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Von Hippel-Lindau Disease:
A Rare Familial Multi-system Disorder
and
The Impact of the Clinical Nurse Specialist

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Abstract

Von Hippel-Lindau disease is a rare familial multi-system disorder that predisposes tumor formation. The lesions that most commonly cause morbidity and mortality are renal cell carcinoma, cerebellar and spinal cord hemangioblastomas, retinal angiomas and pheochromocytomas. The genetics, symptomatology, and medical treatments are reviewed. A case study is presented. Often the psychosocial aspects of a complex illness are ignored. The role of the clinical nurse specialist can be instrumental in a positive outcome for the patient and family affected by such rare multi-system disorders.

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Chapter 1

Introduction

Case Study

A forty-three year old man without prior history suddenly experienced diaphoresis, dizziness, nausea and severe occipital headache and neck pain. A cursory emergency room work-up did not reveal the etiology, but the patient was given a neurosurgery consult for degenerative joint disease of his neck. Over several days, the neck pain, nausea, and vomiting persisted. At that time, a neurological exam revealed tremor of the left upper arm as well as hyperreflexia and muscle wasting. An initial computed tomography (CT) scan of the head was negative. However, a lumbar puncture showed blood was present in the cerebral spinal fluid. The physicians suspected an intracerebral bleed, but an angiogram was negative. Magnetic resonance imaging (MRI) exposed three hemangioblastomas in the cerebellum along with one in the cervical spinal cord. One of the tumors in the cerebellum proved to be the source of the bleeding.

Because of suspicion, the medical team did a thorough work-up and found bilateral pheochromocytomas as well as lesions in both of the patient's kidneys. Cysts existed in the pancreas and epididymis. An

angioma was found in one eye. Von Hippel-Lindau (VHL) disease was diagnosed.

Definition

Von Hippel-Lindau disease is a genetic disorder which causes a predisposition to tumor formation. Collins first described familial retinal angiomatosis in England in 1894, and von Hippel published similar findings in Germany in the early 1900's. In 1926 Lindau associated the retinal manifestations with tumors in the central nervous system as well as visceral organs (Maher et al., 1990). Schuback in 1927 was the first to introduce the term "Von Hippel-Lindau syndrome" to describe patients with retinal or posterior fossa tumors together with cysts or carcinomas in various abdominal organs (Kounis et al., 1989).

Melmon and Rosen (1964) defined the criteria for diagnosis as two or more hemangioblastomas or a single hemangioblastoma in association with a visceral manifestation. Where there is a family history, only one lesion meets the criteria for diagnosis.

Although at least 25 distinct lesions have been described in this disorder, only six frequently produce clinically manifested disease: retinal angiomatosis; cerebellar, medullary, and spinal hemangioblastoma; pheochromocytoma; and renal cell

carcinoma. Clinical variability is characteristic of most autosomal dominant traits, and VHL disease is no exception. Manifest of the entire syndrome is unusual for an individual or even for all the affected members of smaller families (Horton, Wong, & Eldridge, 1976). Manifestation of this disease is delayed and diagnosis is often made after age 30. However VHL disease has been observed in children (Kounis et al., 1989; Filling-Katz et al., 1991).

The disease is often lethal with cerebellar hemangioblastoma and renal cell carcinoma being the most common causes of death. In contrast, the more common cysts and angiomatous tumors of several visceral organs are usually asymptomatic (Hardwig & Robertson, 1984).

Genetics

VHL disease is an autosomal dominant disorder with partial penetrance. Any child born to an afflicted person thus has a 50% chance of being affected (Hardwig & Robertson, 1984). Anyone with an affected parent and an affected child is obliged to have the VHL gene. A patient with combined central nervous system, eye, or systemic lesions but negative family history, if paternity is not in doubt, could still have hereditary VHL, if affected relatives were

undetected, or if it arose by a new mutation (Lamiell, Salazar, & Hsia, 1989). Incidence of VHL disease has been given to range from 1 in 36,000 to 100,000. Expression and age of onset within a family can vary, but studies have shown that if affected, a person will almost always display the disease by the age of 60 (Maher et al., 1991).

Scientists from around the world are studying the genetics of VHL disease. Seizinger (1991) from Harvard in Massachusetts discussed the rationale for this research:

> Many human cancers are known to occur in two different forms: sporadic tumors in the general population and hereditary tumors within families. Hereditary tumor syndromes offer unique model systems for isolating genes whose mutations lead to cancer. Evidence is accumulating that hereditary and sporadic tumors are caused by similar pathogenic mechanisms affecting the same gene loci. The cloning and characterization of these genes- our major goal- may therefore have important implications for diagnosis and treatment of not only the relatively rare hereditary tumors, but also their much more common sporadic counterparts (p. 332).

Maher and colleagues in England analyzed data from 109 patients with VHL disease that present statistical evidence for the cause being an inherited mutation of a 'tumor suppressor gene' (Maher, Yates, & Ferguson-Smith, 1990). Using DNA linkage analysis the primary defect has been mapped to the short arm of chromosome 3p. In one of their studies, Dr. Glenn (1991) and her associates at the National Institutes of Health and the University of Pittsburgh School of Medicine obtained results that suggest that there are mutant alleles at the VHL locus on chromosome 3 associated with distinct tissue specificities.

