



Bartholin's Gland Hyperplasia

Case report and a review of literature



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Bartholin's gland hyperplasia. Case report and a review of the literature

BACKGROUND: Tumors arising from glands of the female ano-genital area, such as minor and major vestibular glands, are very rare. Lesions affecting Bartholin's gland can be divided into two groups: benign and malignant lesions. In the first group we can include nodular hyperplasia, adenoma, adenomioma which can sometimes cause Bartholin's gland enlargement and difficult differential diagnosis. Surgery is considered the treatment of choice, frequently represented by marsupialization with rates of local recurrence.

CASE REPORT: We describe a case of a 50-year-old woman with a several-years history of recurrent episodes of Bartholinitis, previously treated with marsupialization. Patient underwent complete excision of the left Bartholin's gland without operative complications. Pathological findings showed a Bartholin's gland hyperplasia. Post-operative course was regular, free from surgical complications. After one year, the patient is free from any local disease.

RESULTS AND CONCLUSION: In women in postmenopausal age, in those cases in which marsupialization doesn't lead to an improvement in symptomatology and in those cases in which, at physical examination, Bartholin's gland enlargement appeared to be firm and irregular, because of the higher incidence of malignancy in these situations, total excision of the gland is recommended. Total excision of the Bartholin's Gland is a safe technique, given the low incidence of procedure-related morbidities. We do not consider biopsy of the gland a proper strategy for the high percentage of false negative results.

KEY WORDS: Bartholin's Gland, Differential diagnosis Hyperplasia, Local excision, Surgical treatment

Introduction

Tumors arising from glands of the female ano-genital area, such as minor and major vestibular glands (Bartholin glands), Huffman's and Skene's periurethral glands, are very rare¹. Among these lesions, those affecting Bartholin's gland can be divided into two groups:

benign and malignant lesions. Among benign lesions, we can include duct cyst and gland abscess, far apart the most frequent causes of Bartholin's gland swelling². Nodular hyperplasia, adenoma, adenomioma can sometimes cause Bartholin's gland enlargement and differential diagnosis between these anatomo-pathological types can be difficult on simple clinic examination^{1,3-6}. Malignancies of Bartholin's gland, on the other hand, include various types of carcinomas, the most common being adenocarcinomas and squamous cell carcinoma¹. In such cases, cellular atypia, architectural disorganization and invasive growth make differential diagnosis with benign lesion easy to do on histologic basis.

We described a case in which total excision of Bartholin's Gland was performed, and that resulted in a diagnosis of Nodular Hyperplasia.

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Case report

A 50-year-old woman with a several-years history of recurrent episodes of Bartholinitis was brought to our attention. About 1 year earlier, she underwent marsupialization, which guaranteed a partial remission of her symptomatology for one year, after which the same former symptoms presented again. Under general anesthesia, the patient underwent complete excision of the left Bartholin's gland, which was palpated and felt firm and irregular. Postoperative course was uncomplicated and painless.

Macroscopic examination revealed a 2.5 x 1.5 x 1.4 cm whitish oval formation, homogeneous and lobulated at the cut surface.

At microscopic examination, this lesion appeared well circumscribed by fibrous connective tissue and bundles of muscular fibres without atypia. The architecture of

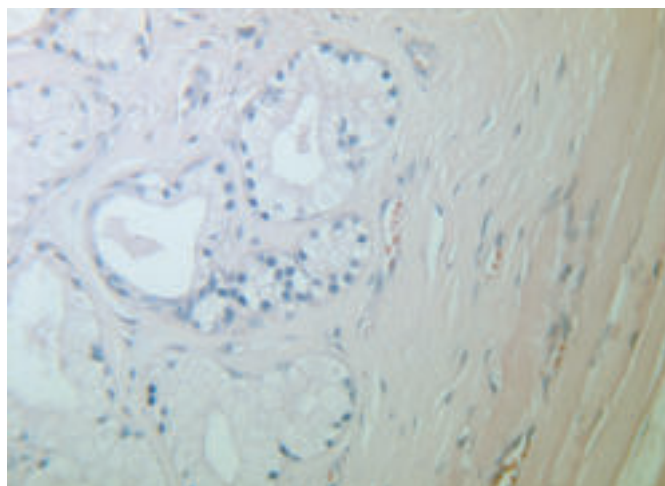


Fig. 3: The acinar lining epithelium is cuboidal without nuclear atypia. X250 hematoxylin/eosin.

