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Age-Associated Structural Changes in Synovial Membranes of Rabbits and Dogs: A Comparative Review

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Abstract: Synovial membrane has considerable importance in the physical activities of all the mammalian. As a consequence, different aspects of synovial membrane have been studied in detail by numerous scientists. As age related changes and deformations are essential in understanding and curing of rheumatic and other illnesses associated with aging, these subjects have the prime importance. General appearance of the synovial membrane changes from small, shiny, smooth and light colored in young dogs and rabbits to large, rough and grayish colored in the olds. The dog's intima get thicker and more layered with aging and in rabbits intima cell types changes only. In rabbits and dogs connective tissue types of subintima changes from areolar, adipose and areola-adipose types connective tissue types to fibrous type with age increase. The collagen fibers are rare and scattered in young animals and the fibers increase gradually and form bundles and bands in middle age and old animals. The elastic fibers increase and thicken with aging in the synovial membrane of dogs. In rabbits trend of decrease occur from young towards old animals. In dog and rabbit synovial membranes capillaries are plenty in young animals and decrease with increasing age. In other members of the synovium age, associated changes are not particularly clear.

Key words: Synovial membrane, dogs, rabbits, age related changes, intima, subintima

INTRODUCTION

Synovial membrane plays a fundamental role in the movements of humans and other mammalian animals. Therefore, various aspects of the synovial membrane have been studied extensively by scientists; Castor (1960), Ghadially and Roy (1966), Krey *et al.* (1973), Levick and McDonald (1989), Rittig *et al.* (1992), Sagiroglu (1991a, b), Sagiroglu *et al.* (1991), Shimizu *et al.* (1996) and Sagiroglu (2012a, b). The pathology of the membrane during rheumatic illnesses are investigated by Bleedorn *et al.* (2011), Chew *et al.* (1990), Hayashi *et al.* (2004), Henderson and Pettipher (1985), Knight and Levick (1984), Levick and McDonald (1989), Malone *et al.* (1991), Rittig *et al.* (1992), Roy *et al.* (1966), Sagiroglu (1991b), Schumacher (1969), Thompson and Stockwell (1983), Watanabe *et al.* (1974) and Wright *et al.* (1989).

Recent studies on synovial membrane concentrated on electron microscopic studies of ultrastructure, changes caused by illnesses, ruptures and treatment (Bleedorn *et al.*, 2011; Cabrera *et al.*, 2008; Comerford *et al.*, 2006; Hayashi *et al.*, 2004).

Age associated changes and abnormalities in morphology of synovial membrane of the dogs and rabbits are investigated by Sagiroglu (2012a, b), Bleedorn *et al.* (2011), Canpolat and Sagiroglu (2000), Chew *et al.* (1990), Fawcett (1986), Henderson and Pettipher (1985), Knight and Levick (1984), Levick and McDonald (1989), Malone *et al.* (1991), Rittig *et al.* (1992), Roy *et al.* (1966), Sagiroglu (1991 b), Sagiroglu *et al.* (1991), Schumacher (1969), Shively and van Sickle (1977), Thompson and Stockwell (1983), Watanabe *et al.* (1974), Wright *et al.* (1989), Wyllie *et al.* (1964) and Wynne-Roberts and Anderson (1978). The studies on age related changes in synovial membrane are extremely valuable for understanding and curing of the rheumatic and other age related synovial membrane illnesses in human and animals.

This investigation reviews age related structural-morphological changes in two commonly used experimental animals; rabbits and dogs. Although, this research is based fundamentally on my earlier researches Sagiroglu (2012a, b), Canpolat and Sagiroglu (2000), Sagiroglu (1991a, b) and Sagiroglu *et al.* (1991), all the earlier researches related to the subject are used. Age associated structural changes in human synovium is also considered in the light of the present literature on the subject. This review studies the synovium as whole and principal members of synovium individually.

AGE RELATED CHANGES IN SYNOVIAL MEMBRANES OF DOGS AND RABBITS

Macroscopic appearance: The synovium of the young animals were pearly white colored, smooth, glistening and

thin (Sagiroglu, 2012a, b; Jilani and Ghadially, 1986; Krey *et al*., 1971; Sagiroglu *et al*., 1991; Wynne-Roberts and Anderson, 1978). In the older dogs the synovium were greyish coloured, rough and pastel. Similar descriptions are made by Jilani and Ghadially (1986), Sagiroglu (1991a, b) and Sagiroglu *et al*. (1991) for the synovium of human and rabbits.

Intima: Synovial intimal layer is observed as made of 1-2 layered cells in young dogs. Intimal cells (Fibroblast-like and macrophage-like) flattened or oval shaped. In middle aged dogs, intima contained 1-2 layered or 3-5 layered lining cells. Synovial intima of the old group formed of 2-6 layered cells. Intimal cell shapes of middle and old animals are cubic or polygonal (Sagiroglu, 2012a, b). However, some studies claim that the thicknesses of synovial cell layers are not associated with the age (Castor, 1960).

Synovial intima of juvenile human is 1-3 layered, chubby and formed of rounded and oval shaped cells. The cells are classified in three groups; A, B and C cells (Wynne-Roberts and Anderson, 1978).

