Lafora disease is a rare neurometabolic condition caused by a mutation in the EPM2A and/or EPM2B genes. The disorder is neurologically progressive, and the disease is eventually fatal. A form of progressive myoclonic epilepsy, it can produce a variety of complications including intellectual disability, various seizure disorders, mental health difficulties, and dementia. The authors describe the symptoms of Lafora disease; a case study of a young male who was diagnosed with the disorder is presented. The etiology of Lafora disease and progression of the disorder are described. Implications for treatment of the disorder and palliative care are briefly discussed.

Keywords: dementia, developmental disability, intellectual disability, Lafora disease, mental retardation, progressive myoclonic epilepsy, psychiatric disorder
Lafora bodies are found in progressive myoclonic epilepsies. They are characterized by a large cell body surrounded by a “clear halo.” (From Rosenblum, 2005, with permission)

epilepticus. Respiratory failure secondary to seizures has been reported, as well as cardiac arrhythmia and arrest. A number of mental health manifestations have been reported including depression, psychosis, and personality changes. Dementia is common with the disorder, as well as intellectual disability.

TREATMENT

The primary focus of treatment is medication management for seizure control. Unfortunately, the disease is fatal and there is no specific treatment to “cure” the disorder. As the disease progresses, treatment takes the form of palliative care. Advances in gene therapy, stem cell research, or protein therapies might provide treatment in the future for this insidious disease.\textsuperscript{12} One area of research is currently being conducted by the National Institutes of Health to determine if a diet limited in carbohydrates will slow progression of the disease and reduce formation of Lafora bodies.\textsuperscript{10,12}

A case report of a young man with intellectual disability and Lafora disease is presented in order to provide further description of medical and psychological aspects of the disorder. It should be noted that the individual eventually died of complications secondary to Lafora disease. Since presentation of the case report involved the examination of archival records, approval to access patient files and present information was obtained from the treatment facility and State Human Subjects Institutional Review Board. Written consent was also obtained from the patient’s guardian.

CASE REPORT

Mr. C was a Caucasian male who died from complications of Lafora disease at 27 years of age. He was reportedly conceived as the result of an incestuous relationship between a 13-year-old girl and her older brother. The patient was placed in foster care, and he was adopted when he was about 6 months old.

His records revealed that disruptive and destructive behaviors were first reported at 8 years old. The first neurological symptoms were also observed, as he exhibited difficulties with visual tracking. Mr. C was diagnosed with a complex partial seizure disorder. He began experiencing auditory hallucinations at 8 years old. His adoptive parents divorced when he was about age 11, and he later went to live with his adoptive father due to behavioral concerns. Because of increasing conduct problems, he was eventually placed in various community residences and treatment facilities for children with behavior disorders. A number of behavioral concerns were noted including assault of other patients and destruction of property. According to
the patient’s guardian, a number of factors likely contributed to behavioral difficulties including the divorce of his adoptive parents, bad experiences with a series of community placements, frustrations with decline in physical/cognitive abilities, and other effects of Lafora disease.

He was referred for psychological, psychiatric, and educational evaluation several times throughout childhood through early adulthood. He was diagnosed with a variety of disorders including reactive attachment disorder of early childhood, conduct disorder, pervasive developmental disorder NOS “with psychosis,” intermittent explosive disorder, and learning disabilities in math and listening comprehension.

At age 14, he was court ordered to a state mental health facility for adolescents. He was then transferred to an adolescent community residence, and he was generally “compliant” with treatment. Occasional “anger outbursts” were noted, and some outbursts reportedly occurred for “no reason.” According to records, professionals attributed outbursts with no identifiable antecedents as occurring secondary to “temporal lobe epilepsy.”

At age 16, he was placed in a community residence. He was reportedly resistant to the program. He was assaultive to other patients, and he was also destructive to property. Frequent noncompliance with treatment was noted, and anger outbursts were sometimes unpredictable.

At age 18, he was placed at a state psychiatric facility due to disruptive behavior. He was diagnosed with “organic personality disorder,” intermittent explosive disorder, mathematics disorder, expressive language disorder, and epilepsy. At the time of his admission to the inpatient facility, he was on several medications including valproic acid, clonazepam, felbamate, ethosuximide, and sertraline.

At age 23, he was transferred to a state institution for persons with intellectual disabilities. Medical staff ordered a skin biopsy for Mr. C, and Lafora disease was diagnosed. Seizure control became increasingly difficult for the patient. Medications prior to death included lorazepam, clonazepam, phenobarbital, valproic acid, lamotrigine, albuterol, and lorazepam PRN.

Intelectual abilities declined over a period of several years. Information regarding progression of cognitive decline is found in Table 2. At age 14, his intellectual abilities were in the low average range (WISC-III Full Scale IQ SS = 85). By age 18, cognitive abilities were in the moderate range of intellectual disability (WAIS-R Full Scale IQ SS = 55). At age 22, he was evaluated for continued eligibility for disability services. During his final evaluation, he was unable to respond to test stimuli; and the evaluator estimated his intellectual abilities in the severe to profound range of intellectual disability. Assessment of adaptive behavior was conducted during his final evaluation, and his score on the Inventory for Client and Agency Planning (ICAP) was severely impaired. His ICAP score placed him in a range of care requiring “total personal care and intense supervision.”

