The first case of autoinflammatory disease caused by de-novo mutation in IL1 receptor antagonist

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Introduction: Autoinflammatory diseases (AIDs) are rare but clinically significant disorders characterized by recurrent fevers and inflammation affecting multiple organ systems. AIDs result from dysregulation of the innate immune system due to mutations causing an exaggerated inflammatory response. We report a case of an acquired autoinflammatory disease caused by de-novo mutation in the interleukin-1 receptor antagonist (IL1-RN) in Korea.

Case presentation: A 47-year-old woman with hypothyroidism woke up with swelling in her left eyelid. The eyelid was red, warm, itchy, and tender. Her head and neck CT showed soft tissue infiltration in the left orbit and neck lymphadenopathies. A biopsy of the affected eyelid revealed multifocal inflammation, showing a mixed population of CD3 T cells and CD20 B cells. Suspecting thyroid-associated ophthalmopathy, treatment with methylprednisolone resulted in partial improvement. After 8 months, following her third dose of the COVID-19 vaccine, she developed spiking fevers, cervical lymphadenopathy, rash, abdominal pain, myalgia, and arthralgia. Extensive infection and malignancy workups, including PET and bone marrow biopsy, ruled out infection and cancer. For FUO possible due to an autoimmune process, empirical treatment with high dose prednisolone 1mg/kg/day was started with a partial response. Her symptoms returned when prednisolone was tapered below 20mg/day. Steroid-sparing agents including tocilizumab, methotrexate and tacrolimus failed. Gene sequencing for autoinflammatory disease revealed a mutation in IL1-RN canonical splicing site. IL1 inhibitor anakinra was started with prompt complete resolution of her symptoms.

Conclusion: To the best of our knowledge, this is first case of acquired autoinflammatory disease due to de-novo mutation in IL1-RN that was successfully treated with the IL1 inhibitor, anakinra. Further studies are required to better understand acquired autoinflammatory diseases in patients who present with fevers.

Figure 1. Recurrent periorbital swelling

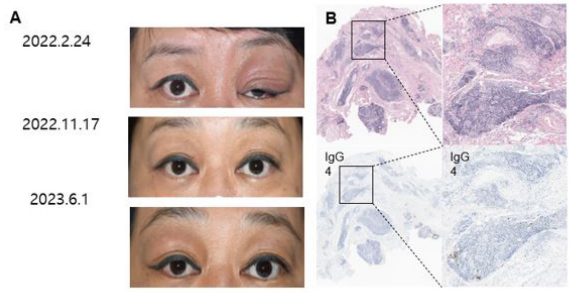

Figure 2. Fever, skin rash, PET/CT

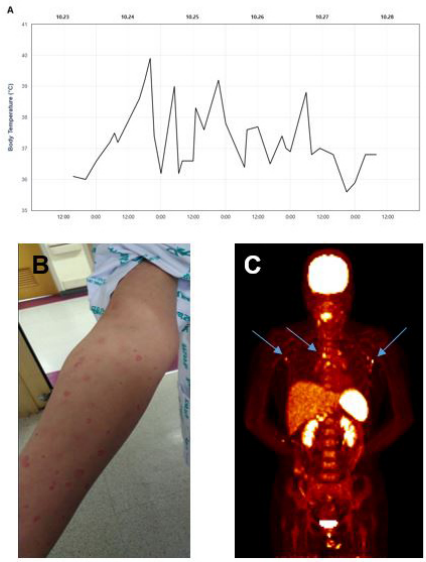

Figure 3. CRP change and treatment

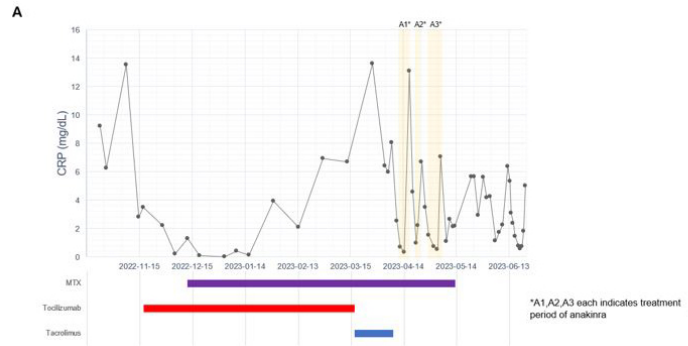

Figure 1. Recurrent periorbital swelling
A. Periorbital swelling change from baseline during treatment course B. Periorbital tissue pathology. Her eyelid biopsy shows Nonspecific lymphoplasmacytic infiltration and scarce IgG4 active cells
Figure 2. Fever, skin rash, PET/CT
A. Spiking fever pattern during her first admission. The fever pattern shows no regular pattern. B. Maculopapular rashes C. PET/CT shows multiple lymphadenopathies, with no sign of malignancies
Figure 3. CRP change and treatment.
CRP change during treatment. CRP level got lower after anakinra treatment, regardless of other treatments.