With strides made in the genetic research, some diagnostic testing procedures have been developed. DNA polymorphism analysis can identify individuals likely to carry the VHL disease gene among asymptomatic members of disease families (Glenn et al., 1992). There are limitations to the application of these techniques, but further breakthroughs including a diagnostic blood test are anticipated in the near future (G. Glenn, personal communication, January, 1993).

Summary of Manifestations

The frequency of involvement of the kidney, brain, spinal cord and adrenal gland in individuals

affected with VHL disease has been described in the literature (Hardwig & Robertson, 1984; Horton, Wong, & Eldridge, 1976; Lamiell, Salazar, & Hsia, 1989; Maher et al., 1990; Malek, Omess, Benson, & Zincke, 1987; Neumann, 1987). These frequencies from various authors are compiled in table 1.

Table 1

Frequencies (in percentages) of Organ Involvement

		Renal Cell	Hemangioblastomas	
Authors	n	Carcinoma	Cerebellar	Spinal
Horton, Wong & Eldridge	50	28	36	4
Hardwig & Robertson	36	22	69	8
Neumann	338	27	46	1
Malek, Omess, Benson, & Zincke	37	21	86	19
Maher et al.	152	28	59	13
Lamiell, Salazar, & Hsia	554	24	55	14

Authors	n	Pheochromocytoma	Retinal Angiomatosis
Horton, Wong & Eldridge	50	10	58
Hardwig & Robertson	36	3	64
Neumann	338	14	46
Malek, Omess, Benson, & Zencke	37	0.3	78
Maher et al.	152	7	59
Lamiell, Salazar, & Hsia	554	19	57

Table 2 includes the mean age when diagnosed with a particular lesion as documented in three studies (Hardwig & Robertson, 1984; Maher et al., 1990; Horton, Wong, & Eldridge, 1976).

Table 2

Mean Age at Diagnosis of Lesions

Type of Lesion	Authors		
	Hardwig & Robertson	Maher et al.	Horton, Wong & Eldridge
Retinal	24	25(±12.7)	28(±2.6)
Spinal cord	18	33.9(±12.6)	25(±1.4)
Cerebellar	33	29(±10.0)	31(±2.9)
Renal	41	44(±10.9)	41(±3.0)
Adrenal	*	20.2(± 7.6)	34(±5.2)

Note: Age at diagnosis for adrenal lesions not included in this report.

Chapter 2

Manifestations and Diagnostics

Ocular Manifestations

Angiomatosis retinae is often the first observed manifestation of VHL disease. Retinal angiomas have been reported in infants and in the ninth decade (Lowden & Harris, 1986; Ridley, Green & Johnson, 1986). This highly cellular vascular tumor of the retina is histologically indistinguishable from a cerebellar hemangioblastoma (Maher et al., 1990).

Both eyes can be affected. In a survey by Neumann (1987) of 338 patients with VHL disease, 29 percent of the tumors were bilateral. In Hardwig and Robertson's (1984) review of 36 patients, the incidence of bilateral disease climbed to 59 percent.

Tumors can be multiple in number and often occur in the mid periphery to the periphery of the retina. The diagnosis is made by indirect opthalmoscopy and fluoroscein angioscopy. The major presenting symptom is blurry vision, but visual acuity can be normal as often as it is severely compromised (Hardwig & Robertson, 1984).

An untreated retinal angioma may increase in size, and the high flow arteriovenous shunt and leaky capillaries lead to exudation of fluid, resulting in

retinal detachment, retinal exudates and visual loss (Maher et al., 1990). The secondary glaucoma resulting from big angiomas can cause severe pain as well.

Central Nervous System Manifestations

Filling-Katz (1991) and colleagues reported the largest cross-sectional study of central nervous system (CNS) involvement in patients with VHL disease. Increased sensitivity of gadolinium-enhanced MRI screening is thought to influence their statistics estimating CNS involvement (72 percent). Their results are greater than in previous studies showing 21 and 42 percent (Melmon & Rosen, 1964; Lamiell, et al., 1989). Conventional CT scanning demonstrates a contrast enhancing mass, but MRI scanning appears to be more sensitive and is preferred when available (Maher et al., 1990).

Lesions are often multiple and occur most often in the cerebellum and cervical spinal cord. These lesions are hemangioblastomas and are not malignant. Histologically hemangioblastomas appear as a network of endothelium and vascular channels and polygonal intervascular or stromal cells (Maher et al., 1990). Hemangioblastomas also occur in the medulla

CNS symptoms relate to the size, number,

locations of tumors and the residual effects of previous surgery. Tumors in the cerebellum and brainstem are often associated with the symptoms of headache, nystagmus, ataxia, and nausea and vomiting. When the spinal cord is involved, focal pain, sensory loss and motor deficit are the major complaints (Filling-Katz et al., 1991). However, patients can often remain clinically asymptomatic in the presence of lesions. When the tumor becomes symptomatic, the course is often one of progressive neurologic impairment that may lead to death if the disease is untreated. The rate at which symptoms progress may be highly variable, ranging from days to years (Horton, Wong, & Eldridge, 1976).