The patient died at age 27 in a state institution for persons with intellectual disabilities. Placement at the state facility was required due to his intensive medical needs. Prior to death, his neurological and cognitive functioning continued to decline. He was nonambulatory, and needed total assistance with sitting and transfers. Mr. C was hypotonic, and deep tendon reflexes of lower extremities were absent. He needed assistance with eating, and a G-tube was required on occasion due to increased seizure activity. Low oxygen saturation was an ongoing problem due to seizure activity. The patient had recently been released from the hospital after his health reportedly improved following a bout of pneumonia. He was generally nonverbal, and was unresponsive to external stimuli. Seizures became increasingly difficult to control, and he went into a coma prior to death. The cause of death was reportedly respiratory failure secondary to Lafora disease.

**DISCUSSION**

Despite the inevitable problems with this disorder, there are still benefits to diagnosis. A number of factors might have contributed to behavioral difficulties including the divorce of his adoptive parents and poor success with a series of community placements. However, many of the behavioral and neurological manifestations could have been explained by the diagnosis of Lafora disease. Early diagnosis might have led to more effective and aggressive treatment for the patient. Proper diagnosis of Lafora disease could have changed habilitative planning for Mr. C, and arrangement of more appropriate community supports might have been possible.

In some cases, the diagnosis of a serious disorder such as Lafora disease can provide
Table 1. Clinical Features of Lafora Disease

1. One type of progressive myoclonic epilepsy
2. Neurometabolic disorder of autosomal recessive inheritance
3. Tonic-clonic and myoclonic seizures most commonly reported
4. Occipital seizures sometimes reported with visual hallucinations
5. Neurological symptoms might include dysarthria, mutism, ataxia, paresis, and/or blindness
6. Neurometabolic disorder of autosomal recessive inheritance
7. Linked to the mutation of the EPM2A and/or EPM2B genes of chromosome 6. A third gene, yet to be identified, is also suspected to cause the disorder.
8. Intellectual disability can be found with Lafora disease; dementia occurs during late stages of the disorder.
9. Other mental health concerns include depression, psychosis, and personality changes.
10. Lafora bodies can be found in the liver, neurons, skin, heart, skeletal muscles, and sweat gland cells.
11. Biopsy of skin cells is usually conducted in order to diagnose the disorder.
12. Lafora disease is always fatal.

Table 2. Progression of Cognitive Decline as described by Intellectual Functioning

<table>
<thead>
<tr>
<th>Age</th>
<th>Intellectual Abilities</th>
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<tbody>
<tr>
<td>14</td>
<td>85</td>
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<tr>
<td>18</td>
<td>55</td>
</tr>
<tr>
<td>22</td>
<td>&lt;40*</td>
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*Estimate of Mr. C’s intellectual abilities. He was unable to respond to stimuli presented on the intelligence measure. Reports of adaptive behavior were in the profound range.

families with insight or “answers” to serious behavioral challenges. When behavioral difficulties appear in the absence of clear external antecedents, proper diagnosis of a disorder can provide validation for families that they are not the “cause” of the behavioral problems. In some cases, proper diagnosis of the disorder might provide a sense of closure for families. Unfortunately, professionals might not recognize or appreciate the importance of making the diagnosis of such a disorder, especially if there is no treatment that will assist the patient. However, diagnosis can prove beneficial for some families as it might provide a reason for the presence of behavioral difficulties, neurological deficits, and cognitive decline.

Lafora disease is an insidious form of myoclonic epilepsy that is very rare. Initial treatment focuses on seizure control through medication management. As the disease progresses, seizure control becomes less successful. During the final stage of the disorder, treatment for the disease is palliative in nature. Unfortunately, the disease is always fatal. In addition to presenting the medical aspects of the disorder, we have also striven to present mental health problems associated with the disorder. One of the more prominent symptoms of the disorder
is the development of dementia. Treatment considerations include seizure control, medications to control psychiatric and neurological aspects of the disorder. Palliative care is necessary for the final stages of the disorder. Long-term prognosis for the patient is poor, and most patients die within 10 years of clinical findings. Although the disease is much more frequent in Asia and Europe, cases are also reported in North America with unknown prevalence. However, it is likely that this disorder is underdiagnosed. As presented in our case study, the disorder was not diagnosed until about two years prior to Mr. C’s death. In some cases genetic tests can be conducted to diagnose the disorder. However, this procedure can be extremely expensive. In addition, genetic screening might not catch all cases of the disorder as it is believed that a third gene yet to be identified is also responsible for the Lafora disease. To date, skin biopsy appears to be the most effective, least intrusive procedure in diagnosing the disorder. A number of mental health concerns have been reported in the literature, which can occur in conjunction with Lafora disease. Mental health problems reported include dementia, depression, and psychosis. As outlined in the case study, Mr. C exhibited several symptoms that have been reported in the literature. At times, his behavior was quite volatile. Environmental factors influenced mental health problems to some degree. Unfortunately, the likely etiology of many of his health concerns was also the presence of a rare disorder. As has been presented, he was diagnosed with a variety of mental health conditions. We have attempted to outline symptoms of Lafora disease in order to educate professionals as to the medical and mental health aspects of this condition.

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