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190
Variable clinical features in Fabry disease in patients with novel mutations

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We report our experience with Fabry disease in a multidisciplinary clinic in UC Irvine. Our cohort comprised of 20 adults and two children (11 M/ 11 F) ranging in age from 6- 62 years, with ages of diagnosis ranging from 3-57 years. The data shows that 63% have angiokeratomas, 58% exhibit corneal whorls, and 80% experience acroparasthesia. There was renal involvement in 37% of patients, most having varying levels of proteinuria with one male requiring a renal transplant. Thirty-two percent of patients had evidence of cardiomyopathy. One male had several strokes with MRI changes of multifocal encephalomalacia and gliosis of the left cerebral frontal and parietal lobes. The data also identified 42% of patients suffering from gastrointestinal problems, 53% had reduced sweating, and 32% had lymphedema. Among the adults 53% had tinnitus, and 41% of adults experienced hearing loss. The majority of males and 44% of the females currently receive enzyme replacement therapy (ERT). Each individual demonstrated different response rates of symptom improvement and slowing of organ deterioration with ERT. Two individuals developed infusion reactions, one male developed ERT associated meningitis which prompted him to end treatment for seven years. He re-initiated ERT later with immunomodulation and has had continued challenges tolerating ERT. Previous studies have shown that early initiation of Fabrazyme infusions may be effective in curbing renal involvement. Indeed Fabrazyme infusions have been effective in clearing GL-3 levels in most patients, however renal involvement has continued to progress in some adult patients despite ERT infusions, especially those diagnosed late. The variability of symptoms and disease progression in patients with Fabry disease was also correlated with their specific GLA mutations. We identified several patients with novel mutations making determination of a phenotype-genotype correlation difficult. Monitoring patients regularly leads to optimization of patient care and provides insight into genotype-phenotype correlations.

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