Circulating sclerostin level in patients with ossification of the posterior longitudinal ligament of the spine

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Introduction

- Ossification of the Posterior Longitudinal Ligament of the spine (OPLL) - OPLL is characterized by pathological ectopic ossification of the posterior longitudinal ligament (Fig. 1A-C).
- OPLL induces compressive myelopathy or radiculopathy by spinal stenosis, and the loss of spinal flexibility by increasing spinal kyphosis (ASH).
- Although the etiology of OPLL has not been fully elucidated, systemic and local bone formation factors may play an important role in its pathogenesis.

Objective

To compare serum sclerostin levels between OPLL patients and controls, and to identify the relationship between serum sclerostin level, Dkk1 level, bone turnover markers, OPLL localization and numbers of ossified vertebra

Subjects and Methods

Study Design: Cross-sectional study

Subjects: Age- and sex-matched Control (n=38) VS OPLL patients (n=78)

Excepting: 1) Non-ambulatory patient, 2) Person with kidney failure (≥ CKD stage 3) 3) Controls with OPLL confirmed by whole spine CT

Study Points

- Serum measurements:
  - Calticotropic hormones and bone turnover markers
  - Serum Sclerostin (ELISA: Biomedica, Vienna, Austria)
  - Serum Dkk-1 (ELISA: R&D Systems: Minneapolis, USA)
- XpCT:
  - Localization of OPLL
  - Numbers of ossified vertebra
  - Presence or absence of ASH

Results

- Patients demographics:
  - Age (years): Control (n=38): 68.0 ± 12.4, OPLL (n=78): 65.5 ± 10.4, N.S.
  - Gender (male/female ratio): 1.35, 1.67, N.S.
  - Height (cm): 157.8 ± 9.9, 162.2 ± 8.3, 0.013
  - Body weight (kg): 59.8 ± 13.6, 65.5 ± 11.6, 0.004
  - BMI (kg/m²): 22.9 ± 3.6, 25.5 ± 3.8, 0.006
  - eGFR (mL/min/1.73m²): 72.3 ± 16.6, 72.1 ± 26.1, N.S.
  - Presence of Hypertension: 47.5%, 32.3%, N.S.
  - Presence of Hyperlipidemia: 17.5%, 20.0%, N.S.
  - Presence of DM: 15%, 35%, 0.022
  - HbA1c (mmol/mol): 5.26 ± 0.56, 5.72 ± 0.78, 0.002

- Statistical analysis using unpaired Student's t-test or Mann-Whitney U test, p<0.05: significant difference (+)

Result 1

Serum sclerostin levels in OPLL patients were significantly higher than controls. Conversely, serum Dkk1 levels in OPLL patients were significantly lower than controls.

- Systemic secretion of sclerostin by osteocytes increased in OPLL male patients with advancing age.
- There will be a negative feedback system by sclerostin to suppress development of OPLL and hyperostosis in OPLL male patients.
- The negative effects on bone formation associated with higher serum sclerostin levels are counterbalanced by the underproduction of Dkk1 in OPLL male patients.

Conclusions

- This work was performed with the aid of the Investigation Committee on the Dissection of the Spinal Ligaments of the Japanese Ministry of Health, Labor, and Welfare.
- None of the authors has any financial interest with any of the commercial entities.
- All authors state that they have no conflicts of interest.

Disclosure

- Bone metabolism centered on sclerostin in controls
- Negative feedback by sclerostin in OPLL male patients
- Suppression of Formation
- Maturation of OPLL
- Development of general hyperostosis

- Statistical analysis using unpaired Student's t-test or Mann-Whitney U test, p<0.05: significant difference (+)

- p-value 0.0001, 0.005, 0.005

- OPLL - Mechanical stress