

Tick Bites – the View from Inside-Out

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Summary

The tick feeding process in humans and its local effects have been studied histologically and in reflection microscopy on specimens of skin lesions, and on tick samples. The mouthparts of the attached ticks, embedded in a cement cone, lined the oral canal. The pharynx was supplied with anti-reflux valves and dilating muscles. The dermis around the mouthparts was, characteristically, replaced by a loose network of fibrin, endothelia, and collagen fibers, soaked with edema and blood, with a dense neutrophilic infiltrate beneath the cone. The vessels showed interruptions, with blood extravasation, endothelial proliferation, and vasculitis. After the tick removal, Erythema Chronicum Migrans-like patches, foreign body granuloma, T- and the B-cell lymphoid hyperplasia, and alopecia areata-like hair loss were recognized.

Introduction

Hard ticks (Ixodidae) are blood-sucking Acari of the order Ixodida, supplied with a scutum and dorsally visible mouthparts. The histologic changes induced in the human skin by these parasites are largely considered aspecific, that is, not distinguishable from those caused by any other arthropod attacks or by trauma (1, 2). However, quite peculiar tick-bite reactions have been observed in the animal hosts by veterinary parasitologists (3, 4)). In order to detect possible specific features in humans, we have conducted a histologic study on a series of acute and chronic tick-bite reactions, and on the feeding apparatus of our collection of tick specimens.

Materials and methods

A few samples of Ixodidae of the genera *Hyalomma*, *Rhipicephalus* and *Ixodes*, and a series of acute and chronic tick bite lesions, documented in reflection microscopy, were processed histologically and their sections were stained with hematoxylin-eosin, orcein-Giemsa, periodic acid-Schiff, Weigert method for fibrin, Bodian's nerve fiber silver impregnation, and Warthin-Starry stain for spirochetes. Immunohistochemical

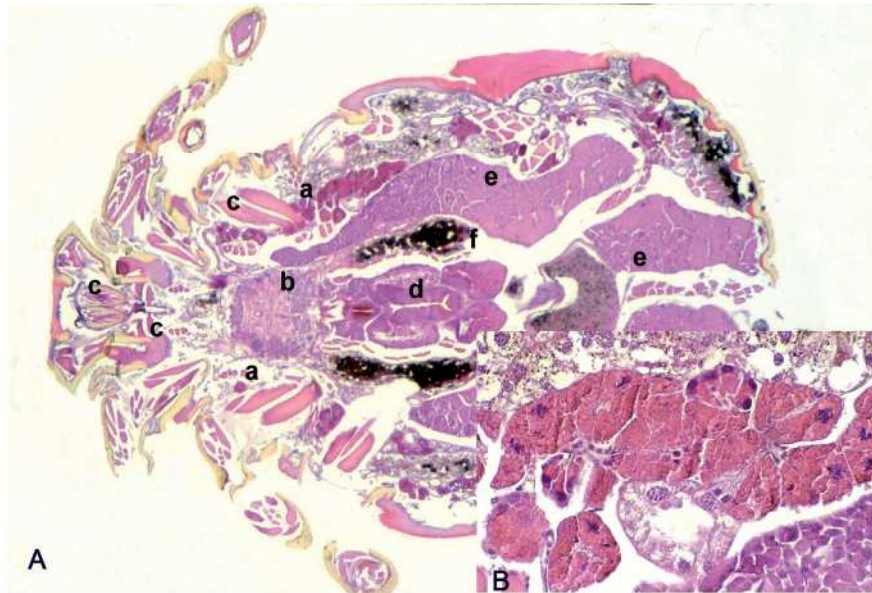


Fig. 1) A: Histologic section of tick body (nymph). a: salivary glands, b: brain, c: muscles, d: uterus, e: ovarium, f: gut. B) Detail of A: Acinar salivary gland.

stains were performed with the following antibodies: 4KB5 (anti CD45RA) and CD10 for B-lymphocytes, UCHL1 (anti CD45RO) for T Lymphocytes, anti CD4 and CD8, for helper and suppressor/cytotoxic lymphocytes, anti-CD68 for macrophages, Bcl-2 for transformed follicular center B-cells.

Results

Reflection microscopy.

The details of the *gnathosoma*, that is, the biting/sucking apparatus, which forms the anterior section of the tick body, were analyzed. The palps, i.e., a pair of segmented appendages with chemical and tactile sensory functions, sheltered laterally the mouthparts, which consisted of a pair of slender chelicerae, located dorsally and ending with mobile pincers, and a toothed hypostome, located ventrally and grooved by a narrow food canal; all held by a mobile *basis capituli*.

