC identified.

Table 1. Diagnosis at histology and incidence in cohort

Diagnosis	Number of cases	Percentage (%)
Non-suspicious	110	42
Inflammation	106	40.5
lichen sclerosis	42	16
Carcinoma	4	1.5

Table 2. Indications for circumcision within sample

Indication	Number of cases
Balanitis	188
Phimosis	122
BXO	42
Paraphimosis	6
Ulcer	3
Warts	1

4. DISCUSSION

This study was performed to determine whether histology obtained from circumcision is useful in identifying sinister pathology in the instance of non-suspicious macroscopic appearance.

This only applies to individuals at low risk for penile cancer with non-suspicious foreskin. Our data demonstrates routine analysis of circumcision specimens for histopathological assessment is not required, and does not alter clinical management. The indications for circumcision in our study are consistent with previous studies, and inflammation was the commonest finding [13-23]. We suggest that the pathologic analysis of non-suspicious foreskin

tissue may be avoided to reduce unnecessary spending.

Notably, case reports of occult penile cancer identified in patients with BXO [22-24]. In our cohort, for cases where penile cancer was not suspected, no sinister pathology was identified. Consequently, it may be necessary for clinicians to selectively send specimens for analysis from individuals at a higher risk for malignancy. Stratifying patients by only sending abnormal looking foreskin may provide cost-savings without diminishing the quality of care and long term pathological outcomes.

This study has several limitations as a retrospective single centre study dependent on documentation. The incidence of occult penile cancer may vary geographically and therefore we recommend local audit of results for all centres to determine, at this stage, whether non-suspicious foreskin may be selectively discounted from costly and unnecessary histological processing. Patients with significant risk factors were not stratified in our analysis, and therefore a risk stratified analysis would be informative when making large scale public health decisions based on which foreskin may be sent for analysis. To this end, large, multi-centre studies are required to construct robust, safe and efficient clinical guidelines.

Considering mounting cost containment pressures within the NHS, the use of clinical resources must be scrutinized. There are at least 10,000 adult circumcisions in England per year, and we estimate the cost around £250 per case, redundant histopathological analysis of non-suspicious looking foreskin represents a huge cost to NHS England and should be scrutinised. There is an additional opportunity cost to current practice in that clinical workload currently is taken up by processing and reporting specimens unnecessarily [25,26].

Box 1. Risk factors for penile malignancy

Age
Immunosuppression
HPV infection with high risk strain
Abnormal looking foreskin eg/ BXO
Previous SCC
Occupational risk (petrochemical, coal and sex work industries)

5. CONCLUSION

There was no benefit in our single centre small study in sending non-suspicious looking foreskin for histopathological analysis. Significant cost savings could be made from only sending appropriately selected foreskin for analysis. We recommend sending foreskin of patients with abnormal looking foreskin / suspicious looking foreskin or high risk for penile malignancy to histological analysis.

CONSENT

As per international standard or university standard written patient consent has been collected and preserved by the authors.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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