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Histopathological Feature and Surgical Outcome of Vulvar Squamous Cell Carcinoma and Lipoma in Female Cattle

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Abstract: Vulvar squamous cell carcinoma (VSCC) is not rare or clinically insignificant health status in cattle, and vulvar lipoma is a benign lesion. These entities need to be differentiated as the prognosis and management differ significantly. Describing clinical presentation, surgical management, and histopathological features of vulvar squamous cell carcinoma and lipoma in female dairy cattle in Wasit province (Iraq). Twenty five of Holstein cows and calves which having a vulvar and/or vaginal mass were subjected initially to clinical examination including rectal palpation, speculum inspection, surgical resection under local or epidural anesthesia, and histopathological analysis of collected tissue sections. The results indicated that such lesions were spread among cows ranging between 10 days (female calf) to 9 years and above; in this case, adult (72%) was significantly higher than young (28%) female cattle. Lesions were found in a wide age category including a 10-day-old calf girl. The clinical manifestations were mass, pain, ulcer, hemorrhage, malodor, and parasite infestation in some animals. Excision was complete in all, one 9-year-old cow had a mass of 0.5 kg. The VSCC cases were histologically characterized by invasive nests and cords containing atypical squamous epithelium with keratin pearl formation, stromal desmoplasia, and irregular necrosis and suppurative inflammation. Lipomas were made up of well-differentiated adipocytes which are organized into lobules. In most animals, postoperative recovery went off without further incident when wound care was provided and there were clear surgical margins that were correlate with positive short-term prognosis. VSCC and vulvar lipoma show a similar clinical presentation but different histopathology and prognosis. Total surgical resection with sufficient margins is a good initial treatment and histopathology optimizes diagnosis and prognostication. Timely surgery and early detection can enhance the outcome of the affected cattle.

Keywords: External Reproductive Lesions, Dairy Cows, Surgical Complications, Iraq

1. Introduction

Cows are relatively rare in terms of neoplasia in the external genitalia, but the lesion is a significant source of discomfort, infertility, and culling [1]. The squamous cell carcinoma (SCCs) are the most common forms of vulvar malignancies in cattle, developing in stratified epithelium at the muco-cutaneous region and in non-pigmented skin. These tumours generally appear in the form of proliferative, ulcerated, or erosive masses that can bleed and have malodour [2]. Contrary to this, lipomas are harmless mesenchymal neoplasms of adult fat cells and are rarely documented in the cow vulva [3]. It has been suggested that exposure to non-pigmented ultraviolet (UV) radiation, the skin, chronic irritation, genetic predisposition, and old age are risk factors of bovine SCC [4]. It is crucial to distinguish VSCC from other vulvar masses (e.g., fibropapilloma, leiomyoma,

fibrosarcoma, melanoma, and lipoma) as the treatment and prognosis of each one of them differ significantly [5]. Other putative factors are chronic irritation/ inflammation and host factors. Cow vulva and vagina tumors have a continuum of benign and malignant tumors; SCC is one of the most common forms of malignant tumors in adult cattle. On the other hand, primary lipomas of the vulva are not very common, and the majority of the reports are of isolated cases [6], [7].

VSCC may present as a mass (lump), which can be either ulcerated, fleshy, warty, or exophytic, or as an ill-defined, erythematous lesion, at the junction mucosal and labial, and is usually accompanied by pain, pruritus, bleeding, and secondary infection [8]. Types of differential diagnoses are fibropapilloma, papilloma, fibroma, leiomyoma/ leiomyosarcoma, hemangioma/ hemangiosarcoma, melanoma, granulomatous inflammation, and lipoma [9]. Before consequential treatment, careful clinical observation and biopsy are thus advised. VSCC presents invasive squamous cell nests/cords of atypical cells that are keratinized (keratin pearls), intercellular bridges, anisocytosis/ anisokaryosis, and inconsistent mitosis [10]. The cytokeratin Immunohistochemistry (IHC) establishes epithelial genesis; the Ki-67 and p53 indices are used to aid grading and prognostication. Lipoma is composed of the lobules of mature adipocytes spaced by fine fibrous septa and exhibits limited atypia and mitosis [11]. Localized vSCC is most commonly treated with wide local excision; surgery (partial/total vulvectomy and, in some cases, partial/total vaginectomy) varies based on the size of the tumor at the time of surgery, depth of tumor, and margin status [12]. Cryotherapy, topical or intralesional chemotherapy (cisplatin, or laser ablation) can be considered when it is a small or superficial lesion, or when the disease has a positive margin [13]. The management of the risk of dehiscence and recurrence relies on the use of postoperative wound care and infection control, and lipomas are usually treated with the help of simple excisions unless they are not removed completely [14], [15]. The current paper provides a summarization of the clinical appearance, surgery, histopathology, and short-term care in 25 cows that were taken to one tertiary veterinary hospital with a mass of the vulva or vagina. We show the diagnostic usefulness of histopathology and IHC to differentiate between VSCC and lipoma and describe clinical practice implications of both field and hospital practice.

