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Letters to the Editor – Brief Communications

Letter to the editor- familial differentiated vulval carcinoma

Dear Editor,

We found that while vulval carcinoma is a rare condition, accounting for less than 1% of all new cancer cases in females [1], we recently had three cases of multi-focal differentiated vulval carcinoma in three women with one degree of familial separation with similar histological characteristics, in the absence of a known genetic mutation. Their characteristics are described in Table 1.

Case 1 and Case 2 have both had protracted clinical courses with three separate episodes of recurrent differentiated squamous cell carcinoma. This was despite frequent clinical review following primary excision which detected no evidence of recurrent disease for initial periods of 6 and 3 years respectively. Given the lack of availability for Next-Generation Sequencing (NGS) nationally outside the research setting, we have been unable to elucidate if there is a genetic predisposition in this family.

To date, there has been no description of non-HPV associated familial vulval carcinoma in the literature, yet here we describe three first degree relatives with similar disease characteristics and recurrence patterns. More significantly, these women are in age groups with a lower incidences of vulval carcinoma. Most significantly, in Case 2, the incidence of vulval carcinoma in this group is 4/1,000,000. While this rate is 53/1,000,000 for those aged 55–59 and 77/1,000,000 in those 60–69, these are significantly lower than the peak rate of vulval cancer cases, at 90 years of age [1].

Some case reports suggest a genetic HLA-mediated predisposition to Lichen Sclerosis [2], which may be true in our family, given histories of HLA-associated conditions of diabetes and vitiligo. However, our sequence of cases may also have other aetiological factors at play.

Given the rarity of familial vulval carcinoma, on the background of vulval carcinoma being uncommon, we propose an increased focus is placed on oncogenetic research in vulval carcinoma to assess treatments that may alter the pathway of progression and recurrence of the disease in affected individuals, which has been highlighted by other recent publications [3].

The area of molecular biology in vulval squamous cell carcinoma is less frequently studied over recent decades, however focus has been placed on directed therapies against cell cycle regulatory molecules, extracellular proteins and the inhibition of angiogenesis [4]. Recent reports have shown successful treatment of recurrent disease with agents such as monoclonal antibodies [5].

However, both diagnostic and therapeutic strategies supporting this form of therapy are less well investigated and a focus needs to be placed on ensuring the availability of these treatments in all major gynaecological oncology centres, and not reserving treatment to elite research centres. Given the lack of availability of NGS in cases such as these, there is a necessity for increased funding and support for research into the management and treatment of vulval carcinoma, particularly in non-HPV associated disease.

Table 1
Summary of cases of vulval carcinoma.

	Case 1	Case 2	Case 3
Relationship (to index Case)	Index Case	Daughter	Sister
Age at diagnosis (years)	59	34	69
Past Medical History	Lichen Simplex Insulin Dependent Diabetes Hypertension Hypothyroidism	Hypothyroidism Hypertension BMI 47.9 kg/m [2] Vitiligo Retinitis pigmentosa	Lichen Sclerosis Insulin Dependent Diabetes BMI 44.0 kg/m [2]
Presentation	Left Labial “Ulcer”	Vulval pain	Right labial mass
Diagnosis	FIGO Stage II moderately well differentiated vulval squamous cell carcinoma	Vulval pseudoepitheliomatous hyperplasia and well differentiated squamous cell carcinoma on a background of Lichen Sclerosis	Poorly differentiated squamous cell carcinoma with multiple foci of intra-abdominal and supra-diaphragmatic disease
Primary Treatment	Triple Incision Vulvectomy and lymphadenectomy	Wide local excision	Excisional biopsy and palliative radiotherapy
Recurrence and Treatment	1 Diagnosis + 6 years: Excision 2 Diagnosis Case +8 years: Anal squamous cell carcinoma excision and radiotherapy 3 Diagnosis + 10 years: Multiple recurrence at right labia, anus and perineal body- re-excised	1 Diagnosis +3 years: Stage IIIA squamous cell carcinoma treated with vulvectomy, lymphadenectomy and radiotherapy 2 Diagnosis +3.5 years: Recurrence Stage II squamous cell carcinoma- complete excision 3 Diagnosis +4.5 years: Recurrence squamous cell carcinoma- complete excision	Died 5 months following diagnosis as not a candidate for chemotherapy

