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Caring for Patients with Hunter syndrome

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Caring for Patients with Hunter syndrome

Hunter syndrome, also known as mucopolysaccharidosis II (MPS II), is one in the family of MPS lysosomal storage disorders. Hunter syndrome is an X-linked-recessive disorder, thus it primarily affects male patients and female carriers are generally asymptomatic (Guffon, Bertrand, Forest, Fouilhoux, & Froissart, 2009). The National MPS Society (2013) estimates that this rare condition affects between 1 in 100,000 to 1 in 150,000 males in the United States. Hunter syndrome involves a deficiency of the enzyme iduronate-2-sulphatase (I2S), which is involved in the catabolism of glycosaminoglycans (GAGs) (Finn et al., 2008). The enzyme deficiency leads to the accumulation of GAGs in the lysosomes of cells, resulting in cell, tissue, and organ dysfunction (Muenzer, 2004). A cure for Hunter syndrome has yet to be discovered, thus the early treatment of patients with Hunter syndrome is vital to prolong their quality of life.

Hunter syndrome is a heterogeneous disorder, both in the age of the onset of symptoms and the severity of the disorder. Depending on the severity of the disease, patients are generally diagnosed between one and five years of age (Guffon et al., 2009, p. 734). Patients can present with a wide clinical spectrum of manifestations due to the range of very severe to mild forms of Hunter syndrome. In the more severe forms of the disease, progressive neurologic deterioration occurs and develops into severe mental impairment. In the milder forms of the disease, clinical signs and symptoms have a slightly later onset, but neurologic deterioration is minimal (Martin et al., 2008). All Hunter syndrome patients, however, experience progressive somatic deterioration (Muenzer et al., 2009). Rohrbach and Clark (2007) estimate that one-third of patients have a milder form of Hunter syndrome with no neurologic involvement (p. 2706). Patients with the more severe forms of Hunter syndrome typically live between 10 and 20 years where patients with the milder forms generally live between 20 and 60 years (Medline Plus, 2011).

This paper focuses on helping nurses to provide the best care for patients living with Hunter syndrome and their families. Clinical manifestations, available resources, requirements for diagnosis, and the management and treatment of Hunter syndrome are discussed. The content included in this paper is important for nurses to review because of the fatality of Hunter syndrome when left untreated. Muenzer (2004) states that children with Hunter syndrome can present in a variety of ways and healthcare providers “need to be alerted to warning signs and symptoms so that patients can be recognized and provided with up-to-date comprehensive care” (p. S33). A nurse may be the first healthcare provider introduced to a patient with an undiagnosed case of Hunter syndrome. In this situation, he or she can best help the patient by being educated to observe the warning signs of the disease and refer the patient and his or her family for further help. Nurses may also encounter patients with Hunter syndrome in the clinical setting. In this situation as well, nurses need to be educated enough to provide competent care. These potential situations cause learning about Hunter syndrome to be an important undertaking for nursing professionals.

Clinical Aspects of Hunter syndrome

Integumentary and Skeletal Manifestations

There are many obvious integumentary and skeletal manifestations that present in patients with Hunter syndrome. The appearance and skeletal abnormalities of patients with Hunter syndrome are similar regardless of the severity of the disease. Patients typically appear normal at birth with progressive manifestations throughout life (Martin et al., 2008). Possible integumentary features of Hunter syndrome include facial dysmorphism, progressive coarsening of facial features, macroglossia, hirsutism, and having a broad nose with flat nasal bridges, flared nostrils, prominent supraorbital ridges, thickened lips, and large jowls (Martin et al., 2008;

Muenzer, 2004; Muenzer et al., 2009). Possible skeletal features of Hunter syndrome include slowed growth, macrocephaly, joint stiffness, contractures, bone and joint deformities, decreased hand fine motor skills, carpal tunnel syndrome, abnormally shaped and stiff ribs, lumbar kyphosis, and having a short neck and unusual gait or stance (Kamin, 2008; Martin et al., 2008; Muenzer, 2004; Muenzer et al., 2009; Roberts, 2008).