2. Materials and Methods

Study design and period

The presented study was approved by the Scientific Committee in the College of Veterinary Medicine (University of Wasit).

Animals and clinical examination

Twenty-five female Holstein cattle (cows and calves) that had clinically visible masses of the vulva and/or vagina were included. Animals that only had lesions caused in the cervix, uterus, or ovaries were not used. In case of their existence, more detailed hospital records were consulted to place the occurrence of tumors in the local population in context. General physical examination, rectal palpation, and vaginal inspection with the help of the vaginal speculum were performed on all animals.

Anesthesia and surgery

Case-based, rely on case requirements, local perilesional infiltration, or caudal epidural anesthesia. Normal aseptic preparation involved hair removal of the perivulvar area, warm water and soap lavage, as well as disinfection of the surgical site. Ligation and mild electrocautery were used to achieve hemostasis in case they were available. There was proper wound closure, which involved the use of appropriate suture material (e.g., chromic catgut, silk, where necessary as a hemostatic) and simple interrupted or mattress designs [16], [17].

Histopathology

Tissues were fixed in 10 per cent neutral buffered formalin, routinely processed, paraffin-embedded, sectioned at a nominal thickness of about 5 μm , and stained with hematoxylin and eosin. Pathologic variables in these cases have involved the type of tumor, differentiation, presence of keratin pearl formation, necrosis, inflammation, and margin status where possible [18], [19].

Postoperative care and outcome assessment

Animals received postoperative analgesia and antibiotic therapy. Wounds were monitored for dehiscence, infection, and fistula formation.

3. Results

The findings revealed that the lesions were distributed among cows aged from 10 days (female calf) to ≥ 9 years; in which, significant increases were reported in adult [72% (18/25)] more than young [28% (7/25)] female cattle, see Figure 1.

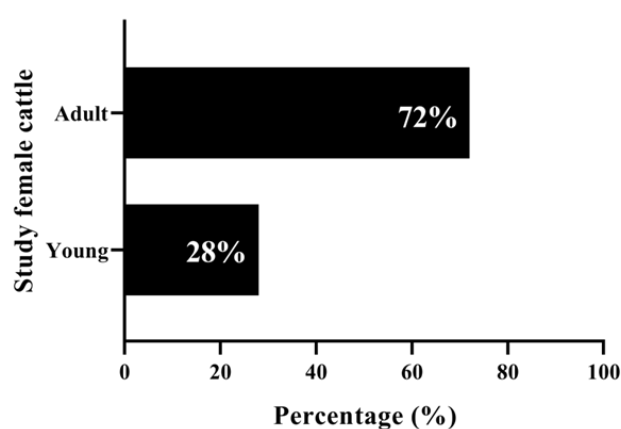


Figure 1. Prevalence of vulvar lesions among study female cattle.

Manifold outcomes were proliferation or nodular exophytic masses of the vulva, and in some instances, spread to the vestibule/vagina. Lesions were often ulcerated, bloody, malodorous, and painful to the touch. Some of the animals had blood-sucking ticks in the perineal area and other body parts, see Figure 2. All cases were operated on using either local or epidural anesthesia via lidocaine 2%. A 0.5-kg mass was excised from a 9-year-old cow through a total excision. There was an objective to clear gross margins; unambiguous margin evaluation was possible in intact specimens, see Figure 3.