Histologic study of the tick bodies.

The capitulum showed the muscles serving the chelicerae, and the pharynx, with its dilating muscles. In the idiosome, two paired salivary glands were visible antero-laterally (Fig.1A). They were of the acinar type (Fig1.B), and were mainly composed of intensely eosinophilic, granular secretory cells. In the engorged specimens, the typical sessile digesting cells were observed in the midgut epithelium. They were characterized by a pinched off appearance, due to the release of membranate vesicles

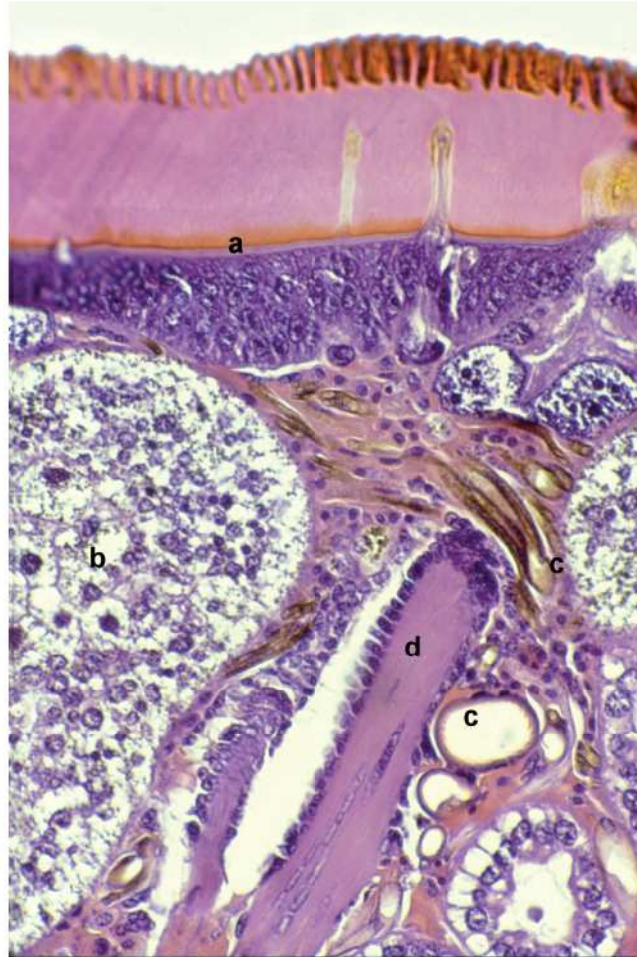


Fig. 2) a: Integument composed of a stratified cuboidal epithelium and a crenellated three-layered cuticle, b: midgut, c: tracheae, d: muscle.

from their luminal side, as well as, by their presence in the form of free, floating cells, in the gut lumen (Fig. 2).

The other organs identified (Fig. 1A) included: the branching tracheae, recognizable for the spiral pattern of their inner surface, the central nervous system, clustered around the esophagus, the uterus, a hollow muscular organ partly encircled by the horseshoe-shaped ovarium, and the motor muscles, which extended from the inner cuticular surfaces of the idiosome to the inner surfaces of the appendages.

The integument (Fig. 2, 3) consisted of a stratified cuboidal epithelium and of an epithelium- secreted cuticle. This was crenellated (the histologic appearance of the fingerprint-like pattern of its surface) and it was decorated with sensory setae, each supplied with a nerve, positive to silver impregnation.