Renal Cell Carcinoma

Significant urological manifestations of this syndrome include renal cysts, renal adenocarcinomas, adrenal pheochromocytomas and papillary cystadenomas of the epididymis (Horton, Wong, & Eldridge, 1976). In the most recent literature, renal cell carcinoma supersedes cerebellar hemangioblastoma as the leading cause of death. Advances in neurosurgical techniques have enabled more patients with VHL disease to survive a cerebellar hemangioblastoma and many of these patients will go on to develop a renal cell carcinoma.

Renal tumors in VHL disease occur at an earlier age than with sporadic non-familial disease, but have a similar clinical presentation and risk of metastasis. The tumors are also often multiple and bilateral (Maher et al., 1990). Also unlike its sporadic counterpart, renal carcinoma in VHL disease is only slightly predominant in males instead of the normal 3:1 male-to-female ratio (Spencer, Novick, Montie, Streem, & Levin, 1987).

Simple renal cysts and solid renal cell carcinomas frequently occur together in VHL disease, but in the past the cysts were assumed to be benign. Christenson, Craig, Bibro and O'Connell (1982) showed that the cysts can be composed of cells consistent with renal cell carcinoma. Loughlin and Gittes (1986) substantiated these findings in their patients. A consistent and characteristic histological feature in VHL disease is the presence of clear cells lining cysts with or without frank carcinoma within the renal cyst walls (Spencer et al., 1987).

Abdominal CT is the recommended diagnostic test as it has been found to be both reliable and safe (Levine, Weigel, & Collins, 1983). Renal cell carcinoma is often silent and diagnosed after other manifestations of VHL disease are apparent.

Presenting symptoms can include flank pain and hematuria. Loughlin and Gittes (1986) recommend initial arteriography, as well as a CT because arteriography may not detect all malignancies. CT is usefull in planning renal-conserving surgery. This strategy is advocated by others as well (Jarvik & Pollack, 1991; Glenn, Choyke, Zbar & Linehan, 1990).

Pheochromocytoma

Interfamilial variation in the predisposition to pheochromocytoma is well recognized in VHL disease. For example, 20 of 38 affected members of a large New Foundland family developed a pheochromocytoma, but none of 43 patients from a large Hawaiian family (Maher et al., 1990).

A pheochromocytoma is a potentially life threatening tumor of the chromaffin cells of the adrenal gland medulla that produces, stores and secretes excessive amounts of catecholamines (Yucha & Blakemen, 1991; Landsberg & Young, 1991). There is a high tendency for these tumors to occur bilaterally in VHL disease. This is also seen in other heritable syndromes in which the tumor occurs: central neurofibromatosis and types 2 and 3 multiple endocrine adenomatosis (Horton, Wong, & Eldridge, 1976).

The presentation is characteristically

unpredictable. Most patients are diagnosed due to hypertensive crisis, paroxysmal symptoms suggestive of a seizure disorder or anxiety attacks, or hypertension that responds poorly to conventional treatment. Less commonly, unexplained hypotension or shock in association with surgery or trauma will suggest the diagnosis. The paroxysmal symptoms, lasting just a few minutes to several hours or longer can include headache, profuse sweating, palpitations, and apprehension, often with a sense of impending doom. The person may experience chest or abdominal pain as well as pallor or flushing. The blood pressure may be elevated to alarming levels, accompanied by tachycardia. (Landsberg & Young, 1991).

Pheochromocytoma is diagnosed with measurement of urinary vanillylmandelic acid and normetadrenaline levels. These levels can be falsely negative if the patient is asymptomatic at the time of collection. Plasma catecholamines and Iodine-131 metalodobenzyl-guanidine (MIBG) scanning may be indicated in patients where there is clinical suspicion (Maher et al., 1990). These tests are more sensitive and result in fewer false negative results.

The usefulness of plasma catecholamine determinations may be increased by agents that

suppress sympathetic nervous system activity. Clonidine and ganglionic blocking agents both markedly reduce plasma catecholamine levels in normal subjects and in patients with essential hypertension. These drugs have little effect on catecholamine levels in patients with pheochromocytoma. In patients with elevated or borderline basal catecholamine values, failure to suppress plasma or urinary levels with clonidine supports the diagnosis of pheochromocytoma (Landsberg & Young, 1991).

Iodine-131 metalodobenzylguanidine ([^{131}I]MIBG) specifically localizes in adrenergic tissues and has proven to be safe, sensitive and most importantly, relatively specific in the detection of pheochromocytoma (Velchik, Alavi, Kressel & Engleman, 1989). Velchik and colleagues found that MIBG, CT and MRI are complementary procedures with MIBG providing more specific functional information and the latter two superior anatomic detail. MIBG scintigraphy is recommended as the initial localizing study of choice.

Other Manifestations

An epididymal cyst is a benign and fairly common finding in VHL disease. Incidence has been determined to be 15 percent and 26 percent in two studies (Neumann, 1987; Lamiell, Salazar, & Hsia, 1989). This

tumor is situated within or in close apposition to the head of the epididymis and is characterized by ectasia (dilitation) of the efferent ducts and by papillar formations, which are usually covered by vacuolated cells with clear cytoplasm. The tumor often occurs bilaterally (Neumann & Wiestler, 1991). Generally, the tumors are asymptomatic and do not require treatment (Glenn, et al., 1990).