Manifestations of the Eyes, Ears, Nose, Mouth, and Throat

Many patients with Hunter syndrome develop clinical manifestations relating to the eyes, ears, nose, mouth, and throat. Problems with the eyes can include photophobia and retinal dysfunction, leading to poor vision (Martin et al., 2008; Muenzer, 2004). Problems involving the ears can include recurrent otitis media and hearing loss (Muenzer, 2004). Problems involving the nose can include chronic rhinitis (Muenzer, 2004). Clinical manifestations of the mouth and throat can include enlarged tonsils and adenoids, dental abnormalities, poor jaw mobility, and macroglossia. The occurrence of these problems can limit the ability to open the mouth, negatively affecting the ability to chew the coordination of swallowing (Muenzer, 2004; Muenzer et al., 2009).

Gastrointestinal and Urinary Manifestations

The GAG storage associated with Hunter syndrome can cause several gastrointestinal and urinary manifestations. Because of the GAG storage, the liver and spleen of patients with Hunter syndrome are often enlarged, resulting in abdominal distention (Martin et al., 2008). Inguinal and umbilical hernias are also commonly seen in patients with Hunter syndrome (Muenzer, 2004). Martin et al. (2008) estimate that approximately half of the patients with a severe form of Hunter syndrome become toilet trained, but most, if not all, will lose the ability as the disease progresses (p. e382).

Respiratory Manifestations

Respiratory abnormalities are a major contributor to the premature mortality experienced with Hunter syndrome. Airway involvement in patients with Hunter syndrome is progressive, first becoming apparent in the upper airway and gradually involving the lower airway (Martin et al., 2008). Obstructive airway disease, obstructive sleep apnea, respiratory insufficiency, reactive airway disease, and restrictive lung disease are major clinical manifestations that are likely in patients with Hunter syndrome (Kamin, 2008; Muenzer, 2004; Muenzer et al., 2009). Features of Hunter syndrome that contribute to these respiratory disorders include enlarged tonsils and adenoids, an enlarged tongue, mucosal thickening, a small chest cavity, abnormally shaped and stiff ribs, enlarged abdominal organs, a short neck, and the skeletal changes of the jaw (Kamin, 2008; Muenzer, 2004; Muenzer et al., 2009). Other potential respiratory abnormalities commonly experienced by patients with Hunter syndrome include frequent pneumonias, frequent upper respiratory tract infections, noisy breath, and snoring (Martin et al., 2008; Muenzer, 2004).

Another important respiratory consideration for patients with Hunter syndrome is the danger with the use of general anesthesia. The anatomic changes seen with Hunter syndrome, such as a short neck, the immobility of the jaw, and the obstruction of the airways by tissues of the throat, may complicate the use of general anesthesia. These changes in anatomy commonly cause difficult intubation and extubation in patients with Hunter syndrome. Patients may even be unable to maintain an airway after extubation (Muenzer et al., 2009). Due to these special considerations, a specialist who is knowledgeable about Hunter syndrome must be consulted if general anesthesia is to be attempted.

Cardiovascular Manifestations

Hunter syndrome can also affect the patient's cardiovascular system. Possible presenting cardiovascular manifestations in patients with Hunter syndrome include a heart murmur, cardiac valves disease, cardiomyopathy, and valvular dysfunction (Muenzer, 2004; Muenzer et al., 2009).

Neurological Manifestations

There are many and varying neurologic manifestations associated with Hunter syndrome. Intracranial findings can include macrocrania, brain atrophy, cysts within the periventricular white matter, corpus callosum, and basal ganglia, enlarged perivascular spaces, ventriculomegaly, communicating hydrocephalus, delayed myelination, and cervical myelopathy (Finn et al., 2008; Iyer & Khanna, 2010; Tarbox & Tjauw, 2012). Spinal cord compression, cervical cord thickening, atlantoaxial instability, median nerve compression, and carpal tunnel syndrome also commonly occur in patients with Hunter syndrome (Muenzer et al., 2009). Tarbox and Tjauw (2012) propose that the cervical cord thickening seen in many patients with Hunter syndrome is secondary to the deposition of GAGs (p. 30B). Developmental findings in patients with Hunter syndrome can include delay, loss of development skills such as speech and learning, mild mental deterioration, behavioral problems, hyperactivity, and communicating hydrocephalus (Muenzer, 2004; Tarbox & Tjauw, 2012). Seizures can be another neurologic finding in patients with Hunter syndrome. Seizures are much less common in patients with a milder form of Hunter syndrome. The initial onset of seizures commonly takes the form of absence seizures, but generalized tonic-clonic seizures are common as the disease progresses (Muenzer et al., 2009).

