Macrophage polarization in aseptic bone resorption around dental implants induced by Ti particles in a murine model

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Background

Titanium particles/ions detected in peri-implant tissues - a potential etiologic factor for crestal bone loss around oral implants.
- Titanium particles could induce marginal bone resorption around dental implants independent of bacterial infection.
- Local adverse inflammation microenvironment leading to peri-implant bone resorption is promoted by macrophage recruitment and macrophage polarization toward a pro-inflammatory M1 phenotype with production of inflammatory mediators.

Methods

- Sprague Dawley rats; 4 groups; titanium screw implanted in bilateral maxillary first molar area for 4 weeks for osseointegration; 20 μg titanium particles in peri-implant tissue to induce aseptic foreign body reaction.
- Macrophages depleted by local injection of 100 μL clodronate liposome (Ti + LipClod group).
- Titanium-injected rats treated with PBS (Ti + PBS) or empty liposome (Ti + Lip) and rats injected with PBS alone included as controls.
- Animals sacrificed at 8 weeks; samples collected; half analyzed radiologically to measure bone level change
- Macrophage markers (CD68, CCR7, CD163) also characterized by immunofluorescence to evaluate number, density, and phenotype distribution (CCR7+M1/CD163+M2).
- The rest of the samples used to determine the relative mRNA expression levels of TNF-α, IL-1β, IL-6, and RANKL with real-time PCR analysis.

Results

Figure. Representative images of hematoxylin and eosin stained sections 8 wk after treatment, 100× magnification. Notice the presence of a dense mixed inflammatory cell infiltrate in the Ti + PBS and Ti + Lip groups as compared to the Control and Ti + LipClod groups

Figure. Quantification of total CD68 + macrophages in 3 randomly selected HPFs of four groups (left), quantification of the M1/M2 ratio in different groups (right)

Conclusion

Titanium particles had a negative effect on peri-implant tissue by activating macrophages which induced an M1 macrophage phenotype promoting local secretion of inflammatory cytokines. It was found that clodronate liposome treatment attenuated the severity of inflammation and bone loss by depletion of macrophages.