


Gynaecological cylindroma in association with CYLD gene mutation

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Abstract

Cylindroma is a benign adnexal tumour that occurs as a solitary pink–red coloured nodule and is usually found on the scalp or neck. There have been few cases reported of these lesions being found on the genitalia. They can be found in single or in multiple form, with the latter usually inherited in an autosomal dominant pattern. CYLD lysine 63 deubiquitinase (CYLD) cutaneous syndrome, also known as Brooke-Spiegler syndrome, is a genetic condition characterized by the growth of multiple benign adnexal skin tumours. The most common tumours are cylindromas, spiradenomas and trichoepitheliomas. The cause of this syndrome can be attributed to mutations in the CYLD tumour suppressor gene. If both copies of this gene are mutated, the cell undergoes uncontrolled cell proliferation and division resulting in the formation of a tumour. Here, we present an unusual case of a female patient presenting with a large cylindroma over the mons pubis.

INTRODUCTION

Cylindromas are benign adnexal tumours found on the scalp, face and neck. They typically occur sporadically in mid-age and elderly patients. Cylindromas often present as pink or red papules or nodules and range from a few millimetres to several centimetres in size. Although usually painless, pain or paraesthesia can occur if nerve compression occurs due to tumour growth. They are more commonly found in females. Multiple tumours are associated with hereditary disorders, and these often manifest during childhood and early adulthood. Brooke-Spiegler syndrome (BSS), otherwise known as CYLD cutaneous syndrome, is an autosomal dominant disorder characterized by the presence of multiple benign skin tumours which develop from adnexal structures of the skin including spiradenomas, cylindromas and trichoepitheliomas. BSS shows variable penetrance between 60 and 100% and is caused by germline mutations on the CYLD gene [1]. The CYLD gene is a tumour suppressor gene, located on chromosome 16q12-13, which encodes an enzyme that interacts with multiple substrates of the nuclear factor kappa B (NF- κ B) signalling pathway and downregulates its activity by removal of Lys-63-linked ubiquitin chain from TRAF2, TRAF6 and IKBKG. Activated NF- κ B signalling, due to CYLD mutations, leads to increased transcription via NF- κ B and subsequent uncontrolled cell proliferation and hence development of tumours associated with BSS [2]. Cutaneous neoplasms

in BSS can gradually increase in size into adulthood, where they may be disfiguring. The form of BSS that is characterized only by the presence of cylindromas is known as familial cylindromatosis. This is a rare phenotypic variant of BSS.

CASE REPORT

A 50-year-old patient presented with a significantly symptomatic large mass arising from the mons pubis. This was identified when the patient presented for review of their utero-vaginal prolapse. The patient first noticed this mass 19 years ago, it has been gradually increasing in size but was previously asymptomatic. There was no history of bleeding or discharge from the lesion. The patient also reported a painful lump on the right upper abdominal wall present since childhood, which has not fluctuated in size.

On examination, the mass measured 15 × 10 cm and covered the mons pubis (Fig. 1). The mass was firm in nature and was tethered posteriorly. There was no lymphadenopathy. An additional 2 cm hard nodule was identified in the upper abdominal wall. Examination revealed a healthy cervix, vagina and vulva but the cervix was found to descend to the level of the introitus on application of abdominal pressure. The patient has been amenorrhoeic for the past 3 years but has recently passed a small amount of blood vaginally. There was no signif-

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Figure 1. Image of growth, in front of mon pubis bone.

icant medical or surgical history other than treatment for a ruptured appendix as a child. There was no relevant family history. The patient has had one vaginal delivery.

Computed tomography (CT) scan identified a large mass over the mons pubis as well as a separate mass on the anterior abdominal wall (Fig. 2 & Fig. 3). Further investigations included an ultrasound-guided biopsy of the mass over the mons pubis. The histology showed lobular nests of basaloid cells, surrounded by a thick basement membrane. Hyaline droplets were also seen within the tumour nests, which were composed of peripheral palisading cells with small dark nuclei, and central larger cells with pale nuclei. These features are in keeping with a benign cylindroma. The 2 cm abdominal wall mass showed similar appearance on histological examination. The patient was referred for surgical excision of the mass.

DISCUSSION

There is little available published literature on cylindromas presenting as a gynaecological condition [3–6]. Cylindromas are benign skin appendageal tumours that arise from pluripotent stem cells in the folliculo-sebaceous apocrine unit with eccrine and apocrine differentiation [7]. Solitary lesions are usually sporadic and non-familial; these are typically slow growing and present as painless, round nodular lesions. Multiple lesions typically present on the head and neck but have been reported to occur on the trunk and extremities and rarely in the pubic area. The identification of germline heterozygous pathogenic variant in CYLD by molecular genetic testing can aid diagnosis.

BSS should be suspected in patients presenting with multiple benign cutaneous adnexal tumours at an early age. A family history of similar multiple tumours may suggest an autosomal dominant inheritance pattern. BSS should be suspected in individuals with any of the following: (i) the presence of one or more cylindromas or spiradenomas on the face and scalp, perinasal



Figure 2. Sagittal CT showing mass lesion in front of mon pubis bone and in upper abdominal wall.

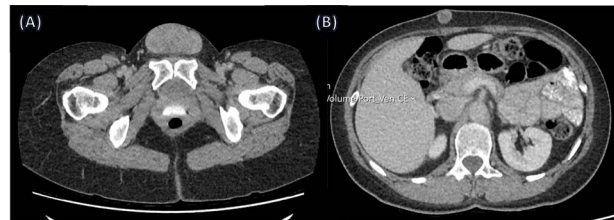


Figure 3. Axial CT showing mass lesion: (A) in front of mon pubis (B) on anterior abdominal wall.

trichoepitheliomas or a combination of these tumour types, (ii) a cylindroma or spiradenoma on the scalp or torso that has been incidentally found on imaging or (iii) a membranous basal cell adenoma-type salivary gland tumour in an individual with a single cylindroma, spiradenoma or trichoepithelioma [8]. Histologic evaluation is needed for diagnosis. Cylindromas are described as nonencapsulated dermal nodules of epithelial cells [9]. Islands of cancer cells are typically reported as having a ‘jigsaw puzzle’ patterned appearance outlined by eosinophilic, membrane-like hyaline basement material that is PAS positive. These islands are mainly within the dermis but may extend into the subcutis.

To diagnose BSS, a mixture of the following is needed, early age onset of skin neoplasms and progression of disease over time, family history of similar neoplasms, histopathologic findings on tissue biopsy, association with tumours in the parotid or salivary glands. Genetic testing should be considered in those who have two or more biopsy confirmed cylindromas, spiradenomas or trichoepitheliomas. Germline mutation in CYLD confirms the diagnosis. If no germline variant is seen

and there is no known family history, mosaicism should be considered.

Although the majority of cases are benign, malignant transformation can occur in 5–10%. Rapid growth, bleeding and ulceration are suggestive of malignant transformation. There have been reported cases of transformation to basal cell adenomas and adenocarcinoma of the parotid glands and salivary glands as well as metastasis to bone, lung and liver [10]. Management is with surgical excision of the tumours to help relieve symptoms and improving cosmesis. Possible novel therapies aim to target and inhibit the NF- κ B signalling pathway. Patients with BSS may develop multiple tumours throughout their lifetime and so multiple surgical procedures may be needed.

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ETHICAL APPROVAL

No ethical approval is required.

CONSENT

Written consent for publication has been obtained from the patient.

GUARANTOR

Dr Chit Cheng Yeoh.

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