

Original Article

Penile Pathomorphologic Entities Seen at A Tertiary Health Facility

Innocent Emmanuel^{1,2}, Philip Ojile Akpa^{1,2}, Barka Vandi Kwaghe¹, Chikwendu Amaike³, Sa'a Jummai Wennie⁴, Tabitha Leslie⁴, Christiana Nwanneka Ibeanu¹, Othman Ishaku Agahu¹, Nanisi Zorto Bahaush¹, James Eveshojiame Ben¹, Emmanuel Jacob Anzaku¹, Lemeche Ezra Nabasu⁵, Titus Nansok Fadok⁶, Barnabas Mafala Mandong^{1,2}.

¹Department of Anatomic Pathology and Forensic Medicine, Jos University Teaching Hospital, Nigeria, Jos, Plateau State, Nigeria, ²Department of Pathology, University of Jos, Jos, Plateau State, Nigeria, ³Department of Community Medicine, Babcock University and Babcock University Teaching Hospital, Illishan Remo, Ogun State, Nigeria, ⁴Department of Nursing Science, Babcock University and Babcock University Teaching Hospital, Illishan Remo, Ogun State, Nigeria, ⁵Nisa Premier Hospital Abuja. ⁶Department of Histopathology, Federal Medical Center Jalingo, Taraba State, Nigeria

ABSTRACT

Introduction: The human penis is a cylindrical cucumberlike external organ that “stands tall,” defining the phenotypic male. The diseases of the penis are rife and may impact heavily on psychosocial well-being of a man. The aim of this research is to study the clinical and histologic patterns of all penile biopsies received at a Nigerian tertiary hospital over a 10-year period. **Methods:** The work was a descriptive study of all histologically diagnosed cases of penile pathologies seen at the Jos University Teaching Hospital between 1st January 2003 and December 31st, 2022. The age, clinical characteristics (site and symptoms) and histological diagnosis were obtained from the records. The data obtained was entered into Microsoft excel and then exported into Statistical Package for Social Sciences (SPSS) 2016, and presented on frequency tables as proportions, simple frequencies, percentages, range, and measures of central tendencies. **Results:** There were 14 histologically diagnosed cases of penile pathologies during the period of the study. The age range was 1-71 years, with a mean age of 28.64±23.11 years. The commonest diagnostic entity was verrucae (condyloma acuminata) accounting for 6(42.9%) cases while Neurofibroma was the least with 1 (7.1%) case. The symptoms of a mass, itching, pain, and ulceration were seen in these patients. The presence of a mass was the symptom with the highest frequency while ulceration had the least frequency. All cases seen were circumcised males. **Conclusion:** This study showed that most histo-pathologically diagnosed penile diseases in our environment are due to pathologies related to sexually transmitted infections with the HPVs, the condyloma acuminata and squamous cell carcinoma. This calls for preventive strategies targeting vulnerable groups amongst our population to control the onset or progression of these histopathological entities on such an important organ.

Keywords: Penis, Warts, Cancer, Inclusion cyst, Neurofibroma.

INTRODUCTION

The human penis is a cylindrical cucumberlike external organ that “stands tall,” defining the phenotypic male. It is located in the urogenital triangle,

a geographical area between the deep perineal fascia inferiorly and the perineal membrane superiorly, and is made of three cylindrical sponges, the corpus spongiosum and the paired corpora cavernosa.¹ It is covered by the penile skin and subdivided into the root (radix), the body (corpus), and the glans (Head),^{1,2} and while erect measure 13.12 cm (5.17 inches) long, and 11.66 cm (4.59 inches) in circumference.³ It serves three very important functions: sexual intercourse, giving sexual satisfaction; intromission, placing

Correspondence:

Dr. Innocent Emmanuel.
Department of Anatomic Pathology and Forensic Medicine,
Jos University Teaching Hospital, and Department of Pathology,
University of Jos, Jos, Plateau State, Nigeria. P.M.B. 2084, Jos.
E-mail: kinapele58@yahoo.com

spermatozoa within the vagina; and micturition, voiding out urine through the urethra.^{2,4}

