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Morphology and histology of the thymus gland in dromedary camel with particular reference to thymic Hassall's corpuscles

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Abstract

The thymus gland is the primary lymphoid organ that undergoes postnatal growth followed by gradual atrophies and functional decline with age progress. The thymus gland has similar morphology across species, with a thoracic portion in the cranial mediastinum and a cervical portion along the trachea. Histologically, the thymus consists of an outer cortex populated with darkly stained T lymphocytes and a pale inner medulla. The medulla contains thymic Hassall's corpuscles (THC), which may function as sites for T cell maturation or as communication points between T cells and antigen-presenting cells. The thymus gland in camels has yet to be well studied, with limited research on its macroscopic and microscopic anatomy. In this study, the thymus glands of camel calves were examined. The thoracic portion was triangular and located in the cranioventral part of the mediastinum. The cervical portion extends cranially to the level of the thyroid gland and, in some cases, to the larynx. Histologically, the camel thymus had a fibrous capsule and connective tissue trabeculae, dividing the gland into incomplete lobules. The cortex was heavily populated with thymocytes, while the medulla contained epithelial reticular cells. A perivascular space (PVS) consisting of mature T lymphocytes surrounding blood vessels was also identified. THCs were present in the medulla, with variable shapes and forms ranging from small-sized to very large-sized with degenerative changes. Further research is needed to fully understand the role of the thymus gland in camels and its implications for vaccination programs and immune health.

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Introduction

The thymus gland is the primary lymphoid organ in which the T lymphoid precursors get matured and programmed through a complex sequence of cell proliferation, selection, death, and maturation (1-3). This gland showed marked postnatal growth due to exposure to different antigens. Once the animal reaches sexual maturity, the thymus begins to involute through gradual atrophy and decline in function with age progression (4-6). Generally, the thymus gland is similar in morphology across species, with some variations among species. It comprises a thoracic portion located at the cranial mediastinum and a cervical portion, which could be seen along the trachea (7-9). The thoracic portion is unpaired in horses and ruminants and paired in dogs and pigs (10). In equine, the thoracic portion lies in the pericardial mediastinal space and extends to the pericardium. The cervical portion showed variability in the extension level but rarely extended to the thyroid region (11). In the cattle calf, however, the cervical portion extends cranially to the larynx (10). In the buffalo calf, the cervical portion extends cranially to the thyroid gland (12). However, the sheep's cervical part extends to the pharynx (13). on the other hand, in the goat, the cervical lobe is the longest part and extends from the thoracic inlet to the level of the larynx (14). Histologically, the thymus showed a consistent appearance across species. This gland comprises an outer cortex of darkly stained, densely packed T lymphocytes and

a delineated inner pale medulla (1,5,9). Within the medulla of the thymus, there is a distinctive structure, the thymic Hassall's corpuscles (THC). This structure is well-developed in humans and guinea pigs but poorly developed in the thymus of mice and rats (5,15). It has been suggested that THC is formed by degenerated epithelial reticular cells (16). Others suggested that it represents the 'cemetery' for dead thymocytes or merely an area for the maturation of medullary thymocytes (17). In sheep, THC passes through cycles of degeneration and regeneration, where the macrophages play a role in this cycle (18,19). These data suggest that THC may actively communicate with developing T lymphocytes and antigen-presenting cells within the thymus. According to the literature survey, there is no research specialized in the anatomy of the thymus of dromedary camel in terms of macroscopic and microscopic anatomy, except for what was previously published in terms of electronic microscopy (20) and immunohistochemistry (21). It was also mentioned in the review papers of Jarrar and Faye (22) and Al-Ramadan (23).

Therefore, this research aims to comprehensively investigate the macroscopic and microscopic anatomy of the thymus gland in the dromedary camel to contribute valuable insights to the existing knowledge base and enhance our understanding of the unique anatomical features of the thymus gland in the dromedary camel with particular emphasis on the thymic Hassall's corpuscles.

Materials and methods

Animals

Eight clinically healthy camel calves were divided into two groups based on age. The first group was 3-4 months, and the second was 5-6 months. All the animals were slaughtered at Al-Omran Slaughter House, Al-Ahsa, Eastern Province, Saudi Arabia. The study was conducted after the approval from the Research Ethics Committee at the Deanship of Scientific Research, King Faisal University, number KFU-REC/2021-01-10.