Figure 2. Preoperative clinical view of vulvar SCC (ulcerated lesion).



Figure 3. Pre- and post-operative clinical view of vulvar lesions.

Histopathology and immunohistochemistry

Invasion nests and cords of abnormal squamous cells that contain keratin pearls, intercellular bridges, and variable pleomorphism, desmoplasia, necrosis, and neutrophilic infiltration with irregular cauliflower-shaped masses that are localized to the lips of the vulva, which is commonly accompanied by a foul-smelling discharge and secondary bacterial infection. The diagnosis of squamous cell carcinoma was confirmed after the histopathological examination revealed the presence of keratin pearls, cellular pleomorphism, and invasive nests composed of squamous epithelial cells. On the contrary, younger cows, including calves younger than one year, were observed to have lipoma cases. The lobular zones exhibited the presence of mature adipocytes, which were divided by thin fibrous septa, which is in line with the diagnosis of benign lipoma. Microscopic observation of lesions showed the existence of fibropapillomatosis, epidermal hyperplasia, or exophytic proliferation in epidermis (squamous and granulosum epithelium) as up

growth lesion. The lesions were also seen as appearing as prominent cords or squamous nodules, which were covered with acanthosis and stratum corneum, and seen as mature, large papillae with down-growing rete pegs, see Figures 4 and 5.

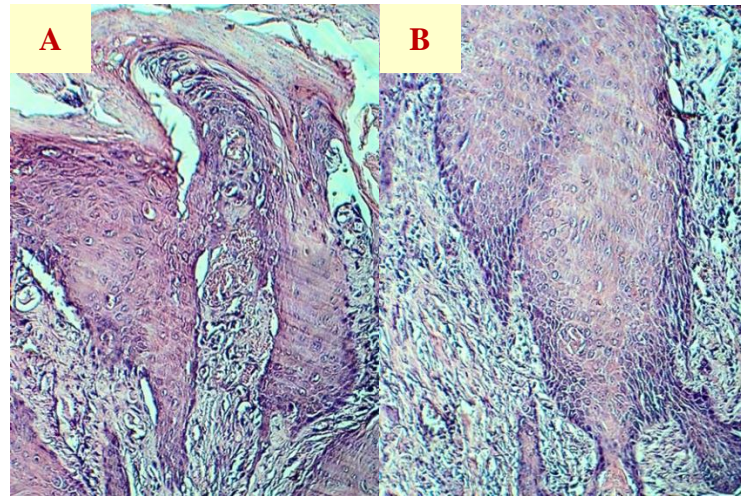


Figure 4. (A) Histopathological section shows acanthosis, hyperkeratosis, and collagenous media with infiltration. (B) Long papillae of hyperkeratosis (H & E stain, 100X & 200X).

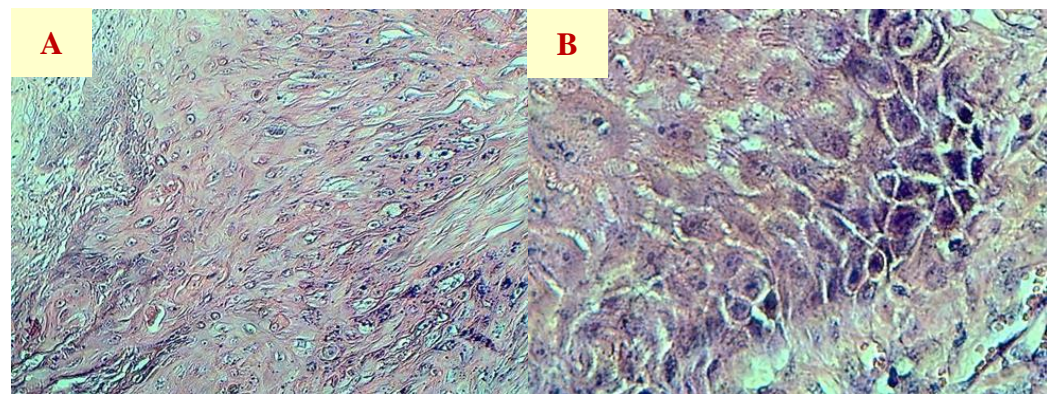


Figure 5. Histopathological section shows hyperkeratosis, acanthosis. (B) Cross-section of papillae with eccentric keratosis (H & E stain, 200X & 100X).