The diseases of the penis are rife and runs a whole gamut: congenital, inflammatory/immunologic, traumatic, and neoplastic.^{5,6} These diseases which might affect the size, shape, or function of the penis impacts heavily on psychosocial well-being of a man.^{7,8,9} As an organ solely dedicated to sexual activities to achieve numerous goals, it is significantly affected by sexually transmitted diseases. On a daily basis, above 1million estimated sexually transmitted diseases are contracted.¹⁰ In 2016, more than 490 million persons were living with herpes of the genitalia.¹⁰ In 2020, a staggering 370 million new infections were reported for just four microorganisms: Syphilis (7.1 million), gonorrhea (82 million), chlamydia (129 million), and trichomoniasis (156 million).¹⁰ The aim of this research is to study the clinical and histologic patterns of all penile biopsies received at the Anatomic Pathology and Forensic Medicine Department of a Nigerian tertiary hospital over a 20 years period.

METHODS

The work was a descriptive study of all histologically diagnosed cases of penile pathologies seen at the Jos University Teaching Hospital between 1st January 2003 and December 31st, 2022. The medical records (data) of patients were obtained from the Anatomical Pathology and Forensic Medicine Department and the Medical Health Records Department of the Hospital. These records were the histopathological reports and folders. Patients with histological diagnosis of penile pathologies were included, while those with inadequate sociodemographic feature (age), clinical information, missing archival slides and tissue blocks were excluded from the study. The age, clinical characteristics (site and symptoms) and histological diagnosis were obtained from the records.

The histologic diagnosis was used to trace archival slides which were retrieved and reviewed to confirm the histological diagnosis, with concordance from at least two anatomic pathology consultant authors in this study. The few variations were harmonized in a joint session. Cases of missing or broken slides were addressed by making new slides from archival tissue blocks. The procedure of making new slides included: cutting of embedded tissue blocks to a thickness of 3micrometres and picking on a glass slide after floating in a warm water bath; immersion in xylene and incubation for 15minutes; immersion of slides in equal portions of xylene and ethanol (xylene: ethanol ratio of 1:1) for 5minutes; immersion in 100% ethanol for 5minutes, then 95%, 85%, 75%, 65% and 55% ethanol, each for 3minutes; rinsing in distilled water for 5minutes; and staining with hematoxylin and eosin.

The data obtained was entered into Microsoft excel and then exported into Statistical Package for

Social Sciences (SPSS) 2016, and presented on frequency tables as proportions, simple frequencies, percentages, range, and measures of central tendencies.

The study was limited by the fact that not all patients in Plateau State with pathologies of the penis seek care from the Jos University Teaching Hospital. Some do visit other tertiary health facilities, others will opt for traditional medical care, and yet others manage the condition at home.

RESULTS

There were 14 histologically diagnosed cases of penile pathologies during the period of the study. The age range was 1-7years, with a mean age of 28.64+23.11years. The commonest diagnostic entity was verrucae (condyloma acuminata) accounting for 6(42.9%) cases while Neurofibroma was the least with 1 (7.1%) case. Table 2. The symptoms of a mass, itching, pain, and ulceration were seen in these patients. Table 2. The presence of a mass was the symptom with the highest frequency while ulceration had the least frequency. All cases seen were circumcised males.

DISCUSSION

Condyloma acuminata (verrucae/genital warts), the commonest pathologic entity in this study and squamous cell carcinoma of the penis shared a common etiological agent and together constituted 57.1% of all cases seen. This is not surprising as the human papilloma virus is the commonest sexually transmitted infection worldwide.¹¹ Generally, the prevalence of penile HPV infection in healthy men is 16–69%,¹² and this may rise to approximately 80% in men with as much as 16 and above lifetime sexual partners.¹³ Considering that up to 57.1 of penile lesions in this study as alluded earlier are linkable to HPV infection, it calls for robust advocacy for vaccination against this agent, a potent public health measure with documented effectiveness in this regard.¹⁴

We earlier in a similar study over a 10years (2011-2020) period reported 215 histologically diagnosed pathologies of the vulva and vagina with 111 (51.6%) cases linkable to HPV (Condyloma acuminata and squamous cell carcinoma).¹⁵ Comparatively therefore, the number of HPV related biopsied and histologically diagnosed pathologies in females in our center is 13.9 times that in males. Research has demonstrated a higher infectivity rate of HPV in men than in women,^{16,17,18} however, the higher prevalence of clinical presentation with lesions in women is due to some factors amongst which is the rate of clearance.¹⁹ Although more than 90% of HPV infections are cleared, the clearance rate is higher in males.¹⁹ Also, more women present themselves for

Table 1: Distribution of penile pathologies according to measures of central tendency for age.