Gross anatomical sample

The thymus gland with its surrounding organs was dissected from the thoracic cavity to study the thoracic portion, while the cervical portion was studied in situ in the neck of the calf-camel after injection of 10% neutral buffered formalin within the common carotid artery. All samples were photographed with a Sony α-550 camera (Sony Corp., Pathumthani, Thailand).

Histological Study

Thymus glands from cervical and thoracic potions were collected from the animals after slaughter and immersed in 10% paraformaldehyde in PBS (pH 7. 3). An automated tissue processor (TP 1020, Leica, Germany) was used to process the tissues after 48 hours of fixation. After Tissue Embedding using Leica Microsystems (St. Louis, MO, USA), a rotary microtome (RM 2135, Leica, Germany) was used to section the tissues. In order to carry out routine histological slides, the sections were floated in a warm water bath (41°C) and mounted onto Superfrost Plus™ microscope slides. After drying, slides were stained with hematoxylin and eosin, according to Bancroft *et al.* (24).

Results

Gross anatomical study

The thymus gland of camel is composed of two parts: thoracic and cervical parts. Thoracic part; it is triangular in outline and located at the cranioventral part of the mediastinum between the trachea and large blood vessels dorsally and the sternum ventrally. Laterally, it is related to the right and left lung cranial lobes. Caudodrosal to thymus is the pericardium, where the external capsule is continued with the pericardium (Figure 1). Cervical part; the cervical part is detected as a ribbon-like structure extended up to the level of the caudal pole of the thyroid gland between the trachea and the left external jugular vein. In some cases, the cervical part reaches the level of the larynx, where it is dilated, forming an oval end (Figure 2).

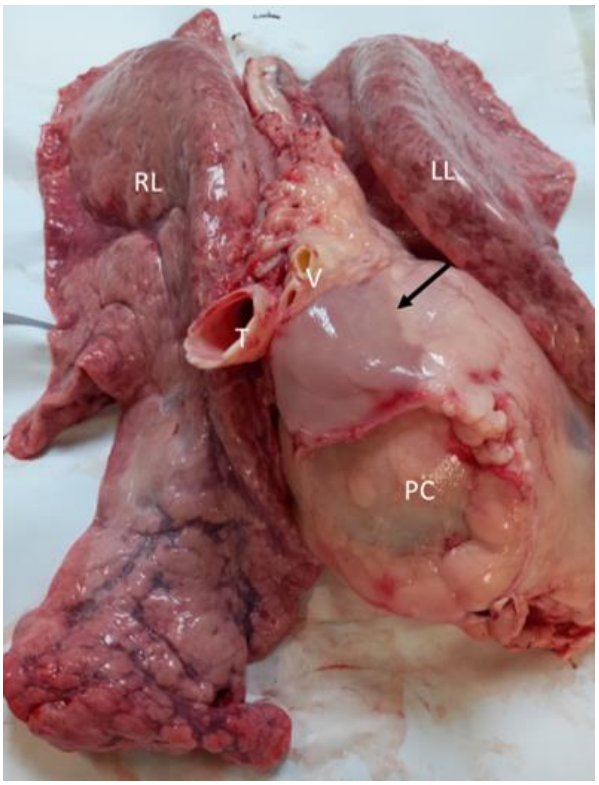

Figure 1: The thoracic portion of the thymus gland (arrow) located in close relation to the ventral to the trachea (T) and large blood vessels (V). Notice that the capsule is continued with pericardium (PC). Right lung (RL), left lung (LL).

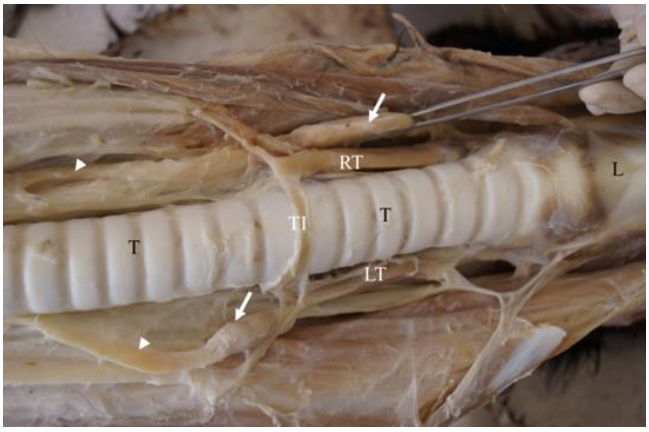

Figure 2: The thymus gland of the camel showing the cranial dilated ends of the cervical portions (arrows) the extended caudally as then ribbon (arrowheads). The right portion is at the level of the right thyroid lobe, while the left portion reaches the caudal pole of the left thyroid lobe. (T) trachea, (L) larynx, (RT) right thyroid lobe, (LT) left thyroid lobe, (TI) thyroid isthmus.