Pancreatic cysts also commonly occur in VHL disease. They are frequently asymptomatic and found during the search for other lesions or during surgery. In the large Freiburg study (Neumann et al., 1991) of VHL syndrome composed of 66 affected individuals, pancreatic lesions were systematically studied. Cystic lesions were found in 15 percent of the patients. Because multiple pancreatic cysts did not cause major clinical symptoms and follow-up examinations over an average period of five years did not show significant progression of the lesions, these researchers concluded that these patients with pancreatic tumors usually do not require surgical treatment.

Angiomas and adenomas of the pancreas may also occur, and rarely there may be a pancreatic hemangioblastoma (Fishman & Bartholemew, 1979). A

case of insulin-dependent diabetes associated with complete pancreatic replacement by cysts has been described (Bird & Krynauw, 1953). Fishman and Bartholemew (1979) report on the rare occurrence of steatorrhea associated with VHL disease, and severe pancreatic involvement in members of a single family.

Lesions have been reported rarely in other organs such as testis (Cendron, Wein, Schwartz, Murtagh, Livolsi, & Tomaszewski, 1991), liver and pulmonary system (McGrath, Gibney, Morris, Owen, & Erb, 1992) spleen, skin, thyroid and pituitary gland (Neumann, 1987).

Polycythemia has also been a finding in patients with other manifestations of VHL disease (Hardwig & Robertson, 1984; Horton, Harsh, Fisher, & Hoyt, 1991). Erythrocytosis occurs in 5 to 30 percent of patients harboring a hemangioblastoma within the posterior fossa (Lamiell, et al., 1989). Using the latest laboratory techniques, Horton and colleagues report the identification of erythropoietin in fluid obtained from a brainstem hemangioblastoma in a patient with VHL disease and erythrocytosis. Pheochromocytoma has also been associated with this finding (Hardwig & Robertson, 1984). In these cases the tumor is thought to be producing ectopic erythropoietin (Horton et al., 1991).

Chapter 3

Medical Management

Goals

A major goal of the medical care of the patient and family with VHL disease is early detection of life-threatening lesions. The entire family must be screened. Life-saving surgical intervention can be more prudently planned with early detection. Since VHL disease is a multi-system disease, the physician who discovers as isolated hemangioblastoma of the retina or cerebellum must search for other, possibly silent lesions of the disease, especially renal cell carcinoma (Hardwig & Robertson, 1984). The diagnostics and symptoms that help to find a particular lesion have been reviewed. Once tumors are diagnosed, the goal of treatment is to maximize function.

Interventions

Early detection and treatment of retinal angiomas should prevent visual impairment. Small lesions (less than 0.8 disc diameter) may be treated by laser photocoagulation, and larger lesions by cryotherapy (Ridley, Green, & Johnson, 1986). Vitrectomy may be indicated in cases with extensive epiretinal membrane formation and traction retinal detachment (Maher et

al., 1990). Some patients' eyes with large angiomas show relentless progression and visual loss despite all forms of treatment. Enucleation is sometimes indicated for pain and blindness (Hartwig & Robertson, 1984).

Treatment for hemangioblastomas of the central nervous system is surgical excision. Advances in neurosurgical techniques have decreased the mortality and morbidity associated with these lesions. However, if the patient is asymptomatic, surgery is generally not indicated.

Traditionally, management of renal cell carcinoma involves a radical nephrectomy. However, due to the nature of VHL disease, where the renal tumors are often multiple and bilateral, a more conservative approach has been advocated. Pearson, Weiss and Tanagho (1980) promulgated the idea of the need for limited surgery and conservation of renal parenchyma in patients with VHL disease to avoid the morbidity and mortality associated with hemodialysis or transplantation.

Another factor favoring a parenchymal-sparing approach is that the majority of these tumors are pathological stage I when detected, as observed by Spencer and colleagues (1987) in 9 of 10 of the

patients they studied. The process of staging categorizes malignant tumors with respect to their degree of differentiation, to their potential for responding to therapy, and to the patient's prognosis. Stage I is the most favorable classification. Loughlin and Gittes (1986) reported favorable results when they directed their efforts toward preserving renal parenchyma without compromising adequate tumor excision. None of their seven patients required dialysis or renal transplantation.

Bilateral nephrectomy followed by hemodialysis has been reported by Fetner, Barilla, Scott, Ballard, and Peters (1976). They have proposed renal transplantation if their patient survives five years on dialysis without evidence of recurrence. Das, Egan and Amar (1981) point out that transplantation necessitates immunosuppressive drugs, which could conceivably increase the likelihood of cancer in VHL patients who are already predisposed to cancer. Peterson, Codd, Cuddihee, and Newton (1977) performed the first reported transplantation in a patient with VHL disease who tolerated hemodialysis poorly. Two years after the surgery, recurrence of the cancer is not evident. However, chronic rejection is a complication. Malek and his colleagues (1987) advocate

radical surgery and autotransplantation of the salvageable portion of the remaining kidney, over Fetner's alternatives. They have been successful in one reported case.

The treatment for pheochromocytoma is surgical as well. It is important for VHL patients to be evaluated for this complication prior to any other surgeries or procedures that could stimulate the adrenal tumor to release catecholamines. The life-threatening effects of excessive catecholamine production may be potentiated by anesthetic agents (Yucha & Blakeman, 1991). Consequences could be devastating, and include hypertensive crisis, stroke, and death.