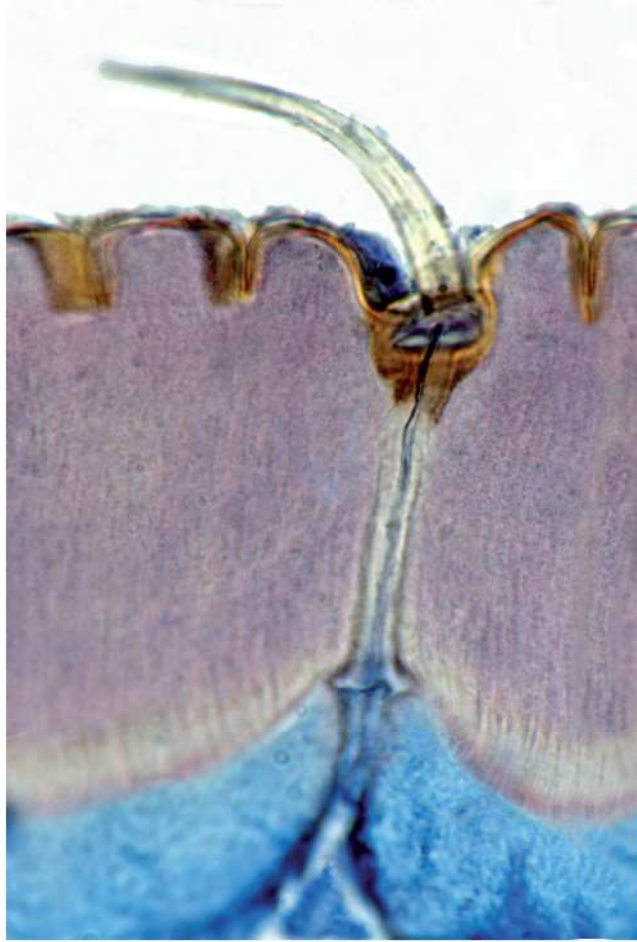


Fig. 3) Seta supplied with a nerve fiber positive to silver impregnation.

Histologic study of the skin lesions. Acute manifestations.

The sections of the brightly erythematous lesions with an attached tick showed the mouthparts embedded in a cement cone, which adhered to the epidermis spreading superficially between the prickle and the horny layer, and encroached irregularly on the dermis (Fig.4).

The one visible chelicera and the hypostome lined the oral canal, which continued with the pharynx and the hypopharynx in the *basis capituli*. Here, the anti-reflux valves and the pharynx-dilating muscles were visible, together with the muscle bundles serving the chelicerae (Fig.4).

The dermis below the apex of the cone was occupied by a dense neutrophilic infiltrate, which streamed along the cone canal and more deeply fragmented in conspicuous foci of neutrophilic and lymphocytic vasculitis and perivasculitis. All around,

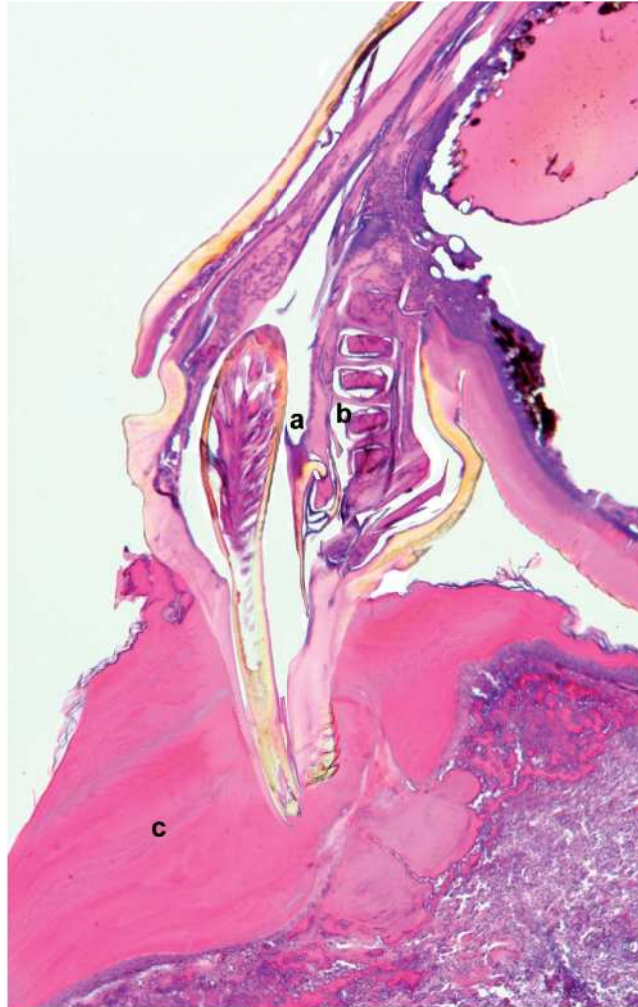


Fig. 4) Attached tick. a: antireflux valvae, b: pharynx dilating muscles, c: cement cone.

a wrecked area, lined by a band of basophilic necrobiotic tissue was noticed. Here, the fabric of the dermis was replaced by a disorganized network of fibrin filaments, endothelial linings, and residual collagen fibers, overwhelmed with blood and blurred by sheets of erythrocytes, as well as, sprinkled with lymphocytes and eosinophils (Fig.5). There was vasodilation, and the small vessels showed gaps of the walls and ruptures, with profuse blood extravasation. Other capillaries and post-capillary venules showed endothelial plumping and proliferation, which produced a vaguely spiral pattern with cribriform appearance of the lumina.