Histological study

The thymus gland of the camel is covered from the outside with a fibrous capsule from which connective tissue trabeculae have emerged, dividing the gland into incomplete connected lobules (Figure 3 a,b). Several lymphocytic cells infiltrate the connective tissue of the capsule and the trabeculae (Figure 3 c). Blood and lymphatic vessels are distributed to the various parts of the thymus along the connective tissue of the capsule and trabeculae before entering deeply with the parenchyma of the thymus gland as smaller vessels (Figure 3 a,b). The parenchyma is divided into several lobules easily demarcated into the cortex and medulla. The cortex of the thymus lobule is heavily populated with T lymphocytes, each with darkly stained round to oval nuclei (Figure 3 d). Several epithelial reticular cells are detected within the cortex due to its distinctive shape. These cells are stellate-shaped with large spherical, lightly stained nuclei (Figure 3 e). The medullary reticular epithelial cells are hardly distinguishable from the surrounding mature T cells. Besides the cortex and medulla, another smaller compartment was also detected within the thymus of the camel, the perivascular space (PVS). This space comprises a group of mature T lymphocytes around the blood vessels that enter and leave the thymus along the trabeculae (Figure 3 f).

THCs could be detected within the medulla besides the mature T lymphocytes and epithelial reticular cells (Figure 4 a-d). Variable shapes and forms of THC have been detected in the thymus of the dromedary camel. The four classes of THC have been identified; (1) small-sized without central acidophilia, necrosis or cellular debris; (2) small-sized with round or oval in shape formed of squamous cells where the centrally located ones have acidophilic cytoplasm and show some degenerative changes; (3) medium-sized THC with necrotic and cystic degenerations and (4) very large-sized THC with calcified, necrotic material and cellular debris (Figure 4). Some of these corpuscles displayed degenerative changes and some granulated and foamy macrophage detected with the center.

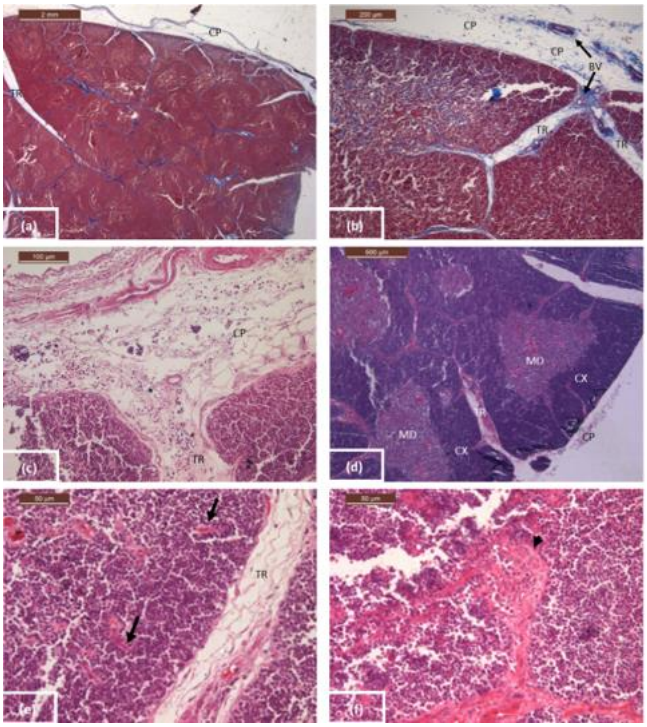

Figure 3: Microscopic section of the thymus gland of dromedary camel showing: (a) general view of the gland; (b) higher magnification of part from (a) showing Connective tissue capsule and trabeculae; (c) high magnification from junction between capsule and trabeculae showing varies lymphocytes; (d) the lobules of the thymus gland demarcated into dark cortex and light medulla; (e) high magnification of the cortex showing the epithelial reticular cells (arrows); (f) high magnification showing the PVS (arrowhead) along the TR of the thymus. Capsule (CP), trabeculae (TR), blood vessel (BV), cortex (CX), and medulla (MD). Trichrome stain (a&b) Hematoxylin &Eosin stain (c-f), Bar= 2, 50, 100, 200, 500 µm.

