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Weber-Christian disease in the patient of acrodysostosis with missense mutation of PRKAR1A gene

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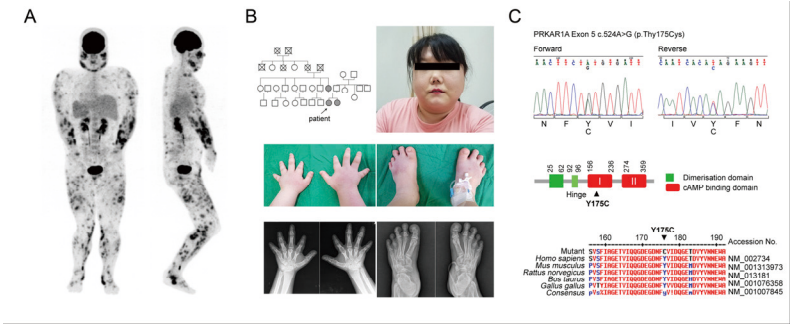
Background/Aims: Acrodysostosis is rare form of skeletal dysplasia with brachydactyly, facial dysostosis, and short stature, which can be accompanied by the resistance to parathyroid hormone or thyrotropin. This complexity of clinical manifestations is known to be originated from the gain-of-function mutation of protein kinase cAMP-dependent type I regulatory subunit alpha (PRKAR1A) gene leading to an attenuated activation of protein kinase A (PKA). Here, we present a case of Weber-Christian disease in the patient of acrodysostosis associated with the heterozygous missense mutation of PRKAR1A gene. **Case report:** A 25-year-old female with a history of hypothyroidism was admitted with fever and generalized erythema nodosum-like skin lesions. On examination, the temperature was 39.0℃ and multiple erythematous nodules with tenderness were observed in both arms, legs, face and trunk which was confirmed on PET-CT scan (figure A). She showed a severe generalized brachydactyly of hands and feet, and nasal hypoplasia with round face (figure B). Skin biopsy finding revealed a septal panniculitis with a mixed cellular infiltrate of lymphocytes, and histiocytes without vasculitis being compatible with erythema nodosum. Together with clinical findings with severe systemic inflammatory response without infectious, malignant or connective tissue disease, we established the diagnosis of Weber-Christian disease. In addition, her acrodysostosis, hypothyroidism and elevated intact PTH level (206.8 pg/ml; normal range 15-65) suggested the diagnosis of acrodysostosis with multiple hormone resistance. DNA sequencing analysis of patient's PRKAR1A gene identified a known heterozygous missense mutation, c.524A>G in exon 5, encoding p.Thy215Cys (figure C). She was treated with steroid in combination with cyclosporine A (3 mg/kg/day), and exhibited a dramatic response, which allowed tapering and cessation of steroid in 2 months. **Conclusion:** This case provides a perspective to the role of gain-of-function of PRKAR1A mutation and PKA inhibition on the inflammation as well as bone and cartilage development.