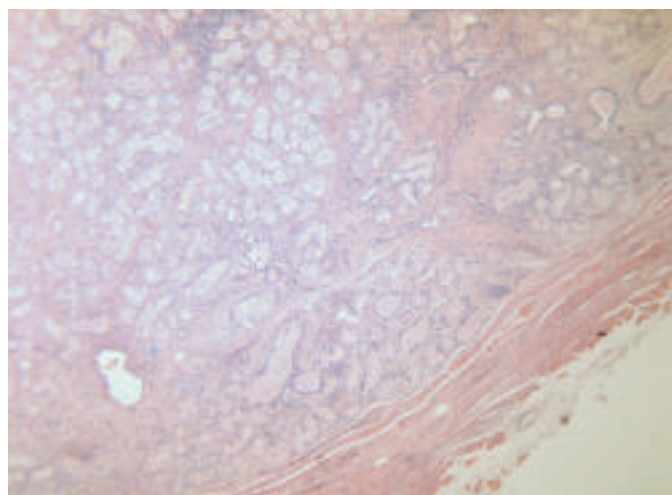


Fig. 1: The lesion is well delimited and has a lobular architecture with preserved tubular/acinar ratio. X40 hematoxylin/eosin.

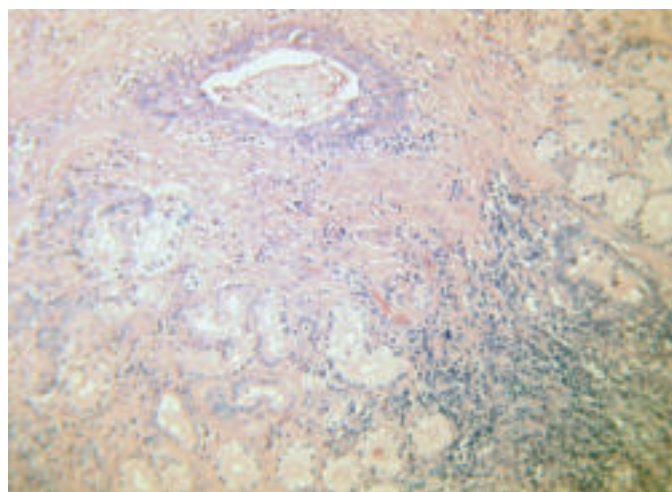


Fig. 2: The lesion shows a mild-moderate inflammatory infiltrate. X100 hematoxylin/eosin.

the lesion was lobulated, with an increased number of acini and a preserved tubular/acinar ratio (Fig. 1). The lining acinar epithelium was formed by mucin-containing cuboidal cells with nuclei free from atypia (Fig. 2). Neither mitotic activity nor necrosis were observed. One ductal structure with focal squamous metaplasia and mild periductal flogosi, with presence of intraepithelial granulocytes and rare intratubular and intracinar microabscess, was found (Fig. 3).

These findings were consistent with a Bartholin's Gland Hyperplasia diagnosis. After a one-year-follow-up, the patient is alive and free from any local disease.

Discussion

Greater vestibular gland, better known as Bartholin's gland, is a tubulo-alveolar gland located at the base of minor labia, that drains with a 2 - 2.5 cm-long duct into the vestibulus at 4 and 8 o'clock positions. They are homologues of the Cowper's gland in males and, at puberty, they begin to function, providing moisture for the lower part of the vestibulus². Normally not palpable, they become clinically evident in case of disease. Among benign lesions, duct cysts and gland abscesses are, by far, the most common pathologies of Bartholin's gland. Two percent of women, during their life, develops a Bartholin's gland abscess or a duct cyst, the first one being almost three times more common than cysts². These nosological entities prevalently occur in women between 20 and 30 for the physiological involution of Bartholin's gland in women older than 30². Moreover, in the group of benign lesions, Nodular Hyperplasia, Adenoma and Adenomioma are very rare. In recent literature, there's no mention of the prevalence and incidence of Bartholin's gland Nodular Hyperplasia, as only 31 cases are reported in modern English language literature.

