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Case Report

Localised Cutaneous Amyloidosis of the Glans Penis: A Case Report and Review of the Literature

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Abstract

Amyloidosis represents a notable cause of morbidity within the developed world. Urological presentations of systemic or localised amyloidosis are rare, with penile amyloidosis being poorly reported. We performed a literature review investigating cases of penile cutaneous amyloidosis via the PubMed database during March 2020, in conjunction with clinical review of a local patient presenting with a penile lesion.

Our patient is a 60 year old uncircumcised, caucasian male presenting with a longstanding history of 2 irregular lesions affecting his glans penis and a further 2 lesions affecting the inner surface of his prepuce. He underwent excision biopsy of the largest lesion which represented cutaneous amyloid deposits. He underwent immunological testing for systemic disease which was negative.

In current literature, there are 13 cases of cutaneous amyloidosis affecting the glans penis, with 1 of those having evidence of extra genitourinary amyloid deposits. All the documented cases were treated with local excision and investigation for systemic disease.

It is important to recognise alternative diagnoses in patients presenting with penile lesions. Despite cutaneous amyloidosis mimicking malignancy macroscopically, the morbidity and mortality is lower in comparison to penile cancer. Treatment remains surgical excision of the lesion and further investigations to exclude systemic disease.

Introduction

Amyloidosis is a notable cause of morbidity, and in some cases mortality within the developed world. Urological presentations of systemic or localised amyloidosis are rare, with primary penile amyloidosis being poorly reported in the literature. It can commonly mimic malignancy on imaging and macroscopically, thus representing an important differential diagnosis to be aware of when examining and investigating a penile lesion.

Case Presentation

CA 60 year old uncircumcised, Caucasian male was referred with multiple longstanding granular lesions of his penis. His past medical history included hypertension and insulin dependent type 2 diabetes. On initial assessment there were two irregular granular lesions on his glans penis and two further similar lesions on the inner prepuce. These were initially thought to be malignant and an excision biopsy of the largest one was performed.

The histopathological examination showed an abundance of relatively amorphous pink material in the superficial to mid dermis with positive Congo red staining and mild apple-green birefringence in keeping with cutaneous amyloidosis. Further analysis with immunohistochemical staining of the sample by the National Amyloidosis Centre confirmed this result and determined this to be of the AL Kappa subtype.

Following investigation under the care of the haematology department with serum free serum light chains, electrophoresis and Bence Jones' protein, there was no evidence of systemic amyloidosis or multiple myeloma. A diagnosis of cutaneous AL amyloidosis of Kappa subtype affecting the glans penis and prepuce was made.

The patient underwent a circumcision for localised treatment of the

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remaining preputial lesions. The remaining glandular one was deemed high risk for meatal stenosis due to its proximity to the urethral meatus and therefore not excised. The patient remains well under yearly review from the National Amyloidosis Centre.

Discussion

The term 'Amyloid' was first coined by Virchow in the 19th century to describe a macroscopic tissue abnormality characterised by a positive iodine staining reaction. Subsequent technological advancements in light microscopy furthered Virchow's description to include distinct birefringence of the amyloid deposits when stained with Congo red dye [1].

The pathophysiology of amyloidosis stems from a failure of proteolysis of misfolded proteins resulting in oligomeric conglomerates referred to as amyloid fibrils. As amyloidosis is caused by misfolded proteins, there are multiple classifications of the disease specifically related to the original protein involved. All of the involved proteins may form extracellular deposits and lead to subsequent organ dysf unction [2]. The most common subtypes of amyloidosis include amyloid light chain (AL), the origin of which is an immunoglobulin arising from plasma cells, and amyloid associated (AA), arising from a non-immunoglobulin synthesised by the liver. Further classification can be made by the clinical presentation of the proteinaceous deposit; whether it be systemic or localised, and the clinical syndrome it produces.

The amyloid Light Chain (AL) subtype is characterized by clonal plasma cell dyscrasia, similarly to multiple myeloma [3]. This results in a failure to produce the classical alpha-helix configuration of either kappa or lambda light chains, instead producing a beta-pleated sheet which is inherently insoluble. Classically there is involvement of the kidneys, heart or nervous system however involvement of many organ systems have been documented.

Cutaneous amyloid deposits can be seen in both systemic and localised disease. Commonly up to 40% of systemic AL amyloidosis sufferers complain of epidermal disease, which reflects amyloid deposition within the capillaries of the skin involved. Cutaneous disease typically presents as petechiae or purpuric lesions, yellow macular or nodular lesions. There are also macular and lichen subtypes which can be associated with systemic connective tissue diseases.

Statistically, within the UK the age-adjusted prevalence of amyloidosis is between 5.1 and 12.8 per 1 million per year*. Approximately 10-20% of cases remain localised, with the remainder of cases being classified as systemic disease. Although the localised form is rarer, it carries a better prognosis [5]. Rarer still is localised penile amyloidosis, with only 14 documented cases, including ours, on literature review.

Merika et al. comments on the low prevalence of systemic disease in those presenting with cutaneous penile amyloid lesions as the primary presenting complaint. Their study also highlights the increased rate of primary nodular amyloidosis amongst those with penile cutaneous lesions [4]. Of the confirmed cases of cutaneous amyloidosis of the glans penis, only one reported a second site affected, namely the trachea. This was subsequently found to be a lone deposit, with no further evidence of widespread disease identified; however, this does not exclude the possibility of this representing systemic amyloidosis [16].

