A case report on alveolar rhabdomyosarcoma in an indigenous dog

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A case report on alveolar rhabdomyosarcoma in an indigenous dog

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List of Abbreviations

Abbreviation and symbol	Elaboration
RMS	Rhabdomyosarcoma
ARMS	Alveolar rhabdomyosarcoma
MF	Mitotic figure
GC	Giant cell
RB	Rhabdomyoblast
Etc.	Et cetera
H&E	Haematoxylin and Eosin

Abstract

A 12 years-old, male indigenous dog was presented to Shahedul Alam Qaderi Teaching Veterinary Hospital (SAQTVH) in Chattogram, Bangladesh with a large tumor on its right front leg. The histopathological findings of the tumor revealed as alveolar rhabdomyosarcoma (ARMS). The tumor was surgically removed from the dog, while there had been no recurrence for five months, the patient died five months post-operatively. The cause of the death would be metastasis which could not be confirmed due to lack of follow up. A histopathological study showed poorly differentiated neoplastic mononuclear cells forming nests in an alveolar pattern. This is the first incidence of ARMS in an indigenous dog in Bangladesh. Despite the limited resources prevented myogenin staining for diagnostic confirmation, the well-contained, defined appearance of the tumor supports the diagnosis of ARMS. This report highlights the challenges in diagnosing and treating ARMS in indigenous dogs and emphasizes the need for further research and diagnostic markers to improve detection and management.

Keywords: Rhabdomyosarcoma, Indigenous dog, Histopathology.

Introduction

Rhabdomyosarcoma (RMS) is an unusual malignant tumor primarily affecting young individuals and originating in skeletal muscle. It poses a diagnostic challenge in both human and veterinary medicine due to its infrequency and its wide variation of macroscopic and microscopic presentations (Caserto, 2013). While RMS typically emerges in skeletal muscle, it can also develop in non-striated muscle organs like the urinary bladder, uterus, and cervix (Kim et al., 2007). In dogs, RMS has been observed in various locations, including the pharynx, larynx, cardiac muscle, gingiva, urinary bladder, larger omentum, urethra, skin, and trachea (Brockus and Myers, 2004).

RMS in animals, especially in dogs, is a relatively rare type of tumor that exhibits considerable variation in its appearance, histology, and cellular characteristics. Common histological subtypes encompass embryonal RMS, alveolar RMS, botryoid RMS, with pleomorphic RMS being less frequent. Due to their rarity, the diagnosis, prognosis, and treatment of these malignancies are challenging. Botryoid RMS is the most prevalent subtype, followed by embryonal, alveolar, and the less common pleomorphic subtypes, as per data from veterinary case reports (Gombert et al., 2020). According to Caserto (2013), 63% (n = 39/62; age was not given in 2 cases) of canine RMS (apart from laryngeal rhabdomyosarcoma) occurs in dogs under the age of 2 years. The remaining 37% are distributed among animals aged 3 to 15years (n = 9/62; 15%), 7 to 10 years (n = 7/62; 11%), and >10 years (n = 7/62; 11%). Eighty-nine percent (n = 55/62) of cases involve dogs under 10 years old.

The diverse phenotypes, age of onset, and cellular structures of RMS make their detection and classification challenging, which might explain their limited presence in the literature. There are three variants of embryonal rhabdomyosarcoma (RMS) based on cytological characteristics. Myotubular RMS, this variant is characterized by multinucleated "strap cells" that produce myotubes (Caserto, 2013); rhabdomyoblastic RMS, this variant features an abundance of round to polygonal cells with eosinophilic cytoplasm (Parham, 2001); spindle-cell RMS, this is a recently identified, uncommon subtype where thin spindyloid myoblast cells typically form bundles and myxoid stroma (Cooper, 2002). Botryoid RMS, mainly appears as

a polypoid, grape-like mass primarily in the urinary bladder that has histological characteristics including strap cells and undifferentiated rhabdomyoblasts inside a myxoid matrix (Kobayashi *et al*., 2004). Histologically, alveolar RMS can be divided into two categories: solid and classic, the classic type is characterized by small, poorly differentiated cells with little cytoplasm and the formation of an "alveolar pattern" (Cooper, 2017). Pleomorphic RMS, the least common RMS form in humans and typically found in adult dogs, is characterized by spindle cells with abundant eosinophilic cytoplasm, an absence of embryonal or alveolar patterns, unusual mitotic figures, and a high degree of pleomorphism (Caserto, 2013).

