Table e-1. Clinical characteristics of patients in the validation cohort

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| --- | --- | --- | --- | --- | --- | --- |
|  | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 | Patient 6 |
| Sex | F | F | F | F | H | F |
| Age (yrs) | 21 | 34 | 21 | 66 | 65 | 18 |
| First sign, age (yrs) | Exercise intolerance, 9 | Unexplained falls, 8 | Subacute proximal weakness, 13 | Asymptomatic hyperCKemia, 65 | Asymptomatic hyperCKemia, 59 | Exercise intolerance+myalgia, 15 |
| Duration (yrs) | 12.5 | 26 | 8 | 1 | 6 | 3 |
| Pattern of weakness | Shoulder and hip girdle | Shoulder and hip girdle, axial | Shoulder and hip girdle | Normal strength initially then slight shoulder and hip girdle weakness (4/5) | Slight hip girdle weakness (4/5) | Normal strength |
| Scapular winging | Absent | Present | Absent | Absent | Present | Absent |
| Ambulation Status | Independent | Wheelchair | Independent | Independent | Independent | Independent |
| CK (IU/L) | 9,832 | 12,000 | 17,000 | 1,866 | 6,000 | 1,200 |
| EMG/NCS | Myopathic | Myopathic | Myopathic | Myopathic | Myopathic | Myopathic |
| Muscle Pathology Findings | Atrophy and chronic myopathic changes (fibrosis, fiber size variability), myofiber regeneration, inflammatory infiltrate, MHC-1 sarcolemmal staining | Chronic myopathic changes (fibrosis, fiber size variability), myofiber necrosis and regeneration, no inflammatory infiltrate, no MHC-1 staining | Chronic myopathic changes (fibrosis), myofiber necrosis and regeneration, small perivascular inflammatory infiltrates, no MHC-1 staining, no C5b-9 deposition | No chronic myopathic changes, myofiber necrosis and regeneration, small perivascular inflammatory infiltrates, no MHC-1 staining, sarcolemmal C5b-9 deposition | Chronic myopathic changes (fiber size variability, internalized nuclei), no myofiber necrosis and regeneration, no inflammatory infiltrate, slight MHC-1 staining, no C5b-9 deposition | No chronic myopathic changes, myofiber necrosis and regeneration, no inflammatory infiltrate, no MHC-1 staining, no C5b-9 deposition |
| Genetic and molecular testing | LGMD panel (IHC+WB), FKRP, anoctamin 5 | LGMD panel (IHC+WB), acid maltase | LGMD panel (IHC+WB), calpain/anoctamin 5 mutations | LGMD panel (IHC+WB), DM1, DM2, anoctamin 5 mutation | LGMD panel (IHC), acid maltase | LGMD panel (IHC+WB), anoctamin 5 mutation |
| Anti-SRP | Negative | Negative | Negative | Negative | Negative | Negative |
| HLA-DRB1 | unknown | unknown | unknown | unknown | unknown | unknown |
| Echocardiogram | Normal | Normal | Normal | Normal | Slight concentric ventricular hypertrophy | Normal |
| PFT | FVC 3.4 L (66%) | FVC 71% | unknown | FVC 3.05 L (118%) | FVC 3.73 L (102%) | FVC 3.40 L (99%) |
| Other comments |  | Heterozygote factor V Leiden mutation and protein S deficiency (no thrombotic event) | Hashimoto thyroiditis | Dyslipidemia, statin exposure | Coronary artery disease with statin exposure | Heterozygote factor V Leiden mutation (no thrombotic event) |

