Case 2002-2

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Reference number: 00-481

Clinical History: This patient was well until the sixth decade, when he developed progressive shortness of breath, severe fatigue and excessive daytime somnolence. He would fall asleep at dinner, during conversation and had difficulty remaining awake while driving. At age 55, he did not complain of dyspnea, but his wife reported that he exhibited "heavy breathing". Respiratory function deteriorated to the point that by age 56, exercise tolerance was less than one-half block of ambulation and, by age 57, he required 24 hour ambulatory oxygen and ventilatory assistance at night.

Concurrently with the development of the respiratory disorder, he noted progressive weakness in the lower extremities, which interfered with walking up stairs and turning over in bed. Treatment with Mestinon for a few days was of no benefit.

He had worked as an installer of telephone lines, transferred to a desk job and finally retired due to disabling somnolence and weakness. He was married with five children; there was no family history of pulmonary or neuromuscular disease. There was a 35 pack-year history of smoking cigarettes, which was discontinued at age 54.

At age 56, he was mildly cyanotic at rest. There was mild bilateral ptosis and full extraocular movements. There was mild weakness (4-5-/5) of the proximal muscle groups of the upper extremities and moderate to severe weakness (3/5) in the proximal lower extremities with diminished muscle mass in buttocks and thighs. There was normal strength of distal musculature. Muscle stretch reflexes were 1+/4+ and symmetrical. Sensory examination was normal.

The serum glucose, thyroid function tests, BUN and creatinine were normal. Creatine kinase 268 u/l (0-235), aldolase 13 u/l (0-8.1). Serologic testing for antinuclear, Jo-1 and anti-mitochondrial antibodies was negative.

Pulmonary function tests at age 56 revealed Total Lung Capacity 3.69 liters (47% of predicted value), Vital Capacity 2.22 liters (41%), Forced Vital Capacity 2.22 liters (41%), FEV1 1.88 (43%) and ABG of 7.40/59/62 on room air with normal CXR and computed tomography of the chest.

Electrodiagnositic testing (age 56) revealed evidence of myopathy and impaired neuromuscular transmission with normal nerve conduction velocities and borderline sensory nerve amplitudes.

The patient visited a rheumatologist and a muscle biopsy was arranged.

Material submitted: One H&E section of *Vastus lateralis* muscle

Points for discussion:

1. Diagnosis
2. Clinical presentation
3. Differential diagnosis of the key light microscopic pathological finding
4. Pathogenesis