**ONLINE SUPPLEMENTAL MATERIAL**

**Clinicopathological appearance of epidermal growth factor-containing fibulin-like extracellular matrix protein 1 deposition: An autopsy-based study**

Shojiro Ichimata1, Yukiko Hata1, Koji Yoshida1, Naoki Nishida1

1 Department of Legal Medicine, Faculty of Medicine, University of Toyama, Toyama, Japan

**List of Supplemental material**

Supplemental Table: 3**Supplementary Table 1.** All clinical and pathological information of the cases.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| # | Age | Sex | Type of death | Cause of death | Const\* | LBD\*\* | Thyroiditis | ATTR-CA | S-SI | S-Colon |
| 1 | 88 | M | Accident | Asphyxia | None | Negative | Negative | Negative | A | A |
| 2 | 81 | M | Accident | Drowning | None | 1 | Negative | Positive | A | A |
| 3 | 80 | M | Illness | ACI | None | Negative | Negative | Negative | A | A |
| 4 | 83 | M | Accident | Trauma | None | Negative | Negative | Positive | A | A |
| 5 | 82 | M | Illness | SAH | Unknown | Negative | Negative | Negative | NA | A |
| 6 | 94 | M | Accident | Drowning | None | Negative | Negative | Positive | A | A |
| 7 | 89 | F | Suicide | ADP | None | Negative | Negative | Negative | NA | A |
| 8 | 100 | F | Illness | Lund cancer | Unknown | 3 | Negative | Negative | A | A |
| 9 | 87 | M | Accident | Trauma | Positive | Negative | Negative | Negative | A | A |
| 10 | 90 | M | Accident | Hypothermia | None | Negative | Negative | Negative | A | A |
| 11 | 85 | F | Accident | Trauma | Possible | 5 | Positive | Negative | A | A |
| 12 | 83 | M | Accident | Drowning | None | 4 | Negative | Negative | NA | A |
| 13 | 88 | F | Accident | Drowning | Possible | Negative | Negative | Negative | A | A |
| 14 | 90 | F | Accident | Burn | None | 5 | Negative | Negative | NA | A |
| 15 | 84 | F | Accident | CMP | Possible | Negative | Negative | Negative | A | A |
| 16 | 80 | F | Suicide | Drowning | Unknown | Negative | Negative | Negative | A | A |
| 17 | 83 | M | Suicide | Drowning | None | Negative | Negative | Positive | A | A |
| 18 | 85 | F | Illness | ACI | None | Negative | Negative | Negative | A | A |
| 19 | 82 | F | Homicide | Asphyxia | None | Negative | Negative | Negative | NA | A |
| 20 | 88 | M | Suicide | Drowning | Definite | Negative | Negative | Negative | A | A |
| 21 | 94 | F | Accident | SAH | None | Negative | Negative | Negative | A | A |
| 22 | 83 | M | Accident | ATE | None | Negative | Negative | Negative | NA | A |
| 23 | 97 | F | Accident | Heat stroke | None | 3 | Negative | Positive | NA | A |
| 24 | 86 | F | Accident | Heat stroke | None | Negative | Positive | Negative | NA | A |
| 25 | 90 | F | Accident | Drowning | Definite | Negative | Negative | Positive | NA | A |
| 26 | 80 | F | Suicide | Drowning | None | Negative | Negative | Negative | NA | A |
| 27 | 80 | M | Suicide | Asphyxia | None | Negative | Negative | Negative | NA | A |
| 28 | 82 | F | Accident | Hypothermia | None | Negative | Negative | Negative | NA | A |
| 29 | 88 | M | Illness | ACF | None | Negative | Negative | Negative | NA | A |
| 30 | 86 | F | Accident | Hypothermia | None | 4 | Negative | Negative | A | A |
| 31 | 81 | M | Accident | Trauma | None | 1 | Negative | Negative | A | A |
| 32 | 87 | M | Illness | ACF | Possible | Negative | Negative | Negative | NA | A |
| 33 | 80 | M | Suicide | Asphyxia | Unknown | Positive | Negative | Negative | NA | A |
| 34 | 81 | F | Illness | Infection | Unknown | Negative | Negative | Negative | A | A |
| 35 | 91 | M | Accident | Drowning | None | 3 | Negative | Negative | A | A |
| 36 | 85 | F | Illness | CCF | Unknown | Negative | Positive | Negative | A | A |
| 37 | 84 | F | Accident | SAH | None | Negative | Negative | Negative | NA | A |
| 38 | 84 | F | Illness | Peritonitis | None | 1 | Negative | Negative | A | A |
| 39 | 89 | M | Accident | Drowning | None | Negative | Negative | Positive | NA | A |
| 40 | 86 | M | Accident | Hypothermia | None | Negative | Negative | Negative | NA | A |