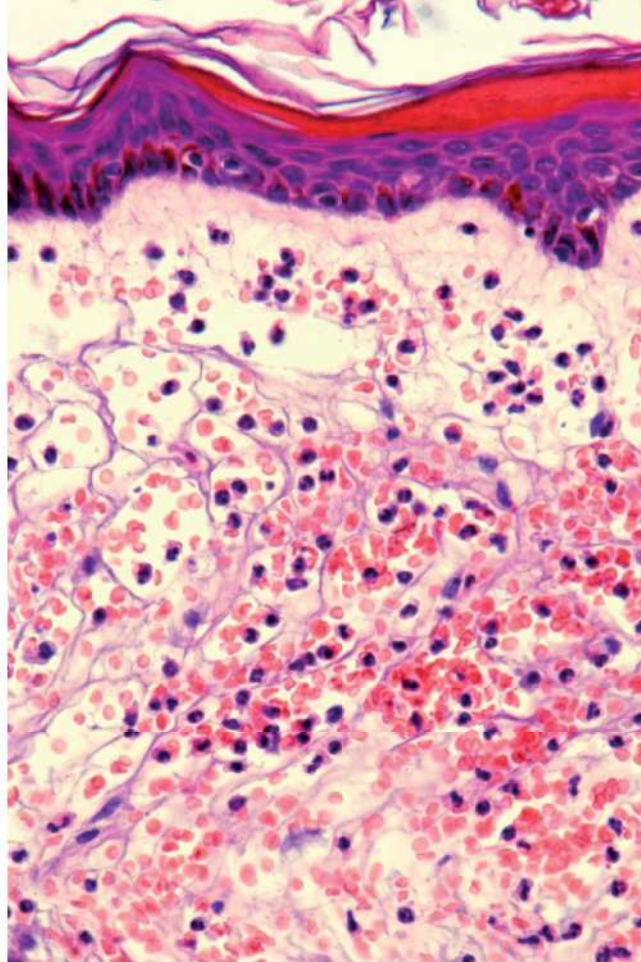


Fig. 5) Cavity: blood-flooded network of fibrin, residual collagen fibers and endothelia, replacing the fabric of the dermis.

Subacute and chronic manifestations.

Erythema chronicum migrans-like patches were noticed in the absence of serologically demonstrated borrelial infection. In these lesions, a mild, T and B lymphocytic or lympho-plasmocytic, perivascular infiltrate was present in the superficial and mid dermis, where the Warthin-Starry stain failed to reveal spirochetes.

Papular and papulopustular lesions were histologically characterized by suppurative and granulomatous inflammation, with giant multinucleated cells phagocytizing foreign body material. Nodular lesions often featured purely granulomatous inflammation, with epithelioid and multinucleated giant cells. Some of these were laden with birefractile foreign body material, which, in one case, consisted of a pair of shafts, recognizable as fragments of mouthparts.

