Huntington’s disease in all (three) siblings and their one parent

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Three siblings (two girls and one boy) and their father are reported who developed Huntington’s disease (HD). The two girls had onset at less than six years of age, while the boy started with symptoms at 12 years of age. The girl, the child number two, has expired and the youngest one is in a vegetative state. The elder brother is still mildly affected. The disease presented in a severe form and early in the females while it remained mild and presented late in the males. This is a rare disease involving all the three surviving siblings and their father. The diagnosis was confirmed after genetic testing.

Key words: Huntington’s disease and siblings or huntington’s disease/genetics and family health or pedigree

Case Report

Three siblings (two girls and one boy) and their father who developed Huntington’s disease are reported. The two girls had onset at less than six years of age, while the boy started with symptoms at 12 years of age. The first child (first daughter) had onset of symptoms at six years of age. She started with failing in school performance, grimacing and dysarthria. Over time she developed dystonia and generalized tonic clonic seizures. Lastly she was bedridden and passed away in 2003 after status epilepticus and aspiration pneumonia at 12 years of age. The younger sibling started with abnormal jerky movements around five years of age. Later she developed dysarthria, dystonia and tonic clonic seizures. Lately the seizures had become refractory and had dystonic/opisthotonic component as well. She is on multiple antiepileptic drugs and gets admitted with recurrent tonic-clonic status epilepticus necessitating phenytoin loading and midazolam infusion to stop the status. At present she is also bedridden. The last surviving boy aged 13 years now, started with grimacing and gait problems over last one year. Examination revealed oculomotor apraxia, generalized rigidity and stooped gait with hyperreflexia. There were no other children in the family. Two years back early symptoms like grimacing and emotional changes were noted in the father (family tree). The parents are consanguineous (first cousins). There was history of dementia and abnormal jerky movements in their mothers (figure of family tree [Figure 1]). CT brain of the siblings had revealed bicaudate atrophy and DNA study using PCR technique showed one abnormal band equivalent to 92 CAG repeats in the Huntington disease gene\(^1\) (IT14.4p16.3) and a second band equivalent to 18 repeats indicating one affected parent. The genetic study was refused by both parents. At that time the father was asymptomatic and the report was not revealed to the family. At present detailed genetic study was refused by

Figure 1: The family tree showing Huntington’s disease in four generations in an Omani family

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the family. An earlier report of HD from Oman had described only one sibling from this family.\[1\] This is the first report of HD in children from this country. HD is known to occur in the Arabs in Saudi Arabia,\[2\] Syria, Egypt and Lebanon.\[3\] HD is an autosomal dominant progressive neurodegenerative disorder characterized by involuntary movements, cognitive decline and behavioral disorders leading to functional disability, a typical presentation in adults.\[4\] In contrast to patients with adult onset, in which abnormal movements, mainly chorea, is the presenting symptom, children present with rigidity, spasticity, school failure and epilepsy.\[4,6\] All these features were seen in our children. Juvenile HD occurs in approximately 10% of affected persons, with onset before the age of 20 years.\[4,5\] The gene causing HD is localized in the short arm of Chromosome 4.\[7\]

We report a family with early onset of childhood (juvenile) HD. In addition to the dystonia severe and refractory seizures were the features in the two siblings and the first affected one died with status epilepticus. The younger one gets frequently admitted with breakthrough seizures (status epilepticus) and needs loading of phenytin sodium/midazolam infusion. At the time of presentation of the first child both parents were asymptomatic. The parents refused genetic testing in other unaffected siblings. Over the course of time the father started choreiform movements, and emotional changes in the last two years, indicating the onset of the disease in him. In juvenile cases, the father is the affected parent three to four times more frequently than is the mother and there is female preponderance.\[8\] Not many reports of three affected siblings and a parent are there in the literature.\[9\] Childhood onset is also labeled as Westphal variant as rigidity is the dominant feature. In addition, both girls were affected at an earlier age (below six years) and the boy at about 13 years. This phenotypic variability suggests that the genetic load may be different in the males and the females. In 65-71% of the HD patients, the number of CAG repeats dictated the age of onset. However, there are familial modifiers, which could determine the age of onset.\[10\]

References


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