**Abbreviations:** A, available; ACI, acute cardiac failure; ACF, acute cardiac failure; ATE, acute thromboembolism; ADP, acute drug poisoning; CCF, congestive cardiac failure; CMP, carbon monoxide poisoning; F, female; LBD, Lewy body disease; M, male; NA, not available; SAH, subdural hemorrhage; S-Colon, specimens from the colon; S-SI, specimens from the small intestine

\* Definite refers to cases with a clinical diagnosis of constipation. Possible refers to cases with no clinical diagnosis but with laxative medications or pseudomelanosis coli.

\*\* Evaluated based on the Braak’s LBD grading [21].

**Supplementary Table 2.** All pathological results of the small intestine evaluation.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| # | SI# | MM | SM (V) | MP | AP | SS (V) | SS (I) | S | TS | Group\* | AGBR | EF | ATTR |
| EM | CR | IHC | EM | CR | IHC | EM | CR | IHC | EM | CR | IHC | EM | CR | IHC | EM | CR | IHC | EM | CR | IHC |
| 1 | 1 | 0 | 0 | 0 | 1 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 2 | 2 | 0 | 0 | 2 | 1 | 2 | 3 | 19 | Intermediate | Positive | Negative | Negative |
| 2 | 2 | 0 | 0 | 0 | 3 | 3 | 3 | 1 | 1 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 2 | 2 | 3 | 3 | 3 | 3 | 45 | Severe | Positive | Negative | Negative |
| 3 | 3 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 2 | 11 | Mild | Negative | Negative | Negative |
| 4 | 4 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 2 | 6 | Mild | Negative | Negative | Positive |
| 6 | 5 | 0 | 0 | 0 | 1 | 1 | 3 | 0 | 0 | 1 | 0 | 0 | 2 | 3 | 3 | 3 | 2 | 2 | 3 | 2 | 2 | 3 | 31 | Severe | Positive | Negative | Positive |
| 8 | 6 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 2 | 1 | 2 | 3 | 1 | 2 | 3 | 0 | 0 | 2 | 0 | 0 | 1 | 19 | Intermediate | Positive | Positive | Positive |
| 9 | 7 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 2 | 3 | 0 | 1 | 3 | 1 | 1 | 3 | 17 | Intermediate | Positive | Negative | Negative |
| 10 | 8 | 0 | 0 | 0 | 0 | 1 | 2 | 1 | 1 | 2 | 0 | 0 | 1 | 1 | 2 | 2 | 1 | 1 | 3 | 2 | 2 | 3 | 25 | Severe | Positive | Negative | Negative |
| 11 | 9 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 2 | 5 | Mild | Negative | Negative | Negative |
| 13 | 10 | 0 | 0 | 1 | 0 | 1 | 3 | 1 | 1 | 2 | 0 | 0 | 1 | 1 | 2 | 3 | 1 | 2 | 3 | 2 | 2 | 3 | 29 | Severe | Positive | Negative | Negative |
| 15 | 11 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 1 | 2 | 0 | 0 | 1 | 1 | 2 | 3 | 1 | 2 | 3 | 2 | 2 | 3 | 25 | Severe | Positive | Negative | Negative |
| 16 | 12 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 2 | 0 | 0 | 2 | 0 | 1 | 2 | 11 | Mild | Negative | Negative | Negative |
| 17 | 13 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 2 | 1 | 1 | 3 | 13 | Mild | Negative | Negative | Positive |
| 18 | 14 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 4 | Mild | Negative | Negative | Negative |
| 20 | 15 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 1 | 3 | 0 | 1 | 2 | 2 | 2 | 3 | 19 | Mild | Negative | Negative | Negative |
| 21 | 16 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 2 | 0 | 0 | 2 | 0 | 1 | 3 | 12 | Intermediate | Positive | Negative | Negative |
| 30 | 17 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 1 | 2 | 0 | 0 | 2 | 1 | 2 | 2 | 1 | 1 | 1 | 2 | 2 | 3 | 23 | Severe | Positive | Negative | Negative |
| 31 | 18 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 1 | 2 | 0 | 0 | 2 | 0 | 0 | 2 | 11 | Mild | Negative | Negative | Negative |
| 34 | 19 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 0 | 1 | 3 | 1 | 1 | 3 | 14 | Intermediate | Positive | Negative | Negative |
| 35 | 20 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 2 | 3 | 1 | 1 | 2 | 1 | 2 | 2 | 18 | Intermediate | Positive | Negative | Negative |
| 36 | 21 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 2 | 0 | 1 | 3 | 11 | Mild | Negative | Negative | Negative |
| 38 | 22 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 5 | Mild | Negative | Negative | Negative |