Of the cases identified, most were diagnosed on a serological and histological basis, more in depth modalities such as serum amyloid protein component (SAP) scintigraphy and genetic testing were not performed routinely. SAP scintigraphy is highly sensitive for AL and AA amyloidosis (90% for both subtypes), with a specificity of 93%. The use of SAP scintigraphy may give a more definitive answer regarding the presence of systemic disease however the modiality itself is often not available in local centres [17, 18].

Treatment of the lesions remains case dependent and requires a multi-disciplinary approach [19]. The underlying amyloid subtype also greatly influences management. In systemic AL amyloidosis, treatment aims to suppress plasma cell production of amyloid which predominantly involves using dexamethasone and mephalan, an oral chemotherapeutic agent, alongside supportive care for the underlying organs involved. Similarly, AA amyloidosis requires management of the underlying disease process often involving immunomodulation [19]. Localised cutaneous amyloidosis is typically managed by surgical excision, or laser ablation, systemic chemotherapeutic agents are usually not employed due to their side effect profile [16]. The majority of cases reported were treated with local excision as in our case.

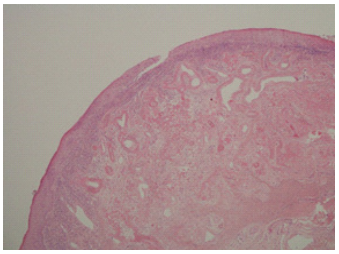

Figure 1: Histopathology showing amyloid in the dermis of glans skin, accentuated round vessels. Magnification X40 H&E.

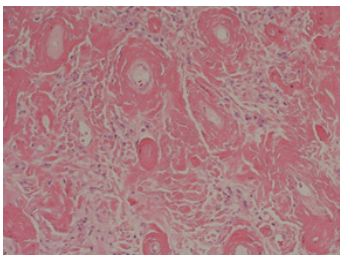

Figure 2: Histopathology with higher power view of amorphous eosinophilic amyloid. Magnification X200 H&E.

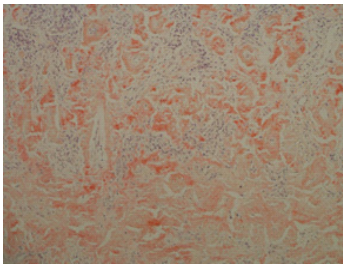

Figure 3: Histopathology showing congo red staining of dermal amyloid x200 H&E.

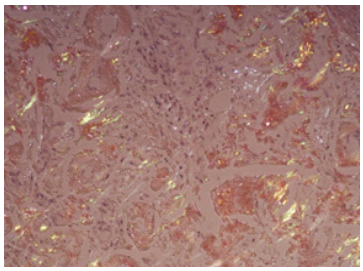

Figure 4: Histopathology showing apple green birefringence of amyloid x200 Congo red.

Table 1

Case Report	Macroscopic appearance of lesion	Histology/Immunocytochemistry
Bodner et al[9]	Glans penis lesion occluding urethral meatus	Deposits of dense eosinophilic amyloid filling lamina propria and adjacent dermis
Degos et al[6]	Painless nodular lesion	N/A
Dominguez-Dominguez et al[14]	Yellow nodule on glans	Dermal deposits of amorphous eosinophilic material. AL and AA. Kappa and Lambda +ve
Floyd et al[5]	Two erythematous raised lesions on glans penis	Lambda Subtype
Friedmann et al[7]	Single painless parameatal lesion, yellow, rubbery	Diffuse dermal amyloid, dilated capillaries; scattered lymphocytes
Hyett et al (this report)	Multiple irregular lesions on glans penis and prepuce	Amorphous pink material in the superficial to mid dermis with positive Congo red staining and mild apple-green birefringence. AL Kappa subtype on immunohistochemistry.
Kawsar et al[13]	Multiple confluent weeping lesions on glans penis	Amorphous material, cuffing of blood vessels beneath epithelium
Lim et al[10]	Tender penile shaft mass and subsequent urethral stricture	Deposits of amorphous, homogenous material with +ve congo red staining,
Merika et al[4]	Waxy plaque on glans penis with haemorrhagic blister	Uniformly globular eosinophilic appearance of the dermis. AL. Cytokeratin 5
Merika et al[4]	Multiple erythematous papules and nodules	Epidermal hyperplasia and deposits of eosinophilic material. AA. Cytokeratin 5+ and 14-
Ritter et al[12]	Multiple painless slowly growing glans penis lesions	Numerous dermal deposits of amorphous fissured eosinophilic material, Amyloid P+
Srinivasan et al[11]	Single painless lesion	Diffuse Subcutaneous Amyloid. AA
Udompaetaikul et al[15]		Nodular amyloid
Wietzner et al[8]	Single painless parameatal nodular lesion	Homogeneous poorly cellular eosinophilic tissue

Conclusion

These cases highlight the importance of consideration of alternative diagnoses in patients presenting with cutaneous penile lesions. Fortunately, despite penile cutaneous amyloidosis mimicking malignancy, the morbidity and mortality is low due to the low incidence of systemic amyloidosis in patients who present with a penile lesion. Treatment remains local excision of the lesion, histological and immunochemical confirmation of the amyloid subtype and further investigations to exclude systemic disease. Consideration could be made for the introduction of SAP scintigraphy in these cases, however the benefit of this remains unclear with such a small demographic to review.

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