The synovial membranes of adult rabbits are made of 1-3 layered lining cells. The membrane cells are described as A (Macrophage-like, M), B (Fibroblast-like, F) and C (Intermediate, I) type cells and discriminating of these cells in rabbits are easier than in human (Krey *et al*., 1973).

Jilani and Ghadially (1986) concluded that B and AB (C) type synovial cells are present in animals and with aging of rabbits A cells increase and B cells decrease in evident amounts.

Traumatic effusions in the synovial membrane cause the disappearance of the differences between A and B type cells (Roy *et al*., 1966).

The synovial intima is separated from the subintimal tissue by an intermediate fibrous zone rich in staining for type III collagen in old human donors (69-94 years of age) (Rittig *et al*., 1992).

Subintima: In dogs, connective tissue types of subintima from the surface towards depths of the subintima changes from areolar, adipose and areola-adipose connective tissue types as the age increases. In the synovial membranes of the old animals subintima areolar mostly change to fibrous connective tissues (Sagiroglu, 2012a, b).

However, connective tissue types are also depending on the history of synovium, especially depending on the functions of and pressures and impacts on the synovium (Fawcett, 1986; Henderson and Pettipher, 1985).

In rabbits the subintima is in general as areolar and areolar-adipose types in young animals and fibrous tissue increases with the increasing age. The cells are full and oval shaped and plenty in young rabbits and they decrease in amount and are flattened in old animals (Sagiroglu *et al*., 1991). Human synovium subintima is made of areolar, fibrous and adipose types (Krey *et al*., 1973).

Collagen fibers: As earlier research state collagen fibers are the basic structural support of the blood and lymph vessels (Castor, 1960; Ghadially and Roy, 1966).

The collagen fibers are rare and scattered in young animals and the fibers increase gradually and form bundles and bands in middle age and old animals. The collagen fibers around capillaries are rare in the young dogs and plenty and as bundles and bands in old dogs (Sagiroglu, 2012a, b).

Collagen fibers in human are very similar to of dogs and according to Castor (1960) they do not show any remarkable changes with aging. In experimental animals, the aging causes in an increase of collagen fibers (Sagiroglu, 2012a, b; Canpolat and Sagiroglu, 2000; Ghadially and Roy, 1966; Sagiroglu *et al*., 1991; Watanabe *et al*., 1974).

Elastic fibers: In the young dogs, thin elastic fibers increase from surficial subintima towards deeper layers. The elastic fibers further increase and thicken in the synovial membrane of the middle and old age dogs. In old dogs, elastic fibers increase in general structure of the synovial membrane and on the walls of the blood vessels and peripheral of the capillaries (Sagiroglu, 2012a, b). In rabbits, the amount of elastic fibers decrease with increasing age (Sagiroglu *et al*., 1991).

Elastic fibers are exceptionally rare in human synovial membrane and increases with age (Castor, 1960; Jilani and Ghadially, 1986; Wynne-Roberts and Anderson, 1978). Earlier resarch (Sagiroglu, 2012a, b; Canpolat and Sagiroglu, 2000; Castor, 1960; Sagiroglu *et al*., 1991; Thompson and Stockwell, 1983) state that elastic fibers are present in synovial membrane of rabbits and dogs and according to Sagiroglu *et al*. (1991) elastic fibers in rabbits synovial membrane decrease with aging.

Capillaries: The capillaries make of a fundamental portion of synovial membrane and earlier describe synovial membrane as a connective tissue with dense capillaries (Ghadially and Roy, 1966; Krey *et al*., 1973; Wynne-Roberts and Anderson, 1978).

In the young dogs, capillaries are present abundantly among intimal cells and layers just under the cells. The capillaries are either absent or rare among the synovial intimal cells of old dogs. However, in a trend from young to middle then to old, capillaries and larger vessels

increased and had larger radii towards the deeper parts of subintima. From young to old dogs, vascularity gradually increase in deeper subintima. The vascularity occurs as capillaries among the intima and as large vessels in the peripheries of old dogs (Sagiroglu 2012a, b). Similar findings are reported for rabbits by Sagiroglu *et al*. (1991).

In human synovial membrane similar age, related structural and changes are reported human by Fawcett (1986), Krey *et al*. (1971) and Wynne-Roberts and Anderson (1978).

In experimental animals, capillaries are more abundant in young animals and show different trends with aging of various animals (Sagiroglu, 2012a, b; Canpolat and Sagiroglu, 2000; Knight and Levick, 1984; Krey *et al*., 1973; Sagiroglu *et al*., 1991; Schumacher, 1969; Shively and van Sickle, 1977). In rabbits, the capillaries are abundant in the young and decrease with increasing age (Sagiroglu *et al*., 1991).

Nerves: Nerve fibers with or without myelin of the dog synovial membranes occur close to the joint capsule in all dogs of different ages. The peripheral nerves occur close to the blood vessels and collagen fibers of the deeper layers of subintima (Sagiroglu, 2012a, b).