Review of the Available Resources

Literary Resources

In a search of the literature relating to Hunter syndrome in CINAHL Plus with Full Text, 26 articles were found. Of these articles, only 3 were in nursing journals. Many nurses and patients are not aware of what Hunter syndrome is and how it affects a patient's life.

Online Resources

There are many online resources available for nurses, patients with Hunter syndrome, and the patients' families. Mayo Clinic (2012), MedlinePlus (2011), and WebMD (2012) are all well-known websites that have webpages about Hunter syndrome. Information on symptoms, causes, risk factors, complications, tests and diagnosis, treatments, and support is provided. These online resources are valuable tools for nurses, patients, and families who need to quickly learn about Hunter syndrome.

One of the most helpful resources for patients with Hunter syndrome and their families is the National MPS Society (2013). Their website, www.mpssociety.org, provides information on all of the MPS diseases, their treatments, and the current research being performed. They also refer patients and families to more resources for education and support. Getting involved with the National MPS Society provides patients and their families an opportunity to contact other families suffering from Hunter syndrome. Because of the wealth of information and resources the National MPS Society provides, they are an important resource for nurses to provide to their patients suffering from Hunter syndrome.

Nursing Implications

Diagnosis of Hunter syndrome

Recognizing signs and symptoms through a history and physical.

Early diagnosis of Hunter syndrome is of the utmost importance so that disease-specific therapies can be initiated before irreversible disease progression occurs. The first step in diagnosing Hunter syndrome occurs when there is suspicion during a history and physical examination. The disease is later confirmed with biochemical and genetic testing (Vedolin et al., 2007). This imperative first step towards diagnosis may fall to a nurse to complete. Recognizing Hunter syndrome through a history and physical is not an easy task, as Hunter syndrome often initially presents subtly. Most children with Hunter syndrome appear normal at birth and only later in infancy or childhood begin to display the clinical features of Hunter syndrome. Findings that are particularly important for follow up include inguinal or umbilical hernias, loss of developmental skills, and any gradual, progressive changes in physical appearance (Muenzer, 2004; Tarbox & Tjauw, 2012). Many times the initial suspicion of Hunter syndrome is based on facial features and is made by a healthcare provider during an examination for other issues that could be causing a child's developmental problems (Martin et al., 2008).

Urine GAG analysis.

Urine GAG analysis can be used to confirm the suspicion of an MPS disorder in general. With MPS, the total urinary GAG level will be increased (Martin et al., 2008). Further, when a specific MPS disorder has not been identified, urinary GAG analysis can be helpful to determine which enzyme should actually be tested for deficiency (Muenzer, 2004).

Enzyme activity.

Unlike a history and physical or urine GAG analysis, documented enzyme deficiency confirms the diagnosis of Hunter syndrome. I2S is present in all cells, except in mature red blood cells, thus enzyme activity can be measured in a variety of cells and body fluids. Assays based on cultures of fibroblasts, leukocytes, plasma, or serum are commonly used for enzyme activity testing (Martin et al., 2008). Patients with Hunter syndrome that have no enzyme production at all can expect a severe form of the disease where patients with a residual enzyme activity as low as 0.1% to 0.3% will have a milder form of the disease. All patients with absent or low I2S activity should have documentation of another normal sulfatase assay before a diagnosis of Hunter syndrome can be made. This will differentiate Hunter syndrome from multiple sulfatase deficiency (MSD), also called Austin's disease (Muenzer, 2004).