The results of all animals were disordered papillary projections with different proportions of epidermal hyperplasia. Papillary projections were oriented all over the section in epidermis with enwrapping of thick collagen fibrous connective tissue and at times between mononuclear inflammatory cells, such as lymphocytes, macrophages, and plasma cells. Besides the intermittent penetration of polymorphonuclear inflammatory cells, a fibrous collagen capsule surrounded the tumor cells and was subdivided into lobules was observed to be with nests of tumor squamous epithelium. In other parts, epidermis lesions that were exposed to irritation and healing demonstrated colossal erosion of squamous-covering epithelium and necrotic dermatitis, extreme and total epidermis lesions, necrosis, and extensive inflammatory cell infiltration, predominantly macrophage. The tumor cells, which look like normal squamous cells of epidermis (spinosum and granulosum), are giant polyhedral cells with a central nucleus and eosinophilic cytoplasm, with the production of keratin either at the surface or in cross sections of tumor papillae. The tumor cells were observed as necrotic polyhedral enlarged cells with hyperchromatic nuclei in other sections, and as having intranuclear inclusion bodies, which are more than one per cell in some cases, see Figures 6 and 7.

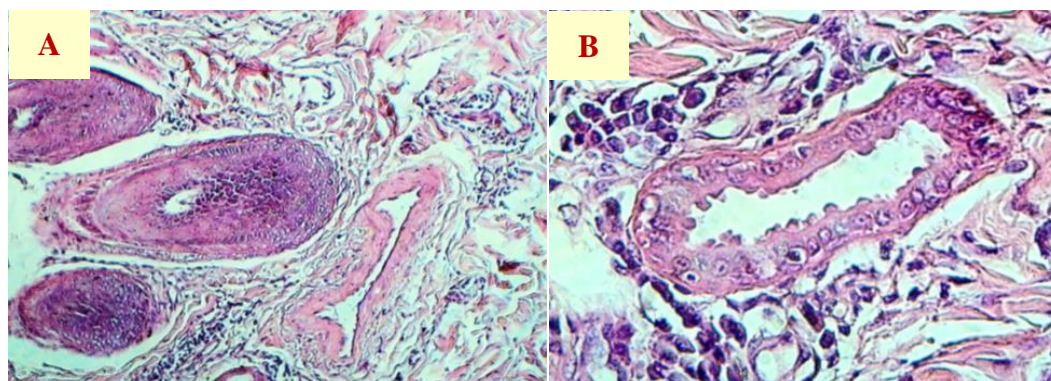


Figure 6. Histopathological section shows (A) Folliculitis, and infiltration of inflammatory cells. (B) Hypertrophy, severe degeneration of lining epithelium, periductal infiltration (H & E stain, 400X & 100X).

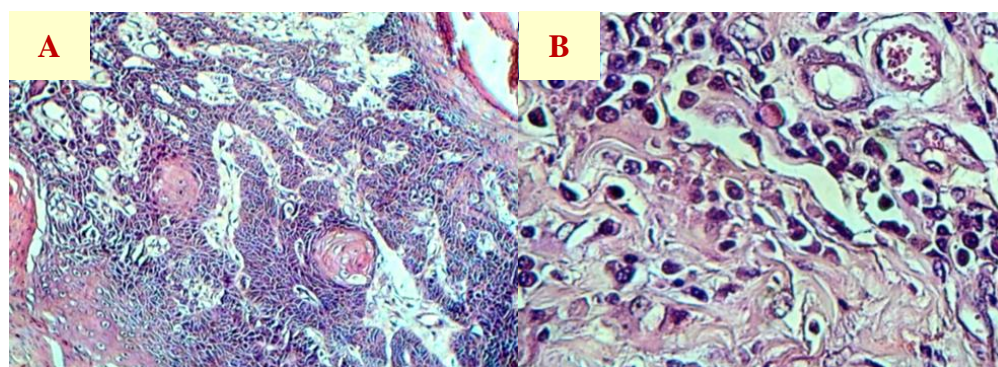


Figure 7. Histopathological section shows (A) Expansion and connection of hyperplastic-basophilic papillary rete. (B) Newly formed hair follicles and infiltration of mononuclear cells (H & E stain, 100X & 400X).