DIAGNOSIS	No. of Cases, N (%)	Measures of Central tendency (Years)			
		Age range	Mean ($\pm$ SD)	Median (IQR)	Mode
Inclusion Cyst	4(28.6%)	2-12	8.00 $\pm$ 4.32	9.0 (10)	2.0
Granulation Tissue	1(7.1%)	49.0	49.00 $\pm$ 0.00	49.0 (NA)	49.0
Verrucae	6(42.9%)	1-45	26.50 $\pm$ 15.23	25.0 (15)	25.0
Neurofibroma	1(7.1%)	20.0	20.0 $\pm$ 0.00	20.0 (NA)	20.0
Squamous cell ca.	2(14.3%)	70-71	70.50 $\pm$ 0.71	70.5 (1)	NA
TOTAL	14(100.0)	1-71	28.64 $\pm$ 23.11	24.5 (35)	25.0

NA= Not Applicable

Table 2: Distribution of penile pathologies according to age, site and symptoms.

DIAGNOSIS	No. of Cases	AGE (Years)								SITE			SYMPTOMS			
		<10	10-19	20-29	30-39	40-49	50-59	60-69	70-79	Glans	Shaft	Root	Mass	Itch	Pain	Ulcer
Inclusion Cyst	4(28.6%)	2	2	-	-	-	-	-	-	-	4	-	4	-	1	-
Granulation Tissue	1(7.1%)	-	-	-	-	1	-	-	-	1	-	-	-	2	1	1
Verrucae	6(42.9%)	1	-	3	1	1	-	-	-	-	6	-	6	4	-	-
Neurofibroma	1(7.1%)	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-
Squamous cell ca.	2(14.3%)	-	-	-	-	-	-	-	2	-	2	-	2	2	2	2
TOTAL	14(100.0)	3	2	3	1	2	-	-	2	1	12	-	13	8	4	3

screening and medical visits to see a physician.^{20,21} Furthermore, 100% of men in this study and 98.9% of men in Nigeria are circumcised,²² and circumcision is shown to offer some benefits over HPV.²³

The most frequently observed symptom in this study is the presence of a mass and it is the commonest symptom for the condyloma and squamous cell carcinoma, the HPV related pathologies. Both low-risk (that causes warts) and high-risk (that causes squamous cell carcinoma) HPVs downregulate growth inhibitory signals, exploiting this pathway to stimulate proliferation of cells leading to a clinically overt mass. The oncogenicity of high risks HPVs is well established,²⁴ but it is now known that low risk HPVs exist in episomal and integrated forms and similarly inhibits the tumor suppressor genes P53 and RB using the viral proteins E6 and E7 respectively.^{25,26} It has been demonstrated that the benignity of low risk HPVs is attributable to the low affinity of binding of the E6 and E7 to the tumor suppressor genes when compared to the avid binding of the high risk HPVs.²⁷ A study demonstrated the degradation of the Na⁺/H⁺ Exchanger Regulatory Factor 1 (NHERF1) by E6 proteins of both low and high risk HPVs which activates the Wnt/ β -catenin signaling.²⁸ Furthermore, another study found that E6 proteins of low risk HPVs degrades the proapoptotic molecule BAK thereby providing a growth advantage for infected epithelial cells.²⁹ Low risk HPVs have also been implicated in the causation of neoplasia in immunocompromised individuals.²⁶ Two of these neoplasms are the Epidermodysplasia Verruciformis and the Recurrent Respiratory Papillomatosis.²⁶