Textbooks state that the nerves in synovial membrane convoyed to the blood vessels (Fawcett, 1986; Shimizu *et al*., 1996).

Although, the existences of nerve tissues in synovium are known (Shimizu *et al*., 1996), the changes due to aging and variations in different species are not described (Henderson and Pettipher, 1985).

Villi: In dogs, synovial villi appearance differ in various sections. Continuous villi are absent and any noticeable change in the amount of villi in different age groups are not detected. However, normal synovial tissue villi are numerous in all the age groups. The villi show variations both in shapes and number of layers, according to locations of sections. In young animals, villi were extending as bump bodies towards articular cavity. The intimal lining cells are 1-3 or 2-5 layered. In general, their inner parts are lined with areolar connective tissues. In dog synovium, synovial filopodia are not detected (Sagiroglu, 2012a, b). Filopodia are detected in several studies on the subject (Ghadially and Roy, 1966; Roy and Ghadially, 1967; Watanabe *et al*., 1974; Wyllie *et al*., 1964).

The villi of middle and old aged dogs are in various shapes and sizes. In old dogs, villi were plenty and lined with multi-layered cells (Sagiroglu, 2012a, b).

Jilani and Ghadially (1986) claimed that villi are not noticeable in normal synovial membrane of human and they increased with aging and disease. However, they could not observe the villus in rabbits.

Basement membrane and tight junctions: Intimal lining cells do not have a basement membrane in villus and other synovial parts of all the age range of dogs (Sagiroglu, 2012a, b).

Tight junctions and desmosome-like structures do not occur in rabbit synovial lining cells (Sagiroglu *et al*., 1991; Knight and Levick, 1984; Thompson and Stockwell, 1983; Watanabe *et al*., 1974).

According to Henderson and Pettipher (1985) basement membrane and desmosomes do not exist in human synovium. Some studies on the other hand Roy and Ghadially (1967), Wyllie *et al*. (1964) and Wynne-Roberts and Anderson (1978) describe desmosomes-like structures in synovial membranes of human and experimental animals.

Membrane-like material associated with synovial lining cells stains for type IV collagen and laminin in old human donors (69-94 years of age) are determined by Rittig *et al*. (1992).

Connective tissue cells/mitotic figure: Various connective tissue cells and fibroblasts of young dogs occur as placed primarily in deeper layers of subintima. The lymphocyte and plasma cells are placed in the neighborhood of blood vessels in the young dogs. In the middle aged dogs, various connective tissue cells occur as collagen fibers and bundles around blood vessels. The connective tissue cells decrease and the cells emplace among collagen and elastic fibers in the fibrous subintima of the old dogs (Sagiroglu, 2012a, b). Similar connective tissue features are described in juvenile and adult human synovium by Wynne-Roberts and Anderson (1978).

In rabbits and different animals variously structured connective tissue cells and different changes with aging are described (Canpolat and Sagiroglu, 2000; Krey *et al*., 1971; Sagiroglu, 1991a, b; Sagiroglu *et al*., 1991; Thompson and Stockwell, 1983).

Although, Castor (1960) did not distinguish mitotic figures in normal synovial tissue of human, Krey *et al*. (1971) and Thompson and Stockwell (1983) determined some mitotic figures.

Mast cells: Few degranulated type mast cells are present as fibrous and areolo-adipose tissues among intimal and subintimal cells of the synovial membrane of young dogs. In the middle aged animals, the mast cells are placed close to blood vessel walls and any mast cells is absent in intimal layer of old age animals. In old aged animals, common degranulated aggregate of the mast cells are observed in the deeper layers of subintima (Sagiroglu, 2012a, b).

Human synovium researches show that the mast cells were the most prominent (about 3% of the total) cells of the subintima. The studies prove that mast cells decrease with aging and they are rare in fibrous type synovium. The mast cells are usually placed just under the intimal cell layer and as attached capillaries and fat cells (Castor, 1960). Castor (1960) in his study of variously (14-68) aged human synovial tissues concluded that although some changes were present, the changes not clearly associated with age, gender and intra-articular localization.

In rabbits, macrophage and mast cells are not seen in the young and synovium of adult rabbits contain sparse mast cells (Sagiroglu *et al*., 1991; Krey *et al*., 1973; Thompson and Stockwell, 1983).

Normal mast cells of monkeys were quite similar to those humans in structural and dispersion manners and they placed close to blood vessels (Schumacher, 1969).

CONCLUSION

Age associated structural changes in the synovial membrane of dogs and rabbits can be summarized as follows. Macroscopic appearances of synovial membranes of the young animals are smooth, light colored and small. It changes to large, deformed and dark pastel colored with age increase.

With aging the cell density and capillarity decrease in both intima and subintima. Increases occur in collagen tissues and mast and plasma cells as the age increase. With the age increase, the elastic fibers decrease and fibrous tissues increase. In general, age related changes in synovial membranes of dogs, rabbits and human are quite similar. However, some minor differences in cell type, cell layer numbers, fat cells, degree of capillarity are present. Physical activity history of the animal also plays a decisive role on the deformations and age associated other changes of the synovial membrane.

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