Gene analysis.

Gene analysis relating to Hunter syndrome is generally used to identify female carriers of the disease. Genetic mutation analysis of the I2S mutation may be used to confirm Hunter syndrome in males, but it is necessary to confirm carrier status in females. Gene analysis is the only secure way to identify female carriers and can also be used for prenatal diagnosis (Martin et al., 2008).

Prenatal diagnosis.

Prenatal diagnosis of Hunter syndrome can be performed. Prenatal diagnosis is achieved through an enzyme assay of living tissue obtained by amniocentesis or chorionic villus sampling (Muenzer, 2004). Fetal blood may also be used to assess enzyme activity, but this test is available in only a few laboratories worldwide (Martin et al., 2008).

Management and Treatment of Hunter syndrome

Multidisciplinary management of Hunter syndrome.

Optimal therapy for children with Hunter syndrome involves both disease-specific treatments and symptom-based nonspecific treatments. To achieve this optimal treatment, Hunter syndrome should be managed in a multidisciplinary manner with care coordinated by a physician with experience treating Hunter syndrome. Patients with Hunter syndrome usually have many different disease manifestations, so their overall care is best overseen by a physician who can refer them to specialists, as needed, and who can ensure that optimal care is being received on all fronts (Muenzer, 2004). Most patients with Hunter syndrome will require care from a broad range of specialists, including cardiologists, neurologists, pulmonologists, otolaryngologists, ophthalmologists, orthopedic surgeons, physical therapists, speech therapists, and more. All of the specialists involved in the care of a patient with Hunter syndrome should have a basic understanding of the disease and how other disease manifestations may interfere with and/or affect treatment decisions (Muenzer, 2004).

Enzyme replacement therapy.

The discovery of using enzyme replacement therapy (ERT) to treat Hunter syndrome provided a treatment option that was not solely palliative. Idursulfase (Elaprase®), the first product developed for the treatment of Hunter syndrome, is a treatment used to significantly improve the quality of life for patients who suffer from Hunter syndrome (Roberts, 2008). Idursulfase was approved by the Food and Drug Administration (FDA) in July 2006 at a dose of 0.5 mg/kg per week (First treatment for Hunter syndrome, 2006; Martin et al., 2008). The most serious adverse effects reported with the use of idursulfase are hypersensitivity reactions that could be life-threatening, including respiratory distress, drop in blood pressure, and seizure.

Other frequent, less serious side effects of idursulfase include headache, pyrexia, joint pain, erythema, flushing, urticarial, and rash (First treatment for Hunter syndrome, 2006). Because of the potential for severe hypersensitivity reactions, appropriate medical support should be readily available when idursulfase is administered (Treatment for Hunter syndrome approved, 2006). The safety, effectiveness, and toleration of ERT for patients with Hunter syndrome have been demonstrated in well-designed clinical trials, and the treatment is now commercially available throughout the world (Rohrbach & Clarke, 2007).

Idursulfase is believed to benefit only the somatic manifestations experienced with Hunter syndrome. In general, the sooner treatment with ERT is initiated, the better the results of the treatment are. Ideally, ERT should begin before the onset of irreversible changes and before significant disease progression (Muenzer et al., 2009). Some tissues, such as the brain, are inaccessible to ERT as the enzyme is unable to pass through the blood brain barrier. This indicates that the cognitive involvement of the disease will not improve or stabilize (Guffon et al., 2009; Muenzer et al., 2009; Rohrbach & Clarke, 2007). The goal of ERT is to administer a form of I2S intravenously that is distributed to affected tissues in amounts sufficient to reverse, or at least prevent, GAG storage and the resulting disease manifestations (Rohrbach & Clarke, 2007). Da Silva, da Silva, Strufaldi, Andriolo, and Silva (2011) completed a literature review to evaluate the effectiveness and safety of ERT with idursulfase compared to treatment with a placebo or no treatment. The study found that ERT with idursulfase led to some improvement in the patients' ability to walk, a reduction in the excretion of abnormal GAG in the urine, and reduced liver and spleen volume (p. 2).