Canine rhabdomyosarcoma is uncommon in veterinary medicine; there are only 65 case reports so far have been published. Botryoid RMS (n = 28; 43%) is the most common RMS, followed by embryonal RMS (n = 15; 23%), and pleomorphic RMS (n = 2; 3%) is the least common. Alveolar RMS (n = 7; 11%) is the second least common type of RMS in dogs, after pleomorphic RMS. The rates of metastasis (50%) were similar for alveolar (n = 3/6) and embryonal RMS (n = 4/8) (Caserto, 2013).

In veterinary medicine, achieving a prognosis and proper diagnosis for canine RMS is challenging due to its rarity and frequent misinterpretation. The prognostic significance of canine RMS remains a challenge for veterinary professionals due to limited follow-up and post-mortem evaluation. In this case, based on clinical sign, the case was suspected that it would be a connective tissue tumor. There has no published research on RMS in indigenous dog in Bangladesh. Accordingly, the case was investigated and analyzed through histopathological study.

This study aims to explore the histological and cytological characteristics of canine rhabdomyosarcoma, with a specific focus on the diagnostic and prognostic aspects of this rare condition in veterinary medicine with its diverse manifestations.

Materials and method

A twelve-year-old, male indigenous dog was brought to the Shahedul Alam Qaderi Teaching Veterinary Hospital (SAQTVH), Chattogram, Bangladesh due to the growth of a sizable lump on its right front leg near the elbow joint. The lump felt hard and could not be moved. To remove this large lump, the dog underwent surgery on the upper part of its right front leg under general anesthesia. The procedure began with standard preparation of the area, followed by the removal of the lump through blunt dissection after making an incision in the skin. The wound was closed by suturing the skin and underlying tissues separately. Parenteral antibiotics were administered for five days following the operation, and topical povidone-iodine ointment was applied. After 10 days, the skin sutures and bandage were removed. The patient was monitored for five months, and there was no sign of the lump recurring, however, patient died five months post-operatively. The lump was semi-soft, fleshy, friable with irregular margins, almost round shape, a solid texture, and the lump had a mixed whitish-pink color (Figure 1).

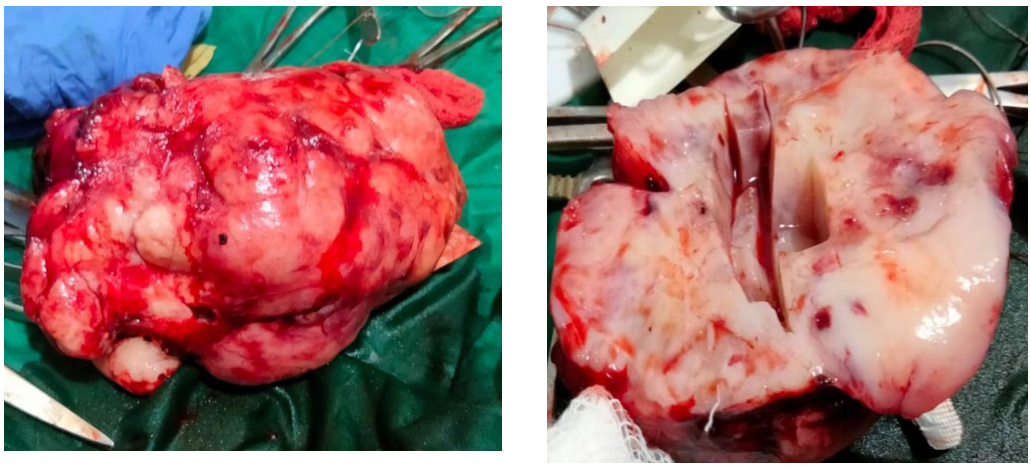

Figure 1: Mass excised from the right forelimb near elbow joint region. The excised large mass is characterized by a smooth surface, semi-soft, fleshy, almost round, solid texture and reddish in appearance.