The induction of stable alpha-adrenergic blockade is the basis of preoperative management and provides the foundation for successful surgical treatment (Landsberg & Young, 1991). Phenoxybenzamine hydrochloride competitively blocks the effects of catecholamines on alpha-adrenergic receptors. Because of the long duration of action, the effects are cumulative and the optimal dose must be achieved gradually with careful monitoring of supine and upright blood pressures (Landsberg & Young, 1991). When the vasculature relaxes due to the effects of this

drug, the patient experiences a relative hypovolemia. Increasing salt intake and fluids restores adequate blood volume.

Phenoxybenzamine should be administered for at least 10 to 14 days prior to surgery. Before adequate alpha-adrenergic blockade with phenoxybenzamine is achieved, paroxysms may be treated with intravenous phentolamine. Nitroprusside is the only other antihypertensive agent that reliably reduces blood pressure in patients with pheochromocytoma, and may be useful on occasion (Landsberg & Young, 1991). Beta-blockers can be used to treat reflex tachycardia after alpha-blockade and the resultant vasodilation is achieved, and if the patient has adequate blood volume.

Surgical removal can be complicated because of fluctuations in blood pressure. Surgery is best performed in centers with experience in the preoperative management of pheochromocytoma patients. In experienced hands surgical mortality is below 2 or 3 percent (Landsberg & Young, 1991).

Most of the other lesions in VHL disease are benign and silent, requiring no treatment. Periodic screening keeps track of these lesions.

Chapter 4

Implications for the Future of the Patient and Family

Diagnosis of a genetic disorder is devastating for a patient and family. When cancer at an early age is the manifestation, as in VHL disease, the impact is compounded. Not only is there an acute crisis, there is chronic anxiety in dealing with the long term effects and the possibility of other family members being afflicted.

The threat or diagnosis of cancer often implies pain, disfigurement, helplessness, loss of independence, deterioration, and death. The social stigma associated with cancer can extend to all family members by association, and will influence all of their responses to the disease. Fear and denial of the existence of symptoms may occur, and delay needed medical consultation. Studies of cancer-prone families show that fear is the most prominent reaction, with other common responses including denial, evasion, guilt, apathy, fatalism, pessimism, regression, and acceptance (McGuire, 1979).

The genetic component of VHL disease brings with it added feelings of guilt because parents feel responsible if children are affected. Uncertainty is another major emotional trigger experienced by

families with genetic disorders if a diagnostic blood test is unavailable. This necessitates life-long screening for manifestations. Fear, guilt, blame, anxiety, depression, and fatalism were often exacerbated by the screening that is necessary for families with VHL disease. A report was recently published in the New England Journal of Medicine on patients with Huntington's disease, another genetic disorder in which manifestations are delayed until adulthood. The delayed onset is like that of VHL disease, so the psychological consequences may also be similar. In this study, the anxiety created by uncertainty was actually greater than that experienced by those informed of an increased risk of disease development (Wiggins et al., 1992).

It has long been evident that any serious and prolonged illness, such as cancer, functions as a source of stress demanding a major adjustment not only by the patient, but also by family members. Family as well as individual reactions are crucial in coping with acute stress since the family has a unique responsibility for mediating the reactions of its members (Kaplan, 1982).

Families pass through a sequentially developmental life cycle with different stages each

composed of tasks that must be negotiated by the family as a whole. When a serious illness occurs during one of these natural transitions, families may experience greater difficulty managing and coping with the illness (Feldstein & Rait, 1992).

When an adult within a family is diagnosed with such an illness, the ramifications extend to the children. Because the family is a system, what effects one member will effect everyone. While the children may not intellectually understand, they are experiencing the anxiety, perhaps the hospitalization of a parent along with the inherent separation, as well as diagnostic tests themselves. The amount of stress the family must cope with is overwhelming.

Sources of stress not only include the diagnosis, hospitalization, and testing of family members, but also changes within the family that are necessary to cope. Family roles may change either temporarily or permanently. The breadwinner may be hospitalized, or the major provider of child care. There may be financial implications due to health care costs as well as loss of income. Physical disability, either acute or chronic, is a potential outcome. Feelings of loss of control and dependence on health care providers occur. Other family members must take on

additional responsibilities and this increases anxiety.

It is obvious that the diagnosis of VHL disease places an incredible burden on the family. Studies on the psychological impact of this disorder are extremely rare. Langsley, Wolton, and Goodman (1964) investigated individual reactions of 24 family members to the threat of premature death, and attitudes toward VHL disease. They found a greater degree of psychopathology than would be expected by chance. Denial was the major coping mechanism employed by these families, but it was not always successful in allaying the anxiety. As a result the investigators found the subjects to have generalized disturbances of personality and as a group they were a relatively disturbed kindred (p. 648).

Only one other study can be found that examines the psychosocial impact of VHL disease on knowledge and attitudes within a family (Yuen, Jewell, Lamiell, & Hsia, 1984). Once an individual has been diagnosed as having VHL disease, a much greater impact on family planning attitudes was seen than with those who were just at risk. Parents associated this diagnosis with the threat of inability to provide adequately for their children. Young parents at risk for VHL disease exhibited little restraint in family

planning attitudes, whereas parents already afflicted with VHL disease showed much stronger inclinations to limit family size (p. 144). The researchers attributed these attitudes to some defense mechanisms such as denial and rationalization which may reduce the subjective perceptions of risk and severity of a condition.