Discussion

The gross anatomical results showed that the thoracic portion is located at the cranioventral part of the mediastinum. The camel's thoracic part is triangular in outline without a clear distinction between the left and right lobes. In the cattle calf, the thoracic portion of the thymus is described as significant with a lobular structure. The lobs are

well-defined and triangular-rounded in shape (5). However, the right, left, and intermediate lobes have been described in the thoracic portion in cattle and pigs (7). Therefore, the current study showed the thoracic part of the camel thymus as an indistinct right and left portion, which might be due to the intermediate lobe connecting both lobes. A similar description was reported from the thymus of the horse. In this latter species, the thymus gland is represented by the thoracic portion, which is situated at the precardiac mediastinum region. However, there is no clear distinction between the right and left lobes (7). In the dog, however, the thoracic part formed of a larger right lobe and a smaller left lobe. It is located in the cranial mediastinum, laying over the sternum and extending caudally to the pericardium (5).

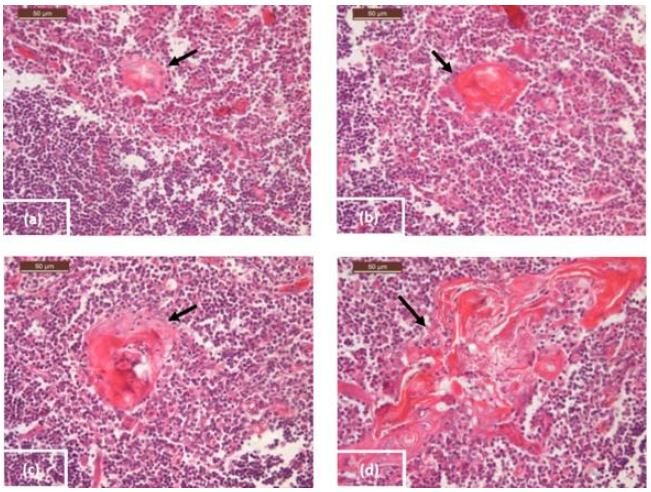

Figure 4: Histological types of thymic Hassall's corpuscles (arrows) (a) small-sized without central acidophilia notice the nuclei of the large epithelial cells; (b) small-sized with deeply acidophilic cytoplasm and some degenerative changes; (c) medium-sized THC with necrotic and cystic degenerations at the center; (d) large-sized THC with calcified, necrotic material and cellular debris. Hematoxylin &Eosin stain, Bar= 50 µm.

Interestingly, the cervical portion in the examined camel calves extends cranially up to the level of the thyroid gland and up to the larynx in some cases. In a previous study, the right and left portions of the thymus gland in the camel were reported to be located between the trachea and the left external jugular vein, but there was no mention of its extremities (16). In the horse and dog, the thymus might extend up to the middle of the neck (5). In ruminants and pigs, the cervical portion is represented by a V-shaped structure that might extend cranially along the trachea (7).

The thymus gland of the camel is covered with a connective tissue capsule, which is projected inside the gland, forming trabeculae and dividing the organ into several cellular compartments housing T lymphocytes. According to the previous study (15), the parenchyma of the thymus formed several incomplete lobules connected. This image is similar to the microscopic description gained from different animal species, including primates (6,19). In the current study, each lobule is demarcated into cortex and medulla. The cortex is darker than the medulla because it is highly populated compared to the medulla. The cortical cells have darkly stained nuclei, a phenomenon similar to other animal species (2). The T lymphocytes at the medulla are more significant than those at the cortex, with large spherical, lightly stained nuclei. Banks (20) has mentioned that the thymocytes of the medulla are not as densely packed as those of the cortex, resulting in a lighter appearance of the medulla compared to the cortex.

The PVS reported currently within the camel's thymus has also been reported in equine (21). The later authors also reported the presence of eosinophils within the PVS among other mature T cells spanning this compartment. In this respect, the PVS has been suggested to be a space where hematopoietic cells that enter or leave the thymus must cross when leaving the thymus to the blood vessels (22). Moreover, in a recent study, the authors suggested that the endothelial cells lining the blood vessels in the PVS of the thymus play a crucial role in the homing of early thymocyte precursors (23). This might be the same role for PVS in the dromedary camel. However, more in-depth studies need to be performed.