The finding of penile warts in early years of life and squamous cell carcinoma in later life supports the

theory of tumor progression in which a stepwise acquisition of driver mutations over time facilitates the acquisition of the molecular hallmarks of cancer.³⁰ A study showed mutations in PIK3CA, KRAS, HRAS, NRAS, and PDGFA genes in both P53 and non P53 expressing penile cancers.³¹ Another study identified 11 genes to include the already known FAT1, HRAS, NOTCH1, TP53 and PIK3CA and new genes, CASP8, SLITRK2 and TRRAP.³² Other genes include: CDKN2A, MYC and EGFR.³³ A study found 76 patients with penile cancer having an average age of 66 years $\pm$ 17.10; 98.68%, all being squamous cell carcinoma; and 63.15% HPV related, mostly the high risk HPV.^{16,34} Similarly, and in tandem with our finding of advance age for penile cancer, a study of 116 patients with penile carcinoma found an average age of 60.4 $\pm$ 16.51 years in which 100% were squamous cell carcinomas.³⁵ Also a younger mean age was reported for genital warts in studies by Motazedian et al,³⁶ 28.84 $\pm$ 8 years, and Cho et al,³⁷ 32.63 $\pm$ 12.78 years.

The penis is a rare site for the occurrence of epidermal inclusion cyst.³⁸ In this location, it could be primary (congenital) owing to the abnormal closure of the median raphe during intrauterine growth,^{39,40} or secondary to trauma with surgical intervention likely for circumcision or correction of hypospadias the major culprits.^{39,41} In this study, all cases were circumcised males. A rate of 0.0015% has been reported for the development of inclusion cyst following circumcision in a study of 1,900 circumcised males.⁴² The commonest symptom of presence of a painless mass for inclusion cyst was corroborated by a study with 11 cases of post circumcision and 10 cases of post hypospadias repair.⁴³ Of great concern is the mass so formed to mimic another pathology. A mimic of ectopic testes, and cancer have been reported.^{38,44} In our study, the intervention was early

as the age range was 1years to 12years for epidermal inclusion cyst. This is necessary to forestall complications as was seen in a report of a 32years old who develop intra-cystic stones and urethra-cutaneous fistula.⁴⁵ Another rare disease of the penis is neurofibroma with a case seen in this study and several reports published documenting its different histologic subtypes and clinical presentation.⁴⁶⁻⁵⁰

As stated earlier this study is limited by the fact that not all cases of penile pathologies present to the hospital. A combination of factors has been shown to contribute this. Chalya et al attributed delays in presentation of penile cancer to the hospital to ignorance and sociocultural taboos.⁵¹ Indeed, there is a significant emotional, psychological, and social sequela accompanying penile HPV related disease.⁵² There is therefore a need to beat these barriers in a bid to improve the control of the disease.

CONCLUSION

This study showed that most penile diseases in our environment are due to pathologies related to sexually transmitted infections with the HPVs, the condyloma acuminata and squamous cell carcinoma. This calls for preventive strategies targeting vulnerable groups among our population to control the onset or progression of these histopathological entities on such an important organ.