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| --- | --- | --- | --- | --- | --- | --- |
|  | Patient 7 | Patient 8 | Patient 9 | Patient 10 | Patient 11 | Patient 12 |
| Gender | F | H | F | F | H | F |
| Age (yrs) | 52 | 17 | 44 | 31 | 63 | 30 |
| First sign, age (yrs) | Asymptomatic hyperCKemia, 47 | HyperCKemia +myalgia, 14 | Proximal weakness, 21 | Exercise intolerance, 14 | Elevated LFTs, 47 | Difficulty rising from a chair+myalgia, 15 |
| Duration (yrs) | 5 | 3 | 23 | 16 | 16 | 15 |
| Pattern of weakness | Shoulder and hip girdle | Shoulder and hip girdle | Shoulder and hip girdle | Shoulder and hip girdle | Shoulder and hip girdle | Shoulder and hip girdle |
| Scapular winging | Absent | Present | Present | Present | Absent | Absent |
| Ambulation Status | Independent | Independent | Wheelchair | Independent | Independent | Independent for short distance with cane |
| CK (IU/L) | 4,000 | 10,858 | 7,000 | 5,985 | 1,851 | 5,890 |
| EMG/NCS | Myopathic | Myopathic | Myopathic | Myopathic | Myopathic | Myopathic |
| Muscle Pathology Findings | Chronic myopathic changes (fibrosis, fiber size variability, internalized nuclei), myofiber regeneration, no inflammatory infiltrate, slight MHC-1 staining, sarcolemmal C5b-9 deposition | Atrophy and chronic myopathic changes (fibrosis, fiber size variability, internalized nuclei), myofiber regeneration, inflammatory infiltrate, positive MHC-1 staining, no C5b-9 deposition | Chronic myopathic changes (fibrosis), myofiber necrosis and regeneration, small perivascular inflammatory infiltrates, no MHC-1 staining, no C5b-9 deposition | Chronic myopathic changes (fibrosis, fiber size variability, internalized nuclei), myofiber necrosis and regeneration, no inflammatory infiltrates, slight MHC-1 staining, sarcolemmal C5b-9 deposition | Atrophy and chronic myopathic changes (fiber size variability, internalized nuclei), myofiber necrosis and regeneration, no inflammatory infiltrates, no MHC-1 staining, no C5b-9 deposition | Atrophy and chronic myopathic changes (fibrosis, fiber size variability, internalized nuclei), myofiber necrosis and regeneration, no inflammatory infiltrates, no MHC-1 staining, sarcolemmal C5b-9 deposition |
| Genetic and molecular testing | LGMD panel(IHC +WB), DM2, anoctamin 5, acid maltase, FKRP | LGMD panel (IHC+WB), acid maltase, anoctamin 5 | LGMD panel (IHC+WB), calpain, FKRP and anoctamin 5 | LGMD panel (IHC+WB), FSHD, acid maltase, SMN1/2 | LGMD panel (IHC+WB), acid maltase, anoctamin 5 | LGMD panel (IHC+WB), anoctamin 5, DM1, FSHD |
| Anti-SRP | Negative | Negative | Negative | Negative | Negative | Negative |
| HLA-DRB1 | unknown | unknown | unknown | unknown | unknown | unknown |
| Echocardiogram | Normal | Normal | Normal | Normal | Normal | Normal |
| PFT | FVC 80% | FVC 5.25 L (88%) | FVC 2.67 L (86%) | FVC 2.44 L (74%) | FVC 3.84L (94%) | FVC 3.29 L (85%) |
| Other comments | Statin exposure at the age of 38, nine years before first elevated CK level testing |  |  |  | Red yeast rice (lovastatin) exposure | Raynaud phenomenon |

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| --- | --- | --- | --- | --- | --- |
|  | Patient 13 | Patient 14 | Patient 15 | Patient 16 | Patient 17 |
| Gender | F | F | F | F | F |
| Age (yrs) | 25 | 65 | 60 | 30 | 47 |
| First sign, age (yrs) | Unexplained falls, 14 | Difficulty rising from a chair, 55 | Myalgia+difficulty climbing stairs, 50 | Exercise intolerance, 26 | Proximal weakness, 30 |
| Duration (yrs) | 9 | 10 | 10 | 4 | 17 |
| Pattern of weakness | Shoulder and hip girdle | Shoulder and hip girdle | Shoulder and hip girdle | Shoulder and hip girdle | Shoulder and hip girdle |
| Scapular winging | Absent | Absent | Absent | Absent | Present |
| Ambulation Status | Wheelchair | Independent | Wheelchair | Independent | Independent |
| CK (IU/L) | 4,000 | 3,300 | 10,000 | 5,473 | 5,600 |
| EMG/NCS | Myopathic | Myopathic | Myopathic | Myopathic | Myopathic |
| Muscle Pathology Findings | Chronic myopathic changes (fibrosis, fiber size variability, internalized nuclei), myofiber necrosis and regeneration, no inflammatory infiltrates, slight MHC-1 staining, no C5b-9 deposition | Atrophy and chronic myopathic changes (fiber size variability), myofiber necrosis and regeneration, no inflammatory infiltrate, slight MHC-1 staining | Chronic myopathic changes (fibrosis, fiber size variability, internalized nuclei), myofiber necrosis and regenera tion, no inflammatory infiltrates | Chronic myopathic changes (fibrosis, fiber size variability, internalized nuclei), myofiber necrosis and regeneration, no inflammatory infiltrates, positive MHC-1 staining, no C5b-9 deposition | Atrophy and chronic myopathic changes (fibrosis, internalized nuclei), myofiber necrosis and regeneration, inflammatory infiltrates and sarcolemmal C5b-9 deposition |
| Genetic and molecular testing | LGMD panel (IHC+WB), anoctamin 5 | LGMD panel (IHC+WB), acid maltase, mitochondrial DNA | LGMD panel (IHC+WB) | LGMD panel (IHC+WB), DM2 | LGMD panel (IHC+WB) |
| Anti-SRP | Negative | Negative | Negative | Negative | Negative |
| HLA-DRB1 | Unknown | Unknown | Unknown | Unknown | Unknown |
| Echocardiogram | Normal | Concentric ventricular hypertrophy | Normal | Normal | Normal |
| PFT | Unknown | FVC 2.81 L (95%) | FVC 1.21 L (43%) | Unknown | FVC 4.04 L (143%) |
| Other comments |  | Statin exposure 3 years after first symptoms, Hypertension, Cancer-associated myositis to an squamous-cell esophageal carcinoma | No statin exposure, Hashimoto thyroiditis |  |  |

CK= creatine kinase, LFT= Liver function tests, N.D.= Not done, MHC-1= major histocompatibility complex-1, LGMD= Limb-girdle muscular dystrophy, IHC=immunohistochemistry, WB=western blot, FSHD= Fascioscapulohumeral muscular dystrophy, DM1= myotonic dystrophy type 1, DM2= myotonic dystrophy type 2, FKRP=fukutin-related protein, PFT= Pulmonary function test, FVC= Forced vital capacity