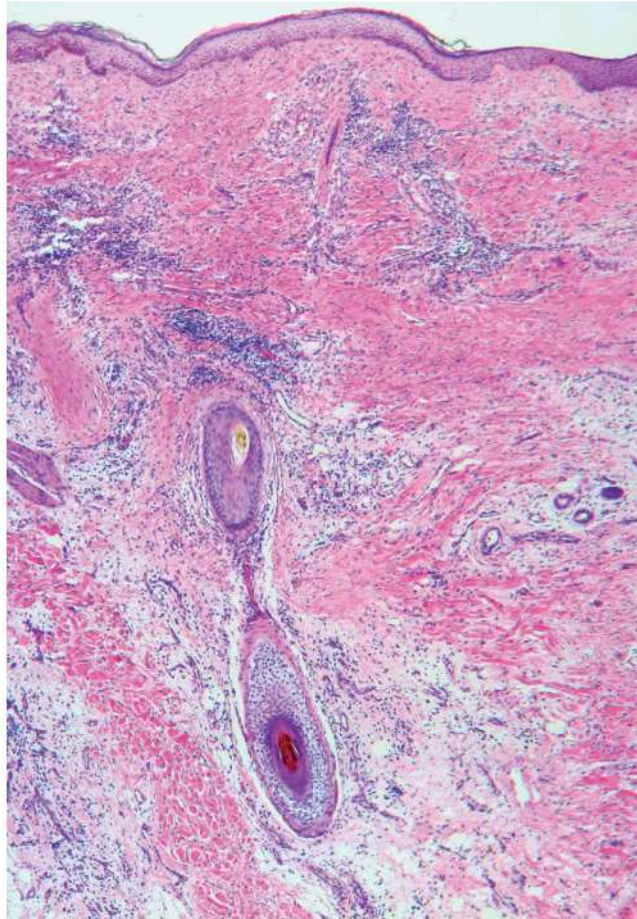


Fig. 6) Tick bite alopecia: catagen hair surrounded by edema, newly formed capillaries, and a sparse lymphocytic infiltrate, huddled in perivascular foci.

Nodular, “persistent arthropod bite reactions” were characterized by a top-heavy infiltrate, mainly composed of CD45RO+ T lymphocytes and admixtures of eosinophils. There was vasculitis with loss of the endothelial cohesion and fibrin thrombi, and nerve infiltration.

Less frequently the nodules displayed the histology of B-cell Cutaneous Lymphoid Hyperplasia, characterized by pseudo-lymphoid follicles with well-developed mantles. The germinative centers were composed of CD10+, CD45RA+, Bcl-2- centrocytes and centroblasts, as well as, of CD68+ tingible body macrophages. A number of eosinophils were mixed to the small lymphocytes. A granulomatous component, with multinucleated giant cells was sometimes detectable. Pericytic proliferation and concentric perivascular fibroplasia in different phases of evolution were detected.

One case of tick-bite induced alopecia of the scalp, was observed in a child. Clinically similar to alopecia areata, it showed, histologically, a wide stretch of skin

virtually devoid of adnexa, outlined by two symmetrical bands with perifollicular inflammation. In the center, there was diffuse edema of the dermis, with numerous newly formed capillaries, and a sparse lymphocytic infiltrate. Few catagen hairs with thickened perifollicular sheaths, surrounded by a denser lymphocytic infiltrate (fig.6), rare remnants of hair follicles and partly phagocytized naked hairs were scattered in this area. On the periphery, miniature anagen hair follicles were present.

On the edge of the lesion, dimensionally unaltered hairs, with multilayered fibrous sheaths, were surrounded by a dense lymphocytic infiltrate, at the height of their isthmus. The infiltrate comprised CD45RO+ T-lymphocytes, both of the T-helper (CD4+) and T-suppressor/cytotoxic (CD8+) types, with a scant admixture of CD20+ B-cells.

Conclusions

The local changes observed in our samples of human skin taken during the tick feeding process, largely match the histologic pictures described by the veterinary parasitologists on the experimentally parasitized cattle. Specifically, the replacement of the normal structures of the dermis with a blood flooded spongiform tissue, the ruptured vessels and the hemorrhagic neutrophilic vasculitis in the action range of the mouthparts overlap the features of the *cavity*, the analogous area of tissue devastation seen in the animal host (3, 4). These alterations, along with the cribriform pattern of the endothelial linings noticed in our specimens, do not appear, to our knowledge, in any other arthropod-induced lesions, with which, the tick-bite reactions share only the rich eosinophilic component.

The whole picture is produced by the negative pressure created by the mouthparts in association with the chemicals injected in the wound with the saliva. The vacuum is achieved through the combined actions of the pharynx dilating muscles and the antireflux valvae, while the cement completes the partial canal formed by the mouthpart and seals the skin breach (5). The chemicals include a number of vasodilatory, anti-hemostatic and antiinflammatory molecules, as well as, hyaluronidases and metalloproteinases, which account for the destruction of the dermal fabric in the cavity (6-12). These molecules are secreted by several types of differently specialized cells in the salivary glands, which include, in addition, the cement producing cells and cells able to extract and excrete excess water from the blood meal (13).

The chronic reactions do not seem specific and the numerous eosinophils present in them are a common clue to any parasitic attack (14). However, the finding of partly phagocytized paired fragments, reminiscent of chelicerae, is suggestive of tick-bite. The self-healing, alopecia-areata like, subacute hair loss, is characterized by a unique histologic picture, and shows clinical features comparable to the forms due to ant and bee attacks (15, 16).

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