**Abbreviations:** AGBR, apple-green birefringence; ATTR, amyloid transthyretin; CR, Congo red grading; EF, elastofibrosis; EM, elastica-Masson grading; I, interstitium; IHC, immunohistochemistry for EFEMP1; MM, mucosa and muscularis mucosa; MP, muscularis propria; S, serosa; SI#, small intestine #; SM, submucosa; SS, subserosa; TS, total score; V, vessel

\* Mild (low-TS (<20) and AGBR-negative); Intermediate (low-TS but AGBP-positive); Severe (high-TS and AGBR-positive)

**Supplementary Table 3.** All pathological results of the colon evaluation.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| # | MM | SM (V) | MP | AP | SS (V) | SS (I) | S | TS | Group\* | AGBR | EF | ATTR |
| EM | CR | IHC | EM | CR | IHC | EM | CR | IHC | EM | CR | IHC | EM | CR | IHC | EM | CR | IHC | EM | CR | IHC |
| 1 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 2 | 0 | 0 | 2 | 1 | 2 | 3 | 0 | 0 | 2 | 0 | 0 | 1 | 15 | Severe | Positive | Negative | Negative |
| 2 | 0 | 0 | 0 | 3 | 3 | 3 | 3 | 2 | 3 | 2 | 2 | 3 | 3 | 3 | 3 | 1 | 1 | 2 | 0 | 0 | 2 | 39 | Intermediate | Negative | Negative | Negative |
| 3 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 2 | 0 | 0 | 2 | 8 | Mild | Negative | Negative | Negative |
| 4 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 7 | Mild | Negative | Negative | Positive |
| 5 | 0 | 0 | 1 | 3 | 3 | 3 | 1 | 1 | 2 | 0 | 0 | 2 | 2 | 2 | 3 | 0 | 1 | 2 | 0 | 0 | 1 | 27 | Severe | Positive | Negative | Negative |
| 6 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 1 | 14 | Intermediate | Negative | Negative | Positive |
| 7 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 2 | 3 | 0 | 0 | 2 | 0 | 0 | 1 | 12 | Severe | Positive | Negative | Negative |
| 8 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 2 | 0 | 0 | 2 | 1 | 2 | 3 | 0 | 0 | 2 | 0 | 0 | 1 | 15 | Intermediate | Negative | Positive | Negative |
| 9 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 2 | 3 | 0 | 0 | 2 | 1 | 1 | 3 | 18 | Severe | Positive | Positive | Negative |
| 10 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 1 | 1 | 2 | 2 | 2 | 3 | 0 | 1 | 2 | 1 | 1 | 1 | 21 | Severe | Positive | Negative | Negative |
| 11 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | Mild | Negative | Negative | Negative |
| 12 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 3 | Mild | Negative | Negative | Negative |
| 13 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 10 | Intermediate | Positive | Negative | Negative |
| 14 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 10 | Intermediate | Positive | Negative | Negative |
| 15 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 1 | 9 | Mild | Negative | Negative | Negative |
| 16 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | Mild | Negative | Negative | Negative |
| 17 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | Mild | Negative | Negative | Positive |
| 18 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 8 | Mild | Negative | Negative | Negative |
| 19 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | Mild | Negative | Negative | Negative |
| 20 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 2 | 3 | 1 | 1 | 2 | 1 | 1 | 2 | 18 | Severe | Positive | Positive | Negative |