All of these emotional reactions can also have an impact on the family and compliance to the health care regimen and screening. If the patient and family have difficulty understanding due to stress or feel overwhelming anxiety, compliance will be decreased. More effective coping will enhance understanding and learning, and this will be a positive influence on compliance. The information given to the family will also have a great impact.

In all of the literature published on VHL disease, genetic counseling is advocated for patients and families. By definition, genetic counseling is a process of dealing with occurrence/recurrence risk of genetic disease in a family. Counseling should include the following components:

1. Understanding the diagnosis, outlining the physical findings, reviewing the theoretic causes, and presenting the current medical

management

2. Determining the risk of recurrence in the particular family and the risk of occurrence in their blood relatives

3. Promoting the understanding of options available that would decrease the chance of recurrence

4. Choosing a course of action that is most consistent with the family's belief system (even if it is alien to the counselor's personal values and morals)

5. Helping the family cope with the diagnosis (Lemons & Brock, 1990, p. 21).

Genetic counseling can play an integral part in influencing the impact of a diagnosis of a genetic disorder.

Case Study

Once the diagnosis was made, the patient underwent an extensive evaluation for all the possible manifestations of VHL disease. To the patient it seemed as if each day brought more bad news as the results of each test returned. He was depressed and pessimistic about his future. He was overwhelmed with the thought that he could have passed this on to his two daughters. And he was worried about how his

family was holding up without him, since he was the primary care giver for the children.

CAT scans, MRIs, bone scans, MIBGs, urine tests, blood tests, ophthalmoscopy, and angiograms are just some of the tests performed. The patient felt inadequately prepared for the tests, and coupled with claustrophobia induced by many of the machines, was highly anxious much of the time.

Every day the team for each of the medical specialties involved in his case would visit. First the physicians would discuss his case out in the hall. He could hear every word, as could his roommate, but the physicians behaved as if this weren't so. The different specialties didn't seem as if they communicated with each other very well either. The patient finally asked to see a psychiatrist because he was having difficulty coping. A week went by before the consult was sent to the psychiatric department.

The nursing staff allowed the patient's children unlimited visiting privileges, breaking the rules. They also maintained a private room whenever the unit census permitted. However they were not knowledgeable about VHL disease.

Complicating the patient's condition was an extremely enlarged gall bladder and cysts interfering

with the flow of bile from the liver. The patient became acutely jaundiced and his liver function tests (LFTs) were elevated. The doctors planned early surgery if this persisted, but fortunately the blockage resolved and the LFTs decreased.

Finally a plan of action was outlined for the patient. First he would receive two weeks of alpha-blocking medication to control the effects of the pheochromocytomas. Then a renal arteriogram would be performed to help plan renal-conserving surgery, if possible. He would recover from this procedure in the intensive care unit, and then would undergo removal of both adrenal glands, the renal cell carcinomas, a cholecystectomy and a choledochoduodenostomy for biliary drainage. The pancreas and liver cysts would be biopsied.

This surgical procedure necessitated the insertion of a Swan-Ganz catheter and an arterial line for monitoring. Two incisions, of the abdomen and the flank might be necessary. Potential complications were numerous, including hypotension, hypertension, cerebral bleeding, renal failure, and pancreatitis. After recovery, a craniotomy would be done to remove the hemangioblastoma that had been bleeding.

The psychiatrist helped the patient and his

wife verbalize fears and anxieties. They also received emotional support from extended family.

The patient was in surgery for 12 hours, recuperated in the intensive care unit for seven days, and was discharged two weeks after surgery, after being hospitalized for seven weeks. Life-long hydrocortisone replacement was instituted. During the surgery the patient lost 3000 cc of blood and received six unit of packed red blood cells. Post-operative pain was managed effectively with epidural Fentanyl and then morphine sulfate via patient-controlled analgesia. After a three month convalescence, the patient had a craniotomy and was home within a week.

The patient's siblings have all had negative eye examinations. One brother refused an MRI due to claustrophobia. The other brother and sister have not pursued further work-up. The patient's seven year old daughter is also negative for ocular lesions, and his four year old was too young to tolerate the examination. She will be followed in a year. The family obtained the recommended screening protocol from the National Institutes of Health.

One year after diagnosis, the patient feels well. He continues to be screened by ophthalmology, endocrinology, neurosurgery, urology and radiology.

He is managed closely by an endocrinologist for replacement therapy.

It is unclear which of the patient's parents had VHL disease. His father is believed to have died from renal cell carcinoma, but he was quite elderly at the age of 80. He also had diabetes. The patient's mother had two craniotomies, in 1961 and 1973, but the benign tumors were not in the typical location for VHL hemangioblastomas. She has no other obvious manifestations and has not been evaluated further. She is in failing health and resides in a nursing home.

This case illustrates many areas where the nurse in an advanced practice role of clinical specialist could have a great impact on the care of the patient and family. This case illustrates the experiences of a patient afflicted by a rare, very complex, multi-system genetic disorder.

Chapter 5

Advanced Nursing Practice and Rare Genetic Disorders

Any disorder that is complicated and involves multiple systems provides an excellent opportunity for the clinical nurse specialist (CNS). There is strong evidence that the physician rarely leads or coordinates health care (Brown, 1983). Through various roles, the clinical specialist functions autonomously and in collaboration with other health care team members to lead, be a change agent, be a role model, and act as a patient advocate. The role components of the CNS include advanced practitioner, educator, consultant, manager and researcher. The clinical specialist exemplifies professional nursing practice.