Postoperative management and recovery

Wound care and postoperative monitoring were required to heal well. The cases that were completely excised and with clear-cut surgical margins were the ones that had a good prognosis. A major focus was minimization of recurrence and complications (infection or wound dehiscence).

4. Discussions

Squamous cell tumors, leiomyoma, fibroma, fibro-papilloma, hemangioma, fibrosarcoma, leiomyosarcoma, and melanoma tumors may be found in the vagina and the vulva of cattle [20], [21]. The squamous cell tumors are also common in pigment-free parts of the body, and are much more often identified in old animals [22], [23]. As seen in the case provided, the mass existed on the right side of the vulva only, and vaginal tumors are normally removed using electrocautery. The small-scale masses are easy to sedate and anesthetize, and the big masses need more significant anesthesia [24]. Li et al noted that epidural anesthesia with lower or upper preference is usually used in large-scale gynecologic surgeries in cattle [25]. The surgery in this case was conducted under intrathecal anesthesia, and no pain or anesthetic complications were experienced during the intraoperative period [26]. According to Alam and Mukherjee, squamous cell carcinoma is characterized by the formation of keratin pearls and a good degree of differentiation, as well as by the fact that the tumor also spreads to the closest lymph node nodules [27]. In the current scenario, we observed multiple bleeding as well as necrotic masses, but the clinical examination showed that the lymph nodes (prefemoral, prescapular and supramammary) had a normal size and surface. This is possibly because

the history of tumor is relatively short. It has been proposed in the literature that squamous cell carcinomas are very invasive and spread to the lymph nodes [28]. Nonetheless, Peinado et al indicated that the postmortem examination was not possible on the current case, which is why it was not possible to state whether the tumor metastasized to adjacent tissues and organs [29].

The histopathological examination showed that microscopic results tended to agree with the literature data, and the conclusion that the tumor was squamous cell carcinoma was made [30], [31], [32]. Other authors have also reported epithelial proliferative foci, as well as, keratin pearls in the shape of submucosal islets and cords in the neoplastic epithelial cells of this squamous cell carcinoma [33], [34]. Similarly, Wolfer et al identified that the foci of tumor cells and individual ones typically have keratinization [35]. The literature has referred to the formation of loose connective tissue that was widely prevalent in the tissue in the tumor and has been proposed to be significant in the diagnosis of invasive carcinoma [20], [36]. Chen and Song stated that tumor parenchyma, which is supported by fibrotic tissue of the given case supports this theory, however, Fathima et al stated that ulceration, necrosis, and inflammatory cell infiltration that are observed on a regular basis of the tumor tissue are explained by ulceration and contamination of the surface of the mass [37], [38].

5. Conclusions

Bovine vaginal squamous cell carcinoma (BVSC), is an affliction that is prevalent in cows around the world. BVSC causes are unclear, and there are a number of factors that are thought to cause the disease. The diagnosis of BVSC at an early stage is essential in enhancing the treatment. A good treatment of BVSC is surgical treatment. Nevertheless, bovine vaginal squamous cell carcinoma (BVSC) can be treated but it is best diagnosed at an early stage of the disease via routine screening and screening lab tests and treatment has been found to be better, when diagnosed at an early age. The use of surgical treatment is the most suitable treatment option of BVSC because surgical treatment has been proven to enhance the outcome of treatment. BVSC epidemiological surveillance is advised to ascertain the causes and socioeconomic effects of the disease because epidemiological surveillance has been proved to enhance treatment results. It is suggested that farmers and breeders be educated and sensitized on the significance of early diagnosis and surgical intervention of BVSC, since awareness and education has proven to increase the outcome of treatment. It is also advised to continue scientific research on the bovine vaginal squamous cell carcinoma (BVSC) to enhance the treatment and diagnosis because scientific studies have revealed that it results in better treatment outcomes.

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