REFERENCES

1. Sam P, LaGrange CA. Anatomy, Abdomen and Pelvis, Penis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Retrieved on 21/07/2023 from: <https://www.ncbi.nlm.nih.gov/books/NBK482236/>
2. Thalanjeri P, Jain R. A Study on Male Reproductive System and Male Hormones. *Reprod Syst Sex Disord*. 2022; 11:321.
3. Veale D, Miles S, Bramley S, Muir G, Hodson J. Am I normal? A systematic review and construction of nomograms for flaccid and erect penis length and circumference in up to 15 521 men. *BJU Int*. 2015;115(6):978–986. doi:10.1111/bju.13010.
4. Kelly DA. The Functional Morphology of Penile Erection: Tissue Designs for Increasing and Maintaining Stiffness, Integrative and Comparative Biology 2022; 42(2):216–221. doi.org/10.1093/icb/42.2.216
5. World Health Organization. Diseases of male genital organs (N40–N51). International statistical classification of diseases and related health problems, 10th revision. Fifth edition. 2016; ICD-10:624–627.
6. Netto GJ, Amin MB. In: Kumar, V., Abbas, A. and Aster, J. The lower urinary tract and male genital system. Robbins and Cotran Pathologic Basis of Diseases. 10th Edition. Amsterdam: Elsevier; 2020. p. 953–983.
7. Prause N, Park J, Leung S, Miller G (2015). Women's Preferences for Penis Size: A New Research Method Using Selection among 3D Models. *PLoS ONE* 10(9): e0133079. doi:10.1371/journal.pone.0133079
8. Schover LR. Psychological factors in men with genital pain. *Cleve Clin J Med* 1990;57:697–700.
9. Audenet F, Sfak JP. *Transl Androl Urol*. 2017;6(5):874–478. doi.org/10.21037/tau.2017.0
10. WHO. Sexually transmitted infections (STIs). World Health Organization, 2022. Retrieved on 21/06/2023 from: [https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-\(stis\)](https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis))
11. Kombe KAJ, Li B, Zahid A, Mengist HM, Bounda G, Zhou Y, et al. Epidemiology and burden of Human Papillomavirus and related diseases, molecular pathogenesis, and vaccine evaluation. *Front Public Health*. 2021;8:552028. doi.org/10.3389/fpubh.2020.552028
12. Diorio GJ, Giuliano AR. The role of human papilloma virus in penile carcinogenesis and preneoplastic lesions: a potential target for vaccination and treatment strategies. *Urol Clin North Am*. 2016;43(4):419–25.
13. Deshmukh AA, Tanner RJ, Luetke MC, Hong YR, Sonawane DK, Mainous AG. 3rd prevalence and risk of penile human papillomavirus infection: evidence from the National health and nutrition examination survey 2013–2014. *Clin Infect Dis*. 2017;15;64(10):1360–1366. doi:10.1093/cid/cix159. Erratum in: *Clin Infect Dis*. 2017;15;65(8):1431–1433.
14. Falcato M, Castañon A, Ndlela B, Checchi M, Soldan K, Lopez-Berna J, et al. The effects of the national HPV vaccination programme in England, UK, on cervical cancer and grade 3 cervical intraepithelial neoplasia incidence: a register-based observational study. *Lancet* 2021; 398: 2084. doi.org/10.1016/S0140-6736(21)02178-4
15. Emmanuel I, Akpa PO, Yakubu D, Yakubu EN, Otene BS, Dallang BC, et al. a clinicopathological study of vulvo-vaginal disease at a Nigerian tertiary health facility. *West Afr J Med*. 2023;40(3):241–246. PMID: 37017190.
16. Rezaee Azhar I, Yaghoobi M, Mossalaei MM, Kollaei Darabi A, Nejadeh AH, Jamshidi M, et al. Prevalence of human papilloma virus (HPV) genotypes between outpatients males and females referred to seven laboratories in Tehran, Iran. *Infect Agents Cancer* 2022;17(1):7. doi.org/10.1186/s13027-022-00421-7
17. Palefsky JM. Human papillomavirus infections: Epidemiology and disease associations. Retrieved on 24/07/2023 from: <https://www.uptodate.com/contents/human-papillomavirus-infections-epidemiology-and-disease-associations>
18. Garutti P, Montori S, Bazzan E, Tarabba C. Gender differences in the epidemiology and prevention of human papillomavirus (HPV) and HPV-related diseases. *Ital J Gender-Specific Med* 2018;4(4):152–161.
19. Bosch FX, Broker TR, Forman D, Moscicki AB, Gillison ML, Doorbar J, et al. Comprehensive control of human papillomavirus infections and related diseases. *Vaccine* 2013;22:31–38.
20. Medscape.com [Internet]. New York: WebMD LLC. c1994–2018. Retrieved on 24/07/2023 from: <https://emedicine.medscape.com>
21. Giuliano AR, Anic G, Nyitray AG. Epidemiology and pathology of HPV disease in males. *Gynecol Oncol* 2010;117:15–19.
22. Morris BJ, Wamai RG, Henebeng EB, Tobian AA, Klausner JD, Banerjee J, et al. Estimation of country-specific and global prevalence of male circumcision. *Popul Health Metr*. 2016;14(4):1–13. doi:

