Seminars in Diagnostic Pathology 38 (2021) 1–2

Contents lists available at ScienceDirect

Seminars in Diagnostic Pathology

journal homepage: www.elsevier.com/locate/semdp

EDITORIAL

# Vulvar pathology: diagnostically challenging areas and new developments

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Medical diseases of the vulvovaginal region have been recognized since the first century (1), but for much of early history, there was relatively limited consideration of diseases that primarily affect the vulva. Most publications on vulvar diseases in the 19th century primarily dealt with malformations and infectious diseases (2-4). Although both of these disease categories were undoubtedly of high clinical significance, they nonetheless do not capture the wide spectrum of diseases that are now known to potentially involve the vulva. The third edition of the classic text *Elements of pathological anatomy*, whose first edition was originally published in 1839, and which is arguably the first significant book on pathology that was published in the United States, listed only 5 entities that involve the vulva: hemorrhagic infiltration, warty excrescences, polyps, ulcers and clitoral hypertrophy (5). Other classical texts of the 19th century, if not on the subject of the aforementioned infectious diseases or malformations, discussed the vulva primarily to mention how diseases of the vagina or upper genital tract may secondarily involve it (6). In part due to the increased use of microscopy in the late 1800s, numerous descriptions of various vulvar malignancies were published by the early 20th century, and the basic clinicopathologic profiles of some neoplasms had begun to emerge. In his 1919 text, *Neoplastic diseases, a textbook of tumors*, James Ewing summarized the literature on vulvar neoplasia up to that point, including some distinctive features of vulvar invasive squamous cell carcinoma (referred to in that work as "epidermoid carcinoma") that are now well-recognized today, such as its association with "extensive sclerosis and atrophy" of the skin, the latter a clear reference to the disease that is now classified as lichen sclerosus (7). Notably, there is also mention of neoplasms of sweat gland or Bartholin gland origin, as well as melanomas, three tumor categories that are still considered relatively rare, but which have long been recognized (7).

For most of the 20th century, diseases of the vulva received a moderate amount of consideration in the medial literature that could arguably be considered inadequate, given the significance of the organ and the potentially deleterious impact on quality of life and life itself when it is afflicted with significant disease. This may be attributable to a variety of factors, including the rarity of cancers at this site (8), the fact that vulvar diseases may theoretically be managed by practitioners in numerous disciplines of medicine (including dermatology/dermatopathology, family medicine, obstetrics and gynecology) thereby potentially reducing the sort of sustained, concentrated investigative efforts that typically result in scientific progress, social/cultural issues that may prevent patients from bringing vulvar diseases to medical attention, potentially potentill potentially leading to self resolution of diseases without an understanding of their etiology, pathogenesis or natural history, and disease-specific factors that prevent clinical trials on vulvar cancer from being widely available, among others (9,10). In the diagnostic pathology realm, vulvar specimens are relatively uncommon, and the spectrum of medical diseases that result in many of them are more typically seen by dermatopathologists than by general pathologists, or even specialized gynecologic pathologists. Nevertheless, the past several decades have seen a resurgence in academic analyses of, and accordingly progress on understanding vulvar diseases, including in the pathology literature wherein, for example, numerous textbooks are now available.

This issue of the Journal is wholly dedicated to vulvar pathology, the first such issue in its illustrious history. The nine review articles that comprise this issue are detailed treatises on a selection of topics in vulvar pathology, encompassing newer developments as well as areas that may potentially pose a diagnostic challenge to the practicing pathologist. In their contribution, Shalin et al review lichenoid dermatoses that may involve the vulva, with an emphasis on clinico-pathologic correlation. This reaction pattern may be seen in several disease states, and the authors explore how to navigate this morphologic pattern to generate clinically meaningful interpretations. Zare performs an in-depth review of infectious diseases of the vulva other than the human papillomavirus (HPV), including disorders by a selection of viral, bacterial, fungal and parasitic organisms. The pathologist' recognition of salient morphologic features and the correlation of pathologic with clinical findings may facilitate the prompt diagnosis and treatment of these disorders. There are three articles on squamous cell carcinoma, since these tumors, along with their precursors, constitute the vast majority of primary vulvar malignancies. Precancerous lesions of vulvar squamous cell carcinoma (VSCC) is the subject of the contribution from Jenkins and Mills. The authors discuss classical precursor lesions as well as those that have only recently been proposed in the HPV-independent pathway, including the evidentiary and biologic basis for potentially

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https://doi.org/10.1053/j.semdp.2020.09.008

Available online 22 September 2020

classifying each as a precursor. Chen and Hoang review 15 possible prognostic factors in VSCC, with a detailed consideration of articles that were published during the past decade. Xing and Fadare review molecular events in the pathogenesis of VSCC, including molecular events that are differentially prevalent in the HPV-dependent and HPV-independent pathways. Two contributions deal with the relatively uncommon phenomenon of glandular malignancies involving the vulva. In the first of these, Konstantinova and Kazakov review all clinicopathologic aspects of extramammary Paget disease, with an emphasis on recent developments. The second deals with overtly invasive glandular neoplasia. Approximately half of adenocarcinomas that involve the vulva originated from extra-vulvar locations, but a diverse array of primary vulvar adenocarcinomas may occur. Desouki and Fadare review primary adenocarcinomas of the vulva and related structures, and discuss a conceptual nosologic scheme that is largely based on their histogenesis for analyzing these cases. Mesenchymal tumors of the vulva are evaluated in the contribution by Chapel et al. Some of the lesions in this category may have overlapping pathologic features but notably different clinical behaviors, which necessitates that they are accurately classified. The final contribution is the rare phenomenon of pediatric vulvar malignancies. As reviewed by Strickland and Fadare, the reported cases appear to be classifiable into one of 5 entities, each of whose clinicopathologic features, as discerned from the published cases, are discussed. It is my hope that this issue makes for informative and enjoyable reading for anyone that has an interest in vulvar pathology.

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