In this regard, Koenig and Tavassoli ³, in 1998, reported 27 cases of benign lesions from the consultation files of Armed Forces Institute of Pathology (AFIP), of which 19 were qualified for the study. Among these, 17 were classified as Nodular Hyperplasia, 1 as Adenoma and 1 as Adenomyoma. They defined criteria for distinguishing adenomas from nodular hyperplasia and, nevertheless, they acknowledged the difficulty in the distinction between these two kinds of anatomic-pathological entities, suggesting that clonality studies, which could be helpful in establishing the nature of these conditions, should be performed in doubtful cases. Kazakov et al. ⁷ suggest that PCR studies, effective in defining clonality of the human androgen-receptor gene (HUMARA), could be useful to solve this issue, even though a straightforward equation between clonality and neoplastic process is not allowed yet. In fact, even if the vast majority of tumors are clonal, some have proven to be polyclonal. Moreover, monoclonal groups of cells have been detected in normal human tissues. So, detection of monoclonality in a single case of nodular hyperplasia of Bartholin's gland should be considered together with other lesion characteristic such as large size, expansive growth, severe atypia and complex histological architecture in order to set the lesion worthy of further investigation.

According to these criteria, nodular hyperplasia can be defined as a proliferation of mucinous acini with a preserved duct-acini ratio, as seen in normal gland, without capsulation and with a lobulated or irregular contour. On the other hand, adenoma can be diagnosed if the proliferation of glands, tubules and acini is random or diffuse and sharply circumscribed or capsulated ³.

Differential diagnosis between Nodular Hyperplasia and Adenoma is very important for the well-defined malignant potential of the latter one ¹. In fact, in their study, Koenig and Tavassoli reported one case of transition from adenoma to Adenoid Cystic Carcinoma (ACC) that accounted for 30% of the tumor. They formulated the hypothesis that, in rare instances, Bartholin's gland carcinoma may arise from a benign adenoma, according to the well-known adenoma-to-carcinoma sequence.

Immunoreactivity assay showed the presence of mutated p53 in the ACC (40% of cells positive) but not in the adjacent Adenoma, suggesting the possible role played by p53 as a determining factor in the evolution from Adenoma to ACC ³.

Primary carcinoma of the Bartholin's gland has an incidence of 0.114/100000 woman-year ², representing 0.1-0.7% of all vulvar carcinomas and less than 1 % of all female genital malignancies ⁸. The most common histological types are adenocarcinoma, squamous cell carcinoma, adenosquamous cell carcinoma, transitional cell carcinoma and the adenoid cystic carcinoma, the latter one accounting for 5-15% of all Bartholin's Gland malignancies ⁸. The average age of patients with Bartholin's gland carcinomas is approximately 60 (49 years for

Adenoid Cystic Carcinoma ⁹), with a range from 33 to 93 years ¹⁰ so that the suspect of malignancy should arise in case of post-menopausal women with painless solid or cystic mass of the posterior half of the vulva, localized at the base of the major labia, associated with abnormal bleeding, pruritus, burning sensation and dyspareunia. Given the rarity of these neoplasms, the entire body of world literature consists of single case reports, retrospective case series and review articles, thus justifying the lack of consensus about which therapeutic approach should be chosen in every single case.

As concerns etiology and physiopathology of Nodular Hyperplasia, both Koenig and Axe stated that trauma, previous surgical intervention and local infection could be determining factors in cellular proliferation ^{3,11}.

Several clinical studies show a positive correlation between previous or concurrent inflammation, cyst, duct obstruction and hyperplastic changes of Bartholin's gland. These findings are consistent with the pathogenetic hypothesis according to which duct obstruction, due to epithelial hyperplasia in the duct or to inspissation of secretions, could determine disruption of the duct cellular lining, with spilling of material into the surrounding connective tissue, and superimposed infection, causing tissue fibrosis ⁵. In fact, several histological studies show the presence of mild to severe inflammation with micro-abscess, intraepithelial granulocytes, lymphohistiocytic infiltrate, squamous metaplasia of larger ducts and ruptured ducts with extravasated stromal mucin ^{1,3,7}.

Nevertheless, neoplastic proliferation itself could cause duct obstruction and, secondarily, inflammatory process³. Lastly, HPV has not an assessed role in the pathogenesis of Bartholin's gland carcinoma ¹⁰.