Advanced Practitioner

When a patient is diagnosed with a rare disorder such as VHL disease, many health care practitioners are not familiar with the condition. Multiple specialists are consulted, and each focuses on one manifestation of the disease. The effects of the disease on the total individual and his family, as well as the effects of this kind of fragmented treatment can be easily ignored.

A primary function of the advanced practitioner

is to utilize advanced cognitive and psychomotor capabilities in the diagnosis, treatment, and evaluation of human responses to actual or potential life threatening health problems (AACN, 1989). While everyone else may be focusing on physiological parameters, the advanced nurse practitioner can key in on psychosocial aspects that are equally important and may have a profound impact on physical manifestations.

Patient and family assessment utilizing a genogram and family systems theory will give insight into coping and behaviors, and will point the way to appropriate interventions. This tool will help identify strengths and weaknesses of the patient and family. Past experience of the patient and family can also be determined and may also influence present attitudes and behavior. The advanced practitioner capitalizes on this knowledge and disseminates it to the entire health care team and the patient and family.

Early identification is important because studies of crises suggest that both the individual and the family reactions to the threat of prolonged illness are fashioned one to four weeks after the diagnosis is confirmed. The coping responses evident by then, whether adaptive or maladaptive, tend to persist and

to be reinforced throughout the course of the illness, which may run for years. Therefore the ideal time to discover that families are coping inadequately is during this early phase (Kaplan, 1982). The CNS has the perfect opportunity.

In the critical care unit, immobilization, isolation and interference with communication due to intubation may hinder mobilization of previous effective coping strategies. The unique aspects of this environment must always be kept in mind, and will be, with the CNS to help.

The critical care CNS is vital to the staff in dealing with the physiological consequences of this disease and its treatments. The surgeries required can be very lengthy and the post-operative care is complex. The critical care CNS can help the nursing staff coordinate, prioritize, and prevent complications. While surgery may be performed on one or more organs at one time, other systems may need close monitoring as well, and the critical care CNS can facilitate this process. Medication regimens may also be complex, as is the actions and effects of these medications. Appropriate pain management can also be coordinated by the critical care CNS, and will benefit the patient after transfer out of the

intensive care unit.

Another function of the advanced practitioner in the care of the patient with a complex disorder can be to organize family conferences. In this way the CNS collaborates with the patient and family and health care providers in achieving optimal patient outcomes. When members of the team are focused on their particular specialty, a family conference can widen the view and enlighten. Questions and concerns can be more easily addressed. Coordination of care can be achieved. The CNS can also act as a liaison between the patient and family and other departments within the hospital that may not be included in the conferences. The CNS can recommend and initiate referrals to other health care providers, such as social workers, dieticians, and disability counselors.

Such simple matters as allowing a patient to have visitors outside of visiting hours and to have personal possessions, modifying medical and laboratory routines, and orienting families and patients at nontraditional times can have a positive effect on both patient and family well-being (Noble, 1988). The CNS has an important role in the modification of staff communications as a potential environmental disturbance. First, the CNS can serve as a role

model, thus helping nurses and other staff members watch what they say in the patient's presence. For instance, the staff may need to realize that medical rounds should not be within hearing range of the patients. Nurses also need to explain happenings in the environment that may be distressing to the patient (Noble, 1988).

As an advanced practitioner, the CNS instills value for professional nursing practice including the utilization of standards and the nursing process and patient advocacy (AACN, 1989). The CNS can also play a role in the diagnosis of rare disorders. The CNS may be the first person to recognize a patient's illness as part of a complex disease.

Educator

In the role of educator, the CNS serves fellow health care providers, patients and families, and the community. Oftentimes, there is a population of patients with complex or unusual learning needs who are seen infrequently by staff nurses but are known to the CNS. This population may include patients with rare diseases, patients undergoing radical and/or new surgical procedures, patients treated with new therapies and modalities, and patients on research protocols or nonstandard therapies (Priest, 1989,

p. 157). The CNS as an educator, utilizing teaching skills and theoretical concepts, is vital in these circumstances.

An integral part of education is the identification of learning needs. The CNS is in perfect position to assess the patient, the family, and the staff. Then with comprehensive knowledge, about a rare disorder for example, the CNS can teach the important points with unique application to each student.

The CNS also evaluates the patient and family readiness to learn and prioritizes learning needs (Priest, 1989). By coordinating educational efforts, the CNS can prevent information overload and still meet needs. Education may help to determine adaptation to illness. Information given to social support systems of family and friends may influence skills of adherence to a regimen that a person learns (Bloom, 1982). Lifestyle changes related to illness are frequently overlooked by less experienced staff, but the CNS can help patients anticipate changes and provide a framework for decision-making about issues that arise after discharge (Priest, 1989).

Accurate, understandable information allays anxiety and allows the patient and family to gather

resources in order to make responsible decisions. To facilitate such communication the CNS could set up an information system and either be available by phone during off hours for a true need or delegate other nurses to fill this need (Noble, 1988).

Another important job for the CNS can be to address the anxiety due to diagnostic tests. Certainly discussing fears and anxieties can help, but other techniques can be taught, such as relaxation, imagery, and music therapy. The CNS can also provide the patient and family with information about each test, and be available when results are given to the patient.