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Prolapse mesh complication: large stone on vaginal mesh extruded in the bladder

Dear Editor,

We found an unusual and severe complication of mesh prolapse surgery we will to report. Synthetic meshes augmentation for pelvic organ prolapse repair by vaginal route has been associated with better anatomical outcomes without improvements in terms of symptoms and quality of life. However their widespread use raised a growing awareness of mesh-related complications which lead in 2011 to FDA warning. These complications include infection, fibrosis, shrinkage and exposure [1,2]. In particular mesh extrusion inside the urinary tract is uncommon and has been mainly related to incorrect suburethral tape positioning (bladder/urethra perforation or submucosal placement) [1]. Chronic contact of a foreign body with urine can lead to concretion and calculus, which can bring to recurrent urinary tract infections, urgency and bladder pain. Cystoscopy is the gold standard for diagnosis, but also X-ray imaging, MRI or ultrasound can be useful. Interestingly, bladder stone formation has been described for suburethral tapes but very few reports are reported after vaginal mesh augmentation for pelvic prolapse [3,4]. The treatment consists of the surgical removal of the calculus with the extruded portion of the mesh. This goal can be obtained through open cystotomy, laparoscopic/robotic route or endoscopic approach. The aim of this report is to present iconography of this rare mesh-related complication.

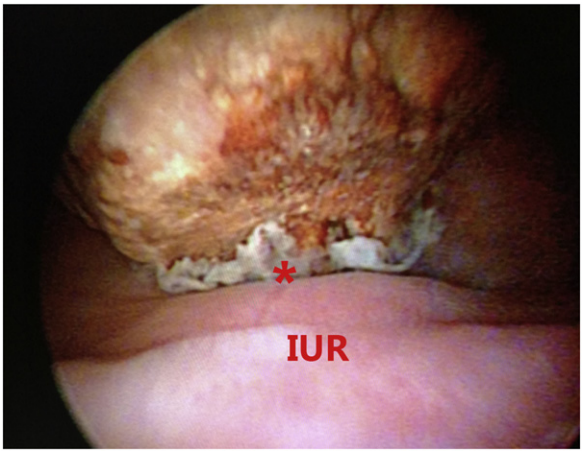

Fig. 1. Cystoscopic view - focus on extrusion site. Mesh erosion is located posteriorly to the interureteric ridge (IUR). In the point of extrusion mesh tissue can be identified (marked with *). IUR = inter-ureteric ridge, *=point of extrusion of the mesh inside the bladder.

The presented case is a 72-year-old lady was referred to the surgical outpatient clinic with recurrent urinary tract infections, bladder pain and overactive bladder syndrome for six years. Ten years before she had a vaginal hysterectomy with anterior mesh-augmented repair. On examination, no vaginal exposure was found. Urodynamic evaluation showed a detrusor overactivity associated to urge incontinence. Pelvic floor ultrasound demonstrated anterior vaginal wall mesh extruded in the bladder from the retrotrigonal region, with stone developed on the eroded mesh measuring 30 mm in its larger diameter (Supplemental Material 1). Cystoscopy confirmed a large stone attached to the mesh extruded in the bladder posteriorly to the inter-ureteric ridge (Fig. 1; Supplemental Material 2). Surgical management was required in order to remove the mesh-stone complex and relief patient's symptoms (due to complexity and stone dimension an open abdominal approach was chosen). This report is meant to rise awareness against this unusual mesh related complication.

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Contribution to authorship

S. Manodoro: project development, manuscript writing.
C. Reato: project development, manuscript writing.
A. Cola project development, manuscript writing.
S. Palmieri project development, manuscript writing.
M. Frigerio project development, manuscript writing.

Consent

Written informed consent was obtained from the patient for publication of any accompanying images.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ejogrb.2019. 02.012.

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