| 21 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 2 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 9 | Mild | Negative | Negative | Negative |
| 22 | 0 | 0 | 2 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | Mild | Negative | Negative | Negative |
| 23 | 0 | 0 | 1 | 2 | 2 | 3 | 1 | 1 | 2 | 1 | 2 | 3 | 1 | 2 | 3 | 2 | 2 | 3 | 0 | 1 | 1 | 33 | Severe | Positive | Negative | Positive |
| 24 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 9 | Mild | Negative | Negative | Negative |
| 25 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 3 | Mild | Negative | Negative | Negative |
| 26 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 1 | 2 | 1 | 1 | 2 | 2 | 2 | 3 | 0 | 0 | 2 | 0 | 0 | 0 | 18 | Intermediate | Negative | Negative | Negative |
| 27 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 5 | Mild | Negative | Negative | Negative |
| 28 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 1 | 3 | 1 | 2 | 3 | 0 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 2 | 19 | Intermediate | Negative | Negative | Negative |
| 29 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 7 | Mild | Negative | Negative | Negative |
| 30 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 2 | 1 | 1 | 2 | 0 | 0 | 1 | 12 | Intermediate | Negative | Negative | Negative |
| 31 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 7 | Mild | Negative | Positive | Negative |
| 32 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 2 | 2 | 2 | 3 | 0 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 17 | Intermediate | Negative | Positive | Negative |
| 33 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 2 | 0 | 0 | 2 | 1 | 2 | 3 | 1 | 1 | 2 | 1 | 1 | 1 | 20 | Severe | Positive | Positive | Negative |
| 34 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 7 | Mild | Negative | Negative | Negative |
| 35 | 0 | 0 | 0 | 0 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 2 | 3 | 0 | 0 | 2 | 0 | 0 | 1 | 14 | Severe | Positive | Negative | Negative |
| 36 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 1 | 1 | 2 | 3 | 0 | 0 | 2 | 0 | 0 | 1 | 15 | Severe | Positive | Negative | Negative |
| 37 | 0 | 0 | 2 | 0 | 1 | 2 | 1 | 1 | 2 | 1 | 1 | 2 | 2 | 2 | 3 | 0 | 0 | 2 | 0 | 0 | 1 | 23 | Severe | Positive | Positive | Negative |
| 38 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 6 | Mild | Negative | Negative | Negative |
| 39 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 2 | 0 | 0 | 2 | 1 | 2 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 14 | Severe | Positive | Negative | Negative |
| 40 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 8 | Mild | Negative | Negative | Negative |

**Abbreviations:** AGBR, apple-green birefringence; ATTR, amyloid transthyretin; CR, Congo red grading; EF, elastofibrosis; EM, elastica-Masson grading; I, interstitium; IHC, immunohistochemistry for EFEMP1; MM, mucosa and muscularis mucosa; MP, muscularis propria; N#, new number; S, serosa; SM, submucosa; SS, subserosa; TS, total score; V, vessel

\* Mild (low-TS (<12) and AGBR-negative); Group 2 (low-TS but AGBR-positive, or high-TS (≥12) but AGBR-negative); Group 3 (high-TS and AGBR-positive