Home treatment with ERT is an attractive alternative to hospital-based ERT. ERT is a lifelong undertaking and the treatment schedule for idursulfase involves weekly intravenous

infusions, with each one administered by a nurse over a period of several hours (Little, Gould, & Hendriksz, 2009). Patients and families who have to travel to the hospital for ERT may find the frequent visits required for chronic care to be stressful, time-consuming, and disruptive to their normal life. There is a growing move to offer ERT at home, supported by many nurse specialists (Little et al., 2009). Home care helps to limit the time spent in the hospital and lost from school and it restores independence to families. Nurses who are willing to be trained and perform home care ERT can help to improve the quality of life of patients with Hunter syndrome (Little et al., 2009).

Psychosocial support.

Counseling and psychosocial support are essential resources to offer to patients with Hunter syndrome and their families. Many families find that maintaining contact with other families struggling with similar issues can help them to cope with feelings of isolation and despair. Several organizations, including the National MPS Society (2013), exist that help Hunter syndrome families connect with one another for support (Muenzer, 2004).

Nonspecific therapies.

Along with the specific treatments aimed at treating Hunter syndrome, there are many other therapies that patients with Hunter syndrome may utilize to treat specific aspects of their disease. Nonspecific therapies do not address the underlying cause of Hunter syndrome, but they can significantly improve the lifespan or the quality of life for many patients and their families (Muenzer, 2004). Common nonspecific surgical interventions for patients with Hunter syndrome include tonsillectomy, adenoidectomy, and tracheostomy to treat obstructive sleep apnea, airway obstruction, or eustachian tube dysfunction, ventriculoperitoneal shunting for communicating hydrocephalus, orthopedic surgery, spinal fusion for spinal cord compression or progressive

kyphosis, median nerve release for carpal tunnel syndrome, hernia repair, and cardiac valve replacement for mitral or aortic regurgitation or stenosis (Kamin, 2008; Muenzer, 2004; Muenzer et al., 2009). Other nonspecific therapies used to treat patients with Hunter syndrome include continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) to treat obstructive sleep apnea, the use of hearing aids, physical therapy to minimize joint contractures and stiffness and improve muscle strength, and speech therapy and behavioral therapy to help children and their families cope with diminishing developmental skills (Kamin, 2008; Muenzer, 2004; Muenzer et al., 2009). Common nonspecific assessments and evaluations for patients with Hunter syndrome can include looking for clinical and radiologic evidence of spinal cord compression, magnetic resonance imaging (MRI) or computed tomography (CT) imaging of the head, MRI of the cervical spine, cervical spine flexion/extension tests, neurobehavioral evaluations, nerve conduction tests, hand function tests, cardiac echocardiography, 12-lead electrocardiogram, and possibly Holter monitoring, standard ophthalmologic, otologic, and audiologic examinations, pulmonary function tests, sleep studies, bronchoscopies, joint range of motion tests, radiograph of spine and hip, clinical evaluations, and standard dental care (Muenzer et al., 2009).

End-of-life management.

Special care and consideration should be taken when planning end-of-life management for patients with Hunter syndrome. Patients will become increasingly disabled, gradually losing the ability to communicate, chew, and swallow. For these reasons, a gastrostomy tube (G-tube) should be considered when poor oral intake results in weight loss and decreased nourishment. Patients' abilities to control bowel and bladder function will be lost completely, and they will

eventually become bedridden. All care should be palliative and directed at maintaining the comfort of the patient, including the use of pain medication, if necessary (Muenzer et al., 2009).

Future Goals for Treatment

Newborn screening.

Newborn screening for Hunter syndrome, especially for families at risk, is a potential future treatment to increase the quality of life for Hunter syndrome patients. To achieve the best long-term outcome for patients with Hunter syndrome, treatment of the disease should be started before the onset of irreversible clinical symptoms (Vedolin et al., 2007). Because of the progressive nature of Hunter syndrome, early initiation of therapy is likely to provide greater benefit than therapy that was started only after signs and symptoms of the disease were noticed (Martin et al., 2008).

