**Supplementary Figure 1** Control staining in brain and muscle tissue Positive and negative (no primary) brain control sections and normal muscle stained using immunohistochemistry for: p62 (A-C), TDP-43 (D-F), α B-crystallin (G-I), ubiquitin (J-K) and myotilin (M,N) and alkalinised congo red (O). (A-C) Negative (A) and positive (B) control sections of AD brain and normal muscle (C) stained for p62. Positive control shows p62 positive neurofibrillary tangles and dystrophic neurites (B). No p62 immunoreactivity is observed in normal muscle (C). (D-F) Negative (D) and positive (E) control sections of FTLD-TDP brain and normal muscle (F) stained for TDP-43. Positive control shows normal nuclear labelling and mislocalised neuronal cytoplasmic staining with neuropil threads (E). Insert shows a neuron with absent nuclear TDP-43 and a cytoplasmic TDP-43 inclusion (E, red arrow and x100 insert). Nuclear TDP-43 staining is observed in normal muscle. (G-I) Negative (G) and positive (H) control sections of CBD brain and normal muscle (I) stained for α B-crystallin. Positive control shows neuropil threads and a balloon cell neuron (H; red arrow and x100 insert). No α B-crystallin immunoreactivity is observed in normal muscle (I). (J-L) Negative (J) and positive (K) control AD brain and normal muscle (L) stained for ubiquitin. Positive control shows dystrophic neurites and neuropil threads (K). No ubiquitin immunoreactivity is observed in normal muscle (L). (M,N) Negative (M) and positive (N) control muscle stained for myotilin. Mild sarcoplasmic staining is observed in normal muscle (N). (O) Positive control section of AD brain showing an amyloid plaque (O). Scale bar represents 100 μm in A-D, F and H-M; and 50 μm in E, N-O. p62 = Sequestosome 1; AD = Alzheimer’s disease; TDP-43 = Transactivation response DNA binding protein 43; FTLD-TDP = Frontotemporal lobar degeneration with TDP-43 positive inclusions; CBD = Corticobasal degeneration.
Supplementary Figure 2 IBM inflammatory score-tool Score tool modified from the published juvenile dermatomyositis inflammatory (JDM) score tool [17] to specifically assess the type, degree and distribution of inflammation in IBM. The inflammatory domain was augmented to include T-cells, T-cell subtypes, B-cells and macrophages. MHC Class I staining was expanded to include three patterns of labelling. The vascular, muscle fibre and connective tissue domains which are present in the JDM score tool were not included.
**Supplementary Figure 3** Sensitivity and specificity of rimmed vacuoles, protein aggregates and mitochondrial changes in IBM+RV compared to PAM. Receiver operating characteristic curves for each test including the area under the curve and optimum cutoff with its associated sensitivity and specificity for rimmed vacuoles (A), myotilin (B), ubiquitin (C), TDP-43 (D), p62 (E) immunoreactive deposits, congophilic deposits (F) and COX/SDH+ fibres (G). COX/SDH HC staining was the most discriminative test for differentiating IBM+RV and PAM (G). However, there was little difference between COX/SDH HC staining, TDP-43 and p62 IHC staining and none were sufficiently discriminative to be considered diagnostic. AUC = Area under the curve.
Supplementary Figure 4 Sensitivity and specificity of protein aggregates and mitochondrial changes in IBMRV compared to PM&DM Receiver operating characteristic curves for each test showing the area under the curve and optimum cut-off with its sensitivity and specificity for myotilin (A), ubiquitin (B), TDP-43 (C), p62 (D) immunoreactive deposits, congophilic deposits (E) and COX-/SDH+ fibres (F). COX/SDH histochemical staining (F) and myotilin (G) IHC were the most discriminative tests for differentiating IBMRV and PM&DM. AUC = Area under the curve.