- 10.1186/s12963-016-0073-5. Erratum in: *Popul Health Metr.* 2016;14:11.
23. Rehmeier CJ. Male Circumcision and Human Papillomavirus Studies Reviewed by Infection Stage and Virus Type. *J Osteopathic Med.* 2011;111 (32):11-18. <https://doi.org/10.7556/jaoa.2011.20024>
24. Hewavisenti RV, Arena J, Ahlenstiel CL, Sasson SC. Human papillomavirus in the setting of immunodeficiency: Pathogenesis and the emergence of next-generation therapies to reduce the high associated cancer risk. *Frontiers in Immunology*, 2023;14. doi: 10.3389/fimmu.2023.1112513
25. Oh ST, Longworth MS, Laimins LA. Roles of the E6 and E7 proteins in the life cycle of low-risk human papillomavirus type 11. *J Virol.* 2004;78(5):2620-6. doi: 10.1128/jvi.78.5.2620-2626.2004.
26. Egawa N, Doorbar J. The low-risk papillomaviruses. *Virus Research.* 2017; 231: 119-127. doi.org/10.1016/j.virusres.2016.12.017.
27. Yim EK, Park JS. The role of HPV E6 and E7 oncoproteins in HPV-associated cervical carcinogenesis. *Cancer Res Treat.* 2005;37(6):319-24. doi: 10.4143/crt.2005.37.6.319.
28. Drews CM, Case S, Vande Pol SB. E6 proteins from high-risk HPV, low-risk HPV, and animal papillomaviruses activate the Wnt/ β -catenin pathway through E6AP-dependent degradation of NHERF1. *PLOS Pathogens* 2019; 15(4): e1007575. doi.org/10.1371/journal.ppat.1007575
29. Underbrink MP, Dupuis C, Wang J, Tying SK. E6 proteins from low-risk human papillomavirus types 6 and 11 are able to protect keratinocytes from apoptosis via Bak degradation. *J Gen Virol.* 2016;97(3):715-724. doi: 10.1099/jgv.0.000392.
30. Netto GJ, Amin MB. The lower urinary tract and male genital system. In: Kumar, V., Abbas, A. and Aster, J. (2020) *Robbins and Cotran Pathologic Basis of Diseases*. 10th Edition. Elsevier: Amsterdam; 2020. P. 951-983.
31. Ferrándiz-Pulido C, Hernández-Losa J, Masferrer E, Vivancos A, Somoza R, Marés R, Valverde C, Salvador C, Placer J, Morote J, Pujol RM, Ramon y Cajal S, de Torres I, Toll A, García-Patos V. Identification of somatic gene mutations in penile squamous cell carcinoma. *Genes Chromosomes Cancer.* 2015;54(10):629-37. doi: 10.1002/gcc.22274
32. Wang Y, Wang K, Chen Y, Zhou J, Liang Y, Yang X. Mutational landscape of penile squamous cell carcinoma in a Chinese population. *International Journal of Cancer* 2019; 145(5):1280-1289. <https://doi.org/10.1002/ijc.32373>
33. Ribera-Cortada I, Guerrero-Pineda J, Trias I, Veloza L, Garcia A, Marimon L, et al. Pathogenesis of Penile Squamous Cell Carcinoma: Molecular Update and Systematic Review. *International Journal of Molecular Sciences.* 2022; 23(1):251. <https://doi.org/10.3390/ijms23010251>
34. de Sousa IDB, Vidal FCB, Branco Vidal JPC, de Mello GCF, Mascimento MDB, Brito LMO. Prevalence of human papillomavirus in penile malignant tumors: viral genotyping and clinical aspects. *BMC Urol.* 2015; 15(13):. <https://doi.org/10.1186/s12894-015-0007-8>
35. Vieira CB, Feitoza L, Pinho J, Teixeira-Júnior A, Lages J, Calixto J, et al. Profile of patients with penile cancer in the region with the highest worldwide incidence. *Sci Rep.* 2020;10(1):2965. doi: 10.1038/s41598-020-59831-5. PMID: 32076037; PMCID: PMC7031540.