Clinical presentation of Bartholin's gland Nodular Hyperplasia is rather aspecific. Most of the cases arise as a slightly painful, rapidly enlarging, cherry-red, regular or irregular, firm or cyst-like lesion of the lower part of the major or minor labium ^{1,3,6,7}. If ulceration is present, entry dyspareunia can be associated ¹. No discharge, dysuria or vulvar sensitivity have been reported ^{3,6,7}. Nodular Hyperplasia can be bilateral ³. Mean presentation age of Nodular Hyperplasia is 35 (range from 19 to 56), while benign neoplasm such as Adenoma and Adenomyoma occur an average of 20 years later ³. According to Koenig and Tavassoli, in their series, 71% of patients had signs or symptoms of Bartholin's duct cyst ³.

Nowadays, the most common procedure used for the treatment of a Bartholin's cyst is the marsupialization or the fistulisation with a Word's catheter, even if recurrence is a frequent event ².

Conclusion

In women in postmenopausal age, in those cases in which marsupialization doesn't lead to an improvement in

symptomatology and in those cases in which, at physical examination, Bartholin's gland enlargement appeared to be firm and irregular, because of the higher incidence of malignancy in these situations, total excision of the gland is recommended. Total excision of the Bartholin's Gland is a safe technique, given the low incidence of procedure-related morbidities. We do not consider biopsy of the gland a proper strategy for the high percentage of false negative results.

Riassunto

Le Ghiandole del Bartolino sono analoghe alle ghiandole bulbo-uretrali di Cooper, nell'uomo. La patologia che si riscontra più frequentemente a loro carico è di tipo infiammatorio, con lo sviluppo nel 2% delle donne nel corso della vita di una cisti o di un ascesso. Invece, di più raro riscontro è la patologia tumorale, sia benigna che maligna.

Tra le neoplasie benigne vi sono l'iperplasia nodulare, l'adenoma e l'adenomioma, e la diagnosi differenziale, spesso difficoltosa, è necessaria per le differenti implicazioni prognostiche: è ben documentata la possibilità che un adenoma possa presentare, nella compagine tissutale, aree di trasformazione adenocarcinomatosa associata a mutazioni di geni oncosoppressori quali p53, possibilità non evidenziata invece per l'iperplasia nodulare o per l'adenomioma. Di qui, la necessità di un corretto inquadramento diagnostico e, di conseguenza, terapeutico.

dal punto di vista clinico il quadro sintomatologico di presentazione dell'adenoma e dell'iperplasia nodulare è molto simile a quello delle cisti del dotto ghiandolare, il che rende ancor più difficile la corretta identificazione della patologia che sottende la tumefazione. la marsupializzazione e/o la fistolizzazione tramite catetere di word, che rappresentano le terapie più frequentemente utilizzate per la patologia della ghiandola del bartolino, sono gravate da un importante tasso di recidiva e non garantiscono peraltro la rimozione di una eventuale lesione neoplastica la quale, nel caso dell'adenoma, potrebbe celare foci di trasformazione carcinomatosa.

Il nostro gruppo ha descritto il caso di una donna di 50 anni che giungeva alla nostra osservazione con una storia di episodi di Bartoliniti ricorrenti e già sottoposta per tale motivo a marsupializzazione circa un anno fa. In anestesia generale, veniva effettuata la completa escissione della ghiandola vestibolare maggiore di sinistra, con decorso post-operatorio del tutto regolare. L'esame istologico definitivo poneva diagnosi di Iperplasia Nodulare,

e naturalmente a distanza di un anno, non si sono manifestati problemi locali di rilievo.

Concludiamo affermando che, in presenza di una tumefazione dura e irregolare a carico della ghiandola del Bartolino, la strategia terapeutica più appropriata da attuare dovrebbe essere l'escissione completa della ghiandola la quale è una tecnica sicura e praticamente scevra da complicanze e garantisce la completa asportazione di una eventuale patologia neoplastica sottostante alla tumefazione. Scoraggiamo l'esecuzione delle biopsie ghiandolari per il rischio di risultati falsamente negativi e le procedure di drenaggio e/o marsupializzazione per l'alto tasso di recidiva.

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