The present study showed the four types of THCs within the medulla. Raica *et al.* (24) previously described those types in the human thymus gland. Their presence within the camel's thymus was early reported in the previous studies Aly *et al.* (25). However, none of the previous studies have given a complete description of the type of THC in the camel. Although their function is not fully elucidated, these corpuscles were said to be a central link for the CD4-CD8 positive and negative selection of T lymphocytes, destroying autoimmune T lymphocyte clones through phagocytosis and subsequent lysis (26,27). The older study suggested a maturation site for the medullary thymocytes (9). Nevertheless, many studies collectively indicate a role for the THC in the communication between antigen-presenting cells and thymic T cells (25-29).

From the macroscopic and microscopic view, much profound and comprehensive research must be performed on the camel's thymus gland. Due to its role as the primary immune organ for maturation and development of the essential cellular immunity cell, the T lymphocyte, there should be concerted efforts between specialists and those interested in the health of the camels to pay special priority to the immune system, especially to one of the essential organs of this system, the thymus gland. More in-depth research is needed to study the molecular events accompanied by the involution of the thymus; hence, these results should be considered when developing any camel vaccination program.

Conclusion

In summary, in the current research, a thorough anatomical examination of the thymus gland in the dromedary camels has been provided, emphasizing thymic Hassall's corpuscles (THCs). Distinctive macroscopic and microscopic features, including the triangular thoracic portion and the presence of epithelial reticular cells, have been identified. The variable forms of THCs have been described, and their attribution in T cell maturation and communication with antigen-presenting cells has been discussed. These findings highlight the need for further research to understand the functional significance of the camel thymus in immunity. By deepening our knowledge, we can enhance camel health management strategies and advance the development of vaccination programs.

Acknowledgments

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Conflicts of interest

The authors declare no conflict of interest.

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مورفولوجيا وأنسجة الغدة الصعترية في الإبل وحيدة السنام مع إشارة خاصة إلى جسيمات هاسل

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الخلاصة

تعتبر الغدة الصعترية من الأعضاء اللمفاوية الأساسية والذي تخضع للنمو ما بعد الولادة يلي ذلك ضمور تدريجي وخمول وظيفي مع تقدم العمر. هناك تشابه في الغدة الصعترية في الشكل عبر أنواع الحيوانات المختلفة، حيث تتكون من جزء صدري في المنصف الأمامي وجزء عنقي على طول القصبة الهوائية. من الناحية النسيجية، تتكون الغدة الصعترية من قشرة خارجية داكنة مزدحمة بالخلايا اللمفاوية ولب داخلي باهت. يحتوي اللب على جسيمات هاسل والتي قد تعمل كمواقع لنضج الخلايا التائية أو كنقاط اتصال بين الخلايا التائية والخلايا المقدمة للمستضد. ورغم أهميتها فإن هذه الغدة لم تدرس في الإبل بشكل جيد بعد، حيث لا يوجد إلا عدد محدود من الأبحاث التي تهتم بالتشريح العياني والمجهري. تم في هذه الدراسة فحص الغدد الصعترية في صغار الإبل حيث أظهرت النتائج أن الجزء الصدري مثلث الشكل ويقع في الجزء القحفي المركزي من المنصف. ويمتد الجزء العنقي الى الأمام حتى مستوى الغدة الدرقية، وفي بعض الحالات، إلى الحنجرة. من الناحية النسيجية، فإن الغدة الصعترية في الإبل تحتوي على كبسولة ليفية وفواصل من الأنسجة الضامة، مما يقسم الغدة إلى فصيصات غير منفصلة تماما. كانت القشرة مكتظة بالخلايا الصعترية بينما احتوى اللب على خلايا شبكية ظهارية. تم التعرف أيضا على مساحة حول الأوعية الدموية تحتوي على خلايا ليمفاوية تائية ناضجة تحيط بهذه الأوعية. كانت جسيمات هاسل موجودة في لب الفصوص الصعترية، بأشكال مختلفة تتراوح من صغيرة الحجم إلى كبيرة الحجم للغاية مع تغيرات تنكسية. ومع ذلك هناك حاجة إلى مزيد من البحث لفهم دور الغدة الصعترية في الإبل بشكل كامل وتأثيراتها المحتملة على برامج التطعيم والصحة المناعية.