Objective: Approximately 1 in every 3000 children is born with multiple congenital contractures (MCC) that cause substantial morbidity. The most common causes of MCC include amyoplasia and the distal arthrogryposis (DA) syndromes. All of the 10 recognized DA disorders are notable for contractures of the hands and feet, but Freeman-Sheldon syndrome (FSS) is distinguished further by severe contractures of the facial muscles. However, the expressivity of FSS is broad, and consequently, it can be difficult to discriminate from other DAs. Our objective was to define the clinical characteristics and natural history typical of children and adults with FSS. This information will facilitate the development of more accurate diagnostic criteria, improve the predictive power of anticipatory guidance, and guide strategies to identify the molecular basis of FSS. Design: Phenotypic information was collected from more than 100 patients who were referred with the diagnosis of FSS. Data from questionnaires and family interviews were collected and analyzed for differences in demographics, clinical features, development, and treatment/outcomes. Results: Only 22 patients met our diagnostic criteria for FSS. All had contractures of the face and the wrists, hands, ankles, or feet. The FSS phenotype changed through adolescence and adulthood but remained quite characteristic. Other notable findings included scoliosis (20/21), dental crowding (13/13), strabismus (10/20), hearing loss (7/22), and cryptorchidism (5/9). Children with FSS walked at an average at 17.9 months of age, and devices to assist ambulation were required in 13/16 patients. Eighteen of 20 individuals underwent an average of 11.8 surgical procedures. Problems with anesthesia/surgery were encountered in 10/17. Feeding was problematic in all children with FSS, with 9/17 requiring a special nipple, 8/18 requiring nasogastric tube feedings, and 3/20 requiring a gastric tube placement. All of the children with FSS were cognitively normal. Conclusions: Most children are diagnosed with FSS erroneously. However, consistent application of existing criteria distinguishes FSS from other DA conditions that have similar phenotypes. Patients with FSS require significant interventions (functional nutrition, orthopedic, surgical, and rehabilitative therapies) that are not required by most children with other DA disorders. Most children with FSS who receive these interventions do reasonably well and eventually function independently as adults.