Experimental molecular therapy.

Molecular therapy is a budding treatment for patients with Hunter syndrome. Researchers at Cincinnati Children's Hospital Medical Center (2013) have developed an experimental molecular therapy that crosses the blood-brain barrier to reverse MPS I, Hurler syndrome, in mice. The researchers discovered that tagging some of the fatty protein, apolipoprotein E (apoE), to the enzyme deficient in Hurler syndrome allowed the modified protein to attach to endothelial cells and cross through the cells to reach brain tissue. The researchers also reported that brain cells in the treated mice exhibited normalized levels of the GAGs and the deficient enzyme. With continued treatment, normalized levels persisted until the end of a five-month observation period (para. 11). These findings may allow for the development of drugs that can be tested for other neurologically-involved diseases, including Hunter syndrome.

The Importance of Knowledge about Hunter syndrome

In a telephone interview with B. Wedehase, MSW, CGC (personal communication, July 2, 2013), Executive Director of the National MPS Society (2013), great insight was gained into the importance of knowledge about Hunter syndrome in order to provide nursing care to patients suffering from Hunter syndrome. During the interview, the importance of knowledge and education about the disease was a topic that was brought up multiple times.

B. Wedehase felt that nurses need to have a general knowledge of Hunter syndrome before coming in contact with a patient with Hunter syndrome. When asked, “What is(are) the most important thing(s) that you feel a healthcare professional should know about Hunter syndrome when first coming in contact with a Hunter syndrome patient?”, B. Wedehase responded, “The most important thing is that they do the background reading, have an understanding of the progression of the disease, the heterogeneity of the disease...and that they be aware of the treatments, ERT, palliative care, and the progression of the disease.” She also stated that it is important to “Be aware that this is a multi-system disease. Be able to go through all of the different systems and talk with the family about these problems. Give the ‘head-to-toe talk’, focusing on all of the problems.”

The importance of nurses being knowledgeable about Hunter syndrome is also important to the family. When asked, “What is(are) the most common complaint(s) that you hear from Hunter syndrome patients and their families in regard to receiving care from healthcare professionals?”, B. Wedehase replied, “The fact that the healthcare professionals are not knowledgeable about the disease. The parents are the ones educating the healthcare professionals. It is imperative that you are knowledgeable about the disease before working with a patient, no matter the rare disease.” She shared that one of the most frustrating things for

families are “the healthcare professionals that do not even look at the chart before coming into the room.”

B. Wedehase also stressed the importance of knowledge and education about Hunter syndrome in order for nurses to best help their patients. When asked, “In what way(s) do you believe healthcare professionals are best able to aid in the care of Hunter syndrome patients and their families?”, she answered, “Being knowledgeable about the disease. By being knowledgeable you are able to talk with parents about what is happening with their child at that point and advising them what may be coming in the future. By educating families about potential future procedures, then they can recognize when the procedure may be needed and be able to recognize when a procedure may be useful before their child gets too far advanced.” B. Wedehase also stressed that when it comes to nurses’ education about Hunter syndrome, “listening to the parents is so important. Parents are the ones who are with these kids all the time. They know this disease.”

Concluding Thoughts

Hunter syndrome is a rare disorder. It is, however, a disease that may affect any patient, and therefore, nurses must be educated about it. Nurses need to be able to recognize warning signs of the disease and be educated enough to provide competent care. With their knowledge, nurses can support patients with Hunter syndrome in many ways. Nurses can help by providing their patients with skilled care, written information, referrals, and suggestions of support groups, but one of the most important roles of the nurse is to provide caring support. Whether a patient has just been diagnosed or he or she has been living with knowledge of the disease for years, it is a stressful and devastating disease to live with. Nurses can care for patients and their families by being there emotionally and by assessing each situation individually and finding the areas where

a specific patient and family could be helped. Nurses may not be able to relate to having or knowing someone who has Hunter syndrome, but they can still provide a sense of comfort in the midst of the always progressing disease.

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