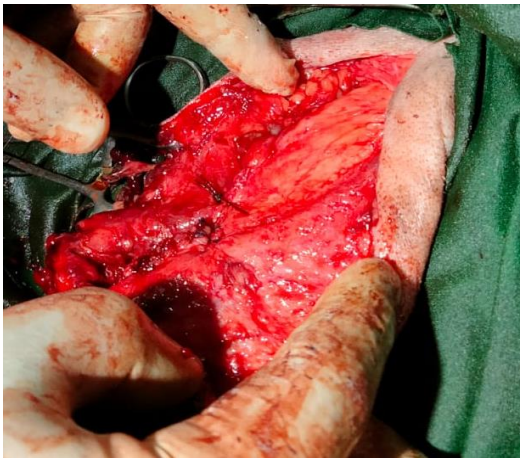

Figure 2: Suturing the skin and underlying tissues separately.

Figure 3: After surgical removal of the tumor from right front leg of the dog.

The excised mass was then referred to the histopathology lab at the Department of Pathology & Parasitology, Chattogram Veterinary & Animal Sciences University for examination for histopathological evaluation. Then three representative tissue samples were taken from the mass, preserved them in 10% formalin, processed them routinely, and embedded them in paraffin wax. Thin sections of paraffin-embedded tissue were stained with hematoxylin and eosin (H&E) for examination under a light microscope.

Result

The cancer did not recur for five months while the patient was being monitored, but the patient died five months following surgery. The dog might have died physiologically because of its advanced age or the cancer might have been metastasized, which could be the cause of death. Because owner did not contact regularly and last two months no imaging and blood testing were performed and after death no post mortem was done, the cause of death could not be ruled out.

The mass was semi-soft, fleshy, friable, with uneven borders, an almost round form, and a solid texture, and it was a mixed whitish-pink in color. Following H&E staining of the tissue sections from the mass, it was examined under a light microscope at different magnifications. Under the microscope, the tissue was found to be consisted of numerous neoplastic mononuclear cells with prominent round-to-ovoid nuclei and scanty cytoplasm, showing signs of being poorly differentiated and having mild variations in nucleus size (anisokaryosis). These neoplastic cells were arranged in an alveolar pattern, forming nests separated by either thick or thin fibrous septa. They were unevenly distributed within the large and small alveolar spaces, either lining or covering the fibrous septa. Additionally, multiple mitotic figures were frequently observed in the less-differentiated neoplastic cells, with four to five mitotic figures present per high-power field (× 100) (Figure 4).