36. Motazedian N, Sayadi M, Beheshti S . Genital Warts Among Men Attending a Dermatology Clinic: Risk Factors and Knowledge. *Int J High Risk Behav Addict.* 2020;9(3):e97530. <https://doi.org/10.5812/ijhrba.97530>.
37. Cho CY, Lo YC, Hung MC, Lai CC, Chen CJ, Wu KG. (2017) Risk of cancer in patients with genital warts: A nationwide, population-based cohort study in Taiwan. *PLOS ONE* 12(8): e0183183. doi.org/10.1371/journal.pone.0183183
38. Firdaus GI, Nurfajri DH, Pramod SV, Safriadi F, Hernowo BS. Penile epidermal inclusion cyst mimicking ectopic testis mass: A case report. *Urology Case Reports* 2022;40: 101962. doi.org/10.1016/j.eucr.2021.101962.
39. Giambanco A, Pensabene M, Giuffrè M, Cimador M. Epidermal inclusion cyst of the penis after urethroplasty causing an urethro-cutaneous fistula: a first case report. *Pediatr Med Chir.* 2013;35:288–289.
40. Shao IH, Chen TD, Shao HT, Chen HW. Male median raphe cysts: serial retrospective analysis and histopathological classification. *Diagn Pathol.* 2012;7:121.
41. Okeke LI. Epidermal inclusion cyst as a rare complication of neonatal male circumcision: a case report. *J Med Case Rep.* 2009;3:7321.
42. Ozkan A, Ozorak A, Oruc M. Retrospective investigation complications in nineteen hundred cases of circumcision. *Konuralp Med J.* 2012;4:8–12. <https://dergipark.org.tr/en/pub/ktd/issue/10304/126417>.
43. Yagmur I, Tekin A, Bağcı U, Yaman B, Avanoğlu A, Ulman I. Acquired Penile Epidermoid Cysts in Children. *Cureus.* 2022;14(7):e27462. doi: 10.7759/cureus.27462.
44. Cormio L, Mancini V, Sanguedolce F, Massenio P, Fucci L, Bufo P, Traficante A, Carrieri G. Epidermoid cyst of the coronal sulcus mimicking penile cancer: a case report. *J Med Case Rep.* 2014 Jun 6;8:179. doi: 10.1186/1752-1947-8-179.
45. El-Shazly M, Ghobashy A, Allam A, Alenezy T, Alenezy N, Yordanov E, et al. Penile epidermal inclusion cyst. *Case Rep Urol.* 2012;2012:191343. doi: 10.1155/2012/191343.
46. Banthia R, Yadav P, Agarwal R, Lal H. Plexiform neurofibromatosis of penis: a rare presentation of type 1 neurofibromatosis. *BMJ Case Rep.* 2020;13(11):e236542. doi: 10.1136/bcr-2020-236542.
47. Cholakkal S, V C S, Nachiketh G. Large Solitary Plexiform Neurofibroma of the Penis Without Erectile Dysfunction: a Case Report from Kerala. *Indian J Surg.* 2018;80(1):90-92. doi: 10.1007/s12262-017-1669-0.
48. Cheng S, Yang J, Zhang Y, Xu An, Dong Li, Yang G. A Rare Case of Myxoid Neurofibroma of the Penis and the Literature Review. *J Urol Nephrol.* 2021;8(1):2.
49. Hirayama T, Matsumoto K, Minami S, Nagi S, Iwamura M. Neurofibroma of the penis due to neurofibromatosis type 1: von Recklinghausen's disease. *Kitasato Med J* 2014;44:104-106.
50. Perafan-Valdes L, Giraldo-Ocampo S, Lores J, Pachajoa H. Neurofibromatosis Type 1 and Hypospadias in a Male 46, XY with a Mutation in the NF1 Gene and a Mutation in NR5A1. *Pharmgenomics Pers Med.* 2022;15:873-878. doi.org/10.2147/PGPM.S380796
51. Chalya PL, Rambau PF, Masalu N, Simbila S. Ten-year surgical experiences with penile cancer at a tertiary care hospital in northwestern Tanzania: a retrospective study of 236 patients. *World J Surg Oncol.* 2015;22(13):71. doi: 10.1186/s12957-015-0482-0.
52. Reitano M. Counseling patients with genital warts. *Am J Med* 1997;102(5A):38-43.