Fluorometric imaging for early diagnosis and prognosis of rheumatoid arthritis

S.Y. Jung, J.J. Choi, S.K. Lee. Division of Rheumatology, Department of Internal Medicine, CHA Bundang Medical Center, CHA University, Seongnam-si, Korea, Republic of Ireland

Background: Early diagnosis and monitoring of disease progress are of significant importance in the effective treatment of rheumatoid arthritis (RA), because the continuing inflammation can lead to irreversible joint damage and systemic complications. However, using imaging modalities for the prognosis of RA remains challenging, because no tissue-specific guidelines are available to monitor the progressive course of RA.

Objectives: We report fluorometric imaging of RA for early diagnosis and prognosis, using structure-inherent targeting of the blood vessel, bone, and cartilage.

Methods: We conducted dual-channel near-infrared (NIR) fluorescence imaging, by using NIR light in the wavelength range of 700–800 nm and NIR fluorophores, to monitor the pathophysiological processes of RA. In RA mice, we intravenously injected two NIR fluorophores—indocyanine green (ICG, 800 nm) and DEX700 (700 nm)—that have the characteristics of vascular perfusion agents in order to identify the severity of joint inflammation and the corresponding changes on the basis of differences in fluorescence intensity. In addition, for monitoring the changes in cartilage and bone on the basis of the progression of arthritis, we also intravenously injected C700-OMe (700 nm), a cartilage-targeting NIR fluorophore with an affinity for hyaluronic acid and glycosaminoglycan and P800SO3 (800 nm), a bone-targeting agent that has a strong binding affinity for bone minerals such as hydroxyapatite and calcium phosphate.

Results: In the acute inflammatory stage of arthritis, ICG with a lower molecular weight showed a significantly higher signal-to-background ratio (SBR) than DEX700 (p<0.05). But, in the chronic inflammatory stage, DEX700 showed a higher SBR value than ICG (p<0.05). The changing tendency of SBR value obtained from ICG showed similar to those of the clinical arthritis score in RA mice. In the fluorescence images of the mouse cartilage with C700-OMe before arthritis induction, very clear and distinct lines were observed in the fore paw and ankle joints. In the images obtained after arthritis was induced, these lines were lost, indicating cartilage destruction due to the progression of arthritis. A fluorescence image of the bone was obtained 24 hours after the injection of P800SO3; in this image, it was difficult to view the bone shape of joints especially in the fore paw before arthritis induction, because of a very low fluorescence intensity, in contrast to the cartilage. However, with the progression of arthritis, the fluorescence image of the bones was dramatically appeared and the SBR value of them increased significantly to clearly display the altered morphology of the joints (p<0.05). In particular, as it was confirmed that bone-specific NIR fluorophore, P800SO3 went only into the osteoclast cells, it was determined that monitoring of bone remodelling caused by arthritis-induced osteoclastogenesis is possible by using NIR fluorescence images.

Conclusions: The fluorometric imaging of RA by using tissue-specific contrast agents plays a key role in the systemic treatment of RA by monitoring structural damage and disease progression.

Disclosure of Interest: None declared