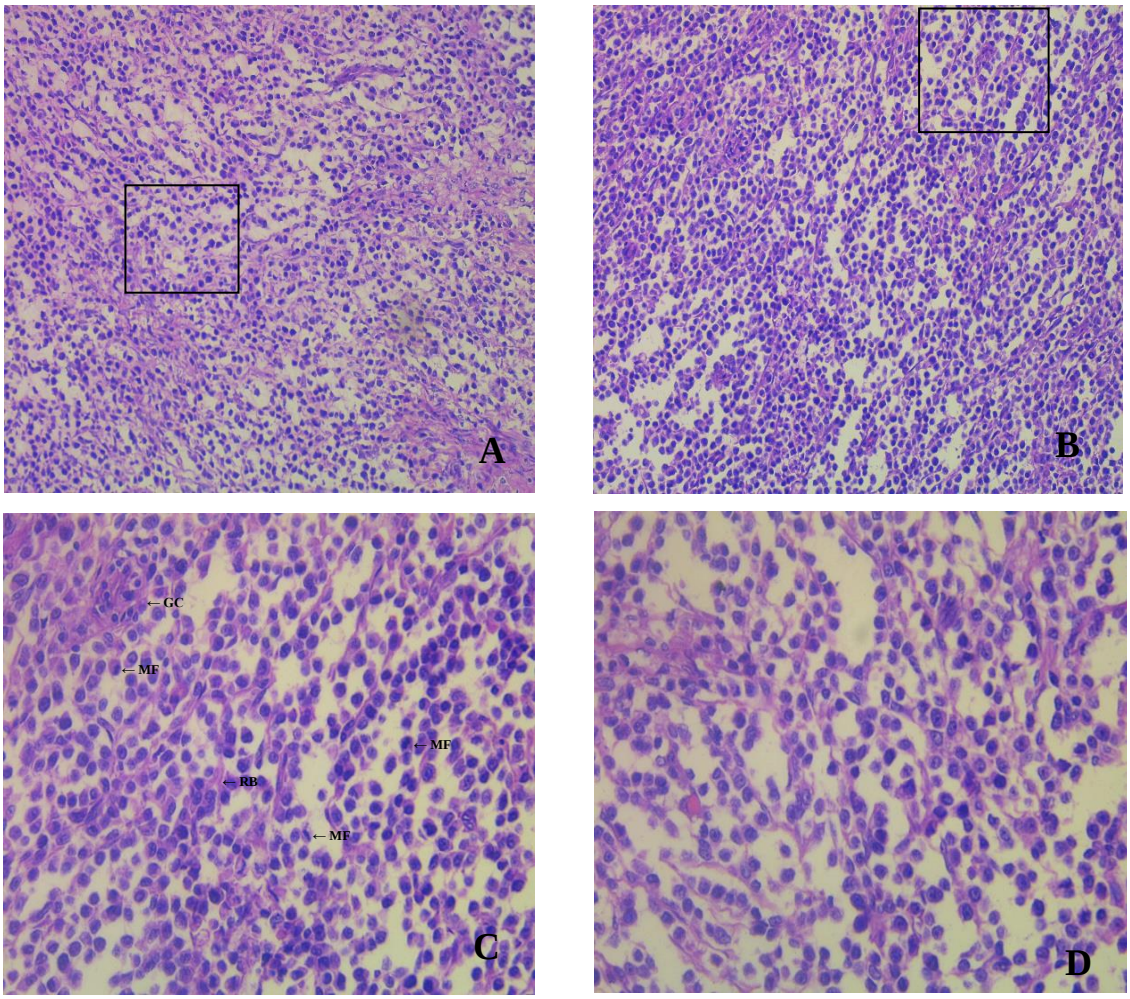

Figure 4. A,B. Large clusters, nests, cords and trabeculae of primitive round cells, separated by variably thick fibro-vascular septa arranged in an alveolar pattern; C. Small to intermediate monomorphic cells with multinucleated tumor giant cells (GC), spindle shaped rhabdomyoblast (RB), and a lot of mitotic figures (MF); D. Neoplastic tumor cells characterized by small and large mononuclear cells with large round-to-ovoid hyperchromatic nuclei and scant cytoplasm were separated by thick or thin fibrous septa and arranged in an alveolar pattern forming cell nests. H&E stain

Discussion

After surgery, the patient passed away five months later. There maybe two explanations for this. This could be because of the age of the dog. Perhaps the dog's older age caused it to die physiologically. The life span of an indigenous dog is average 8 to 15 years. So, it could be a physiological death. The other reason could be the metastasis of the cancer, which was not investigated. According to Caserto (2013), the metastasis rate of alveolar and embryonal rhabdomyosarcoma is about 50%, and in both cases the survival rate is very poor. Murakami (2010) reported that, a dog died because of aggressive metastasis within 100 days while receiving radiation therapy and chemotherapy (Murakami *et al*., 2010).