The CNS often provides continuity of care to a particular population and is in position to evaluate the effectiveness of the teaching process. This feedback can be given to the staff to improve the quality of teaching for subsequent patients. The CNS must be sensitive to the nursing staff's need to be involved in the education process, and negotiation for specific tasks must take place according to patient needs and time constraints of staff. Encouragement of staff motivated to learn and teach is essential to CNS success in the educator subrole (Priest, 1989).

Another strategy that can be used by the CNS in

the role of educator is unit-based nursing rounds designed to meet the identified needs of staff nurses and to ensure comprehensive patient care and documentation (Coleman & Henneman, 1991). These rounds can be lead by the CNS who has knowledge of educational methods, clinical issues, and staff needs. A case study approach to staff education can incorporate research and facilitate collaboration. With a special emphasis on physical and psychosocial needs identification, these efforts will improve comprehensive patient care, which is an important goal of education.

Finally, it is important for the CNS to be involved in education of the public. The CNS can take her wealth of knowledge and share it with church groups, parent-teacher associations, senior citizen groups, the media, and any others interested. The CNS can be assertive and advertise her availability.

Consultant

Consultation is an important aspect of the CNS role, and it incorporates the subroles of practitioner, educator, researcher, and manager. The consultant applies change theory during the consultation process (AACN, 1989). The clients of the consultation may be the patient and family, the nursing staff, other

health care providers, or others outside the hospital. The consultant uses the steps of the nursing process to assess, intervene and evaluate.

With knowledge of a rare disorder, the CNS may be called upon to consult with a variety of people. The patient and family would certainly want to consult with an expert, and then the CNS can also let their concerns be known. The CNS as a consultant can make referrals to other consultants as well, such as social workers, psychiatrists, or genetic counselors. Physicians of one specialty could consult the CNS about aspects of the disease outside their field, including the psychosocial aspects. A specific department, such as radiology, may consult the CNS to improve patient sensitivity or staff interactions.

The nursing staff may wish consultation on many aspects of patient care that are involved in a complex disorder. Dealing effectively with psychosocial aspects is often facilitated by CNS consultation. The mutual and creative problem solving that occurs during a consultation can be a catalyst for the ongoing professional development of both the consultee and consultant, and can profoundly influence nursing practice (Barron, 1989).

Outside the hospital, the CNS can provide

consultation services to genetic support groups and other associations that are available for patients after discharge. The CNS is particularly valuable to facilitate group discussions, provide access to meeting rooms and other resources, and in referring new members. The CNS can be a source of expert information and serve as a speaker at meetings.

Manager

As a manager, the CNS participates in the development, implementation and evaluation of structure standards for care of the patient and family (AACN, 1989). This is particularly important in rare disorders when the CNS may be the only expert that can fulfill this function, and unfamiliarity with the condition among the staff makes standards invaluable.

The CNS is integral in evaluating the performance of the entire staff in meeting the complex and diverse needs of the patient and family. Part of the management role includes ensuring quality care, through quality assurance activities and monitoring, and through the other roles of the CNS. Management involves obtaining results, evaluation, and implementation of change to improve performance. Knowledge of change theory is a handy skill for the

CNS, especially as a manager.

Researcher

In the immediate future, additional studies demonstrating the importance of the CNS on patient and family outcomes and cost of care are needed. Studies that replicate current work or extend it to other patient populations are important (Naylor & Brooten, 1993). Such research is particularly important in our present climate of health care reform with concern for costs while maintaining quality.

The CNS is uniquely qualified to conduct research at the bedside. As an important central figure on the health care team, the CNS is in a position to identify appropriate research questions and to elicit participation among the staff in research. As a result of graduate education, the CNS has skills to conduct the research. The CNS then presents and publishes research findings. Not only does the CNS share the results of her own research, but she also evaluates the research of others. Then the CNS disseminates findings relevant to the staff and concerning patient care and outcomes.

Particular areas where research would be valuable in the area of rare multi-system genetic disorders include:

1. The impact of the CNS on patient compliance with self care

2. The impact of the CNS on family follow-up and adaptation

3. Determination of the interventions that truly benefit the patient and family, and measurement of these benefits

4. Determination of cost-effectiveness of various CNS interventions

5. Impact of the CNS on attitudes and knowledge of staff and patients.

While research on disorders such as VHL disease is conducted, these studies are confined in large part to medical and genetic inquiries. Nursing literature is conspicuously scanty, and nursing research is virtually nonexistent. The CNS can play a major role in improving care of patients with rare multi-system disorders through research.

Summary

The CNS addresses the health care needs of the patient and family with complex multi-system genetic disorders through each of the following subroles: advanced practitioner, educator, consultant, manager, and researcher. High quality patient outcomes are dependent on this unique combination of roles fulfilled by the CNS (AACN, 1989). While genetic multi-system disorders are rare, there are many other diseases that have a genetic component as well, such as breast cancer, diabetes, and heart disease. Certainly these and other diseases also have implications for multiple systems. Some of the strategies and methods of care applicable in VHL disease can be extrapolated to care for many diverse patient populations.

The CNS is influential in coordinating care and ensuring the psychosocial and physiological needs of the patient and family are met. Through advanced practice and research, the CNS will identify even better ways of patient care management.

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