

Appendix V

Correlation of histological and radiological features for the natural history of ALTR/ARMD

The inclusion of the term “natural history” for longitudinal follow-up of pseudotumors in the title of a publication can make it more appealing and four radiological studies aiming at its evaluation with US [1-3] or MRI-MARS examination [4] in asymptomatic patients have been reported. However, the progression or regression of the pseudotumor on radiological longitudinal examination in these studies is based only on the variation in size of the wall thickness, solid component, and cystic component of the lesion, which do not have any threshold for the diagnosis of ALTR/ARMD. Therefore, it is an open question how the natural history of these ALTR/ARMD reactions can be provided only by cross sectional radiological studies performed at different time intervals during implantation and its value for the implementation of surveillance programs.

The figures of various cases of ALTR/ARMD presented here show direct and indirect documentation of the possible variation in the radiological findings and the chronological evolution of the lesion for the three parameters used for MRI classification of the severity of the lesion: fluid component, wall thickness/cystic component, solid component. The parameters depend on the type of wear generated by the implant and the host response (qualitative and quantitative cell composition of the inflammatory infiltrate).

Fluid component. A pure fluid component does not exist because a pseudocapsule/neo-synovial wall is always present, no matter how thin it is and possibly obscured by compression from the fluid. A large amount of synovial fluid is usually linked to the presence of the lymphocytic component of the inflammatory infiltrate (Fig 1, Fig. 7, Fig. 8a-e) and can be enhanced by the presence of eosinophils and mast cells (DHT type IVb) as shown in Fig. 3. The density of the fluid can vary and increase during the implantation time due to (a) soft tissue necrosis (Fig. 7c and Fig. 8a and 8c), (b) hemorrhage of the periprosthetic and/or bursal neo-synovium (Fig. 4a-d), (c) macrophage necrosis (proteinaceous/solid fluid signal), which is variable and can become more prominent during implantation time (Fig. 2c, Fig. 6b and 6c, Fig. 8b, App. III Fig. 1a, Fig. 8b). The fluid component can also regress through dehiscence through the pseudocapsule with possible formation of a bursal, extracapsular reaction (Fig. 3, Fig. 4, Fig. 9).

Wall thickness/cystic component. The thickness of the neo-synovial and pseudocapsular wall is variable and depends above all on the rate of the proliferative growth phase of the neo-synovium, from flat (Fig. 4b, App. III Fig. 1b; App. III Fig. 4c) to various degrees of papillary/polypoid (Fig. 1a and 1b, Fig. 2a and 2b, Fig. 3a and 3b, Fig. 8a, Fig. 9b and 9c). It can occur in a short time (months to less than two years) in presence of immunogenic/toxic wear debris and macrophage/lymphocytic host response (Fig. 3a, Fig. 7a, Fig. 8a) with possible decrease in thickness (“regression”) secondary to partial loss of the papillary component due to tissue necrosis (Fig. 7a-c, Fig. 8a, upper and lower tissue section) or in a long time (several years) due to a steady rate of macrophage necrosis and recruitment and low proliferation index of stromal cells/vessels (Fig. 4b, Fig. 9b, App. III Fig. 1b). Of note is that the thickness of the wall is not an absolute indicator of the severity of the ALTR/ARMD, although the quick development of a thick neo-synovial membrane would be usually associated with abundant lymphocytic infiltrate with possible progression to tissue necrosis and damage of adjacent skeletal muscle and tendon. The cystic pseudotumor is a combination of fluid component and wall thickness and patients can become symptomatic during time by compression of adjacent tissue/neurovascular bundles, especially if large extracapsular masses are formed (Fig. 3a, Fig. 4a; Fig. 9a).

Solid component. The solid part of a pseudotumor cannot “disappear” during implantation time because is composed of reactive fibrovascular tissue with papillary/polypoid configuration (Fig. 1a, Fig. 2a, Fig. 8f), even in presence of massive infarction/necrosis (Fig. 3a and 3b and Fig. 7a and 7b) and can be steady or grow very slowly during implantation time, in part due to the different rate of progressive accumulation of particle laden macrophages with possible spikes due to changes in wear debris (i.e. onset of unintended edge loading versus intended tribocorrosion) as shown in Fig. 5 with correspondent variation in MRI signal (low versus intermediate density).

The cases illustrate that a grading system based on amount of synovial fluid, wall thickness, and size of the pseudotumor can provide indications for implant revision, although it is non-predictive of its biological significance, clinical prognosis, and development of bone involvement (osteolysis/implant loosening) at a later implantation time. Histopathological examination can provide a more precise definition of the type of reaction and its course through different phases (natural history/pathological course), although it is also non-predictive for stratifying cohorts of patients in groups with different prognosis and possible long-term side effects.

References

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