Alveolar rhabdomyosarcoma is characterized by a distinctive alveolar pattern in its tumor cells. These cells tend to form collagenous partitions and are often loosely grouped in the center of the alveolar spaces. In poorly differentiated alveolar rhabdomyosarcomas, observing cross striations can be challenging (Park et al., 2016). The tumor itself is composed of two types of cells: poorly differentiated small cells arranged in a solid pattern, and round to oval cells forming the characteristic alveolar pattern. In this alveolar pattern, cells are grouped into nests separated by fibrous septa, with a central loss of cellular cohesion leading to the creation of pseudo glandular spaces. While cells at the periphery remain attached to the fibrous septa, those in the center tend to be more isolated and have eccentrically located hyperchromatic nuclei. Despite the absence of cross striations in the cancerous cells, the typical alveolar pattern strongly suggests a diagnosis of alveolar rhabdomyosarcoma (Sarnelli et al., 1994). In a case reported by Kimura et al., (2013), a 3-year-old Shih-Tzu, a dog breed, had gingival alveolar RMS, with anaplastic cells arranged in the typical alveolar pattern, numerous mitotic figures, and multinucleated cells with no cross-striations. In dogs, the solid variant of alveolar rhabdomyosarcoma may have thin fibrous septa dividing cell nests, resembling the classic "neuroendocrine pattern," but often lacks this distinction, making it challenging to differentiate from rhabdomyoblastic embryonal RMS (Caserto, 2013).

In this case, there was large clusters, nests, cords and trabeculae of primitive round cells, separated by variably thick fibro-vascular septa arranged in an alveolar pattern, Small to intermediate monomorphic cells with multinucleated tumor giant cells, spindle shaped rhabdomyoblast, and a lot of mitotic figures. Cells of origin for RMS could be mesenchymal progenitors, satellite cells, or endothelial progenitor cells. It is difficult to say as the cells are highly undifferentiated.

There have been no reports of this type of cancer in indigenous dogs in Bangladesh. A relatively small amount of work has also been done with indigenous dogs in other countries. So far, this is the first report on ARMS in indigenous dog in Bangladesh. Therefore, there were some challenges emerged when studying this case. However, ARMS is quite uncommon in other countries, with very low frequency and prevalence.

In this case, considering the observations made during the physical examination, based on the gross findings, microscopic findings, and the knowledge that a lack of cross-striation is frequently observed in poorly differentiated rhabdomyosarcomas, this particular case can be confidently identified as an alveolar rhabdomyosarcoma. It's noteworthy that despite the tumor's well-contained and clearly defined appearance, the evidence still supports this diagnosis.

Limitation

Our research underscores the potential utility of myogenin as a diagnostic marker for canine alveolar rhabdomyosarcoma, a technique that we were unable to implement because of laboratory resource limitations. Although this procedure is auxiliary to ARMS diagnosis.

Conclusion

Canine rhabdomyosarcoma (RMS) is a relatively rare and diagnostically challenging malignancy with several subtypes, including alveolar RMS, botryoid RMS, and embryonal RMS. Histopathological and immune-histochemical examinations are essential in veterinary medicine for identifying rhabdomyosarcomas and screening out other neoplasms. RMS presents a challenge to pathologists and clinicians due to its wide range of variability, the lack of prognostic value of its histologic subtypes, and the few numbers of documented occurrences in animals. The case of alveolar RMS in an indigenous dog in Bangladesh represents prevalence of this type of cancer in this region. More research is required to better understand the biological behavior and useful strategy for its classifications and characterization.

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Farjana Akter

Author, November 2023.

Biography

Farjana Akter, the daughter of Md. Sahab Uddin and Monowara Begum born on 10th October, 1997. She passed her Secondary School Certificate (SSC) examination in 2014 with a GPA of 5.00. Then she passed her Higher Secondary Certificate (HSC) examination in 2016 with a GPA of 4.67. Currently she is an intern student of Faculty of Veterinary Medicine at Chittagong Veterinary and Animal Sciences University. In future she would like to work as a veterinary surgeon and conduct research on zoonotic diseases.