CLINICAL VIGNETTE

Extramammary Paget Disease of the Scrotum – Be on the Lookout

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Clinical History

A 72-year-old male initially presented with scrotal rash 5 years ago. His past medical history included stable CAD s/p stent placement, hyperlipidemia, and osteoarthritis. He was treated with several types of steroid and anti-fungal creams by his primary care doctor and Dermatology. The rash did not improve and worsened in appearance. It was eventually biopsied and proved to be Extramammary Paget disease (EMPD) of the right scrotal region. He received 2 courses of 5% Imiquimod cream, but the rash persisted. He was then treated with topical 5-FU/calcipotriene course without success. The patient was then evaluated for surgical removal of the skin cancer and underwent Moh's surgery with clear margins and followed by reconstruction. He was also advised to screen for underlying malignancy with colonoscopy and urine cytology +/- cystoscopy. Clinically, he is asymptomatic and without complaints.

Discussion

Extramammary Paget disease (EMPD) is a skin lesion characterized by a chronic eczema-like rash seen in the genitals of males and females. It's cell of origin is unclear. Most cases of EMPD occur in women between the ages of 50 to 60 and are located on the vulva and anus; EMP of the scrotum and penis is rare.[1] EMP can be associated with other malignancies anatomically close to or distant in location. It can be mistaken for common skin lesions including contact dermatitis, yeast infection, and eczema. The diagnosis is confirmed histologically after biopsy for recalcitrant lesions. This clinical presentation frequently causes significant delays in diagnosing this disease.

EMPD is rare and is a slow growing intraepithelial malignant neoplasm. It can arise as a primary cutaneous lesion or secondary to visceral malignancies, as epidermal extension of adenocarcinomas or from pluripotent stem cells.[2] This is why an aggressive search for these malignancies is advised. Associated malignancies are usually gastrointestinal or genitourinary origin. Screening these systems should be undertaken once EMPD is confirmed. Common sites of associated malignancies in males include colon, rectum, and prostate while there was no increased risk of associated malignancies in non-invasive primary vulvar EMPD.[3]

Treatment of EMPD include surgery, topical chemotherapy and radiotherapy. Wide local excision has long been regarded as the standard of management of EMPD.[3] Patients who refuse surgery or who are not candidates for surgery can be treated with radiotherapy, topical imuquimod cream, or photodynamic therapy. Currently, there are no recommended chemotherapy regimens but a variety of agents have been used including 5-FU/Cisplatin and docetaxel especially for advanced EMPD. Other treatments that have been considered include hormonal, anti-HER2 antibody, and immune checkpoint therapies. These need further evaluation.

Conclusion

EMPD of the scrotum is a rare condition and is typically observed in older men, with a mean age of 71 years at presentation.[4] Diagnosis is often delayed because of its very benign presentation. Caucasians are more often affected. The cause is unknown and risk factors are not yet established. It is imperative that non-healing scrotal skin lesions be biopsied because that is the only way to definitively diagnose. A search for associated visceral malignancies should be simultaneously.

The prognosis of EMPD depends on a variety of factors including, early diagnosis, extent of surgical margins and associated carcinoma. A higher mortality rate and poorer prognosis is seen in patients with associated carcinoma, perianal disease, invasion into dermal skin layer, and spread of cancer to lymph nodes.[5]

Long-term follow-up is needed to monitor for recurrences and development of concomitant malignancies. There is no standard monitoring protocol. Due to the rarity of this disease and limited experience, there is need for larger global studies to better understand and evaluate treatment standards.

REFERENCES

1. **Juang GD, Lin MY, Hwang TI**. Extramammary Paget's disease of the scrotum. *J Chin Med Assoc*. 2011 Jul;74(7):325-8. doi: 10.1016/j.jcma.2011.05.010. Epub 2011 Jul 13. PMID: 21783099.
2. **Shabihkhani M, Patil P, Murati Amador B, Plaza JA, Osunkoya AO, Lombardo KA, Epstein JI, Matoso A**. Extramammary Paget Disease of the Scrotum: A Contemporary Clinicopathologic Analysis of 20 Cases in the United States. *Appl Immunohistochem Mol Morphol*. 2020 Aug;28(7):524-531. doi: 10.1097/PAI.0000000000000789. PMID: 31290785; PMCID: PMC7458628.

3. **Ishizuki S, Nakamura Y**. Extramammary Paget's Disease: Diagnosis, Pathogenesis, and Treatment with Focus on Recent Developments. *Curr Oncol*. 2021 Aug 5;28(4): 2969-2986. doi: 10.3390/curroncol28040260. PMID: 34436026; PMCID: PMC8395499.
4. **Purohit MP**. Paget's Disease of the Scrotum. [Internet] Available at: https://www.dovemed.com/diseases-conditions/pagets-disease-scrotum/.
5. **Lloyd J, Flanagan AM**. Mammary and extramammary Paget's disease. *J Clin Pathol*. 2000 Oct;53(10):742-9. doi: 10.1136/jcp.53.10.742. PMID: 11064666; PMCID: PMC1731095.