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Lupus Nephritis: A Synopsis of Pathophysiology and Implications for Advanced Nursing Practice

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Introduction of Pathophysiology

Systemic Lupus Erythematosus (SLE) can be described as a chronic, complex, autoimmune disorder (McCance & Huether, 2014). Disproportionately affecting women, and those of Afro-Cuban, Hispanic, Asian, and American Indian descent, SLE has a prevalence of 2.0 to 7.6 cases per 100,000 persons in the United States. Characterized by chaotic autoantibody production, complement alterations, and formation of immune complexes, SLE has the potential to generate devastating damage to multiple organ systems. Formed from the binding of autoantibodies and self-antigens, immune complexes often result in renal damage, a significant complication of the disease. Through careful analysis and synopsis of literature, the writer intends to provide the audience with pathophysiologic concepts defining lupus nephritis (LN). Within ten years of SLE diagnosis, between 50% and 60% of adults diagnosed will go on to develop LN (Richey, 2014). Of those with LN, upwards of 17% will go on to develop end stage renal disease (Bose, Silverman, & Bargman, 2014). The devastating course of this condition prompted the writer's choice of LN as a topic of interest for the purpose of this project, as she wished to gain valuable knowledge regarding the ailment and implications for advanced nursing practice.

Clinical Manifestations

Many patients experience no symptoms at all. Typically, LN is suspected in SLE patients producing abnormal urinalysis results, possibly with an elevated serum creatinine level. Patients may demonstrate persistent proteinuria greater than 0.5 grams per day, random protein/creatinine ratios greater than 0.5 grams, and the production of urine with active sediment consisting of blood cells and/or casts greater than 5 without urinary tract infection. Serum creatinine, blood urea nitrogen, and antiDNA studies may be elevated, while glomerular filtration rates and C3 and C4 complement may be low (Hahn et al., 2012). Interestingly, IgE is also noted to be elevated with both active SLE and LN. A prominent player in type I hypersensitive reactions, IgE has historically been identified in autoimmune illness. Dema et al. (2014) ascertain elevated autoreactive IgE levels to be in significant relationship with active SLE and LN.

The advanced practice nurse should suspect LN in SLE patients presenting with selected symptoms. Hahn et al. (2012) identify these signs as:

- Periorbital edema
- Edema of the upper and lower extremities
- Changes in urine appearance
- Weight gain

Figure 1: Bubbles within urine samples are flag for proteinuria. Retrieved from http://www.kidney-cares.org/nephrotic-syndrome-symptoms-complications/220.html

In addition to the above physical symptoms, patients with active LN typically demonstrate signs of active SLE. As described by Hahn et al. (2012), these symptoms include:

- Malar (Butterfly) rash
- Light sensitivity
- Fatigue
- Arthralgias and arthritis
- Fever
- Gastrointestinal upset
- Ulcerations of the mouth and nose
- Pleurisy
- Hair loss
- Raynaud's Phenomenon

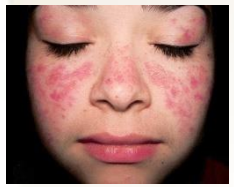
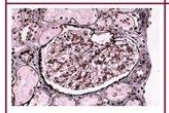
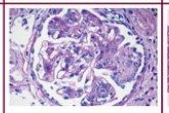
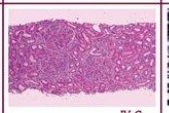
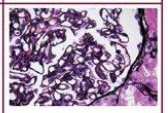
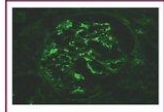
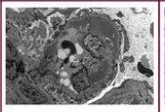
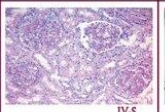
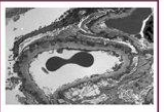


Figure 2: The malar rash associated with active SLE. Retrieved from www.healthsurgical.com

Diagnosis

Definitive diagnosis and classification of LN is made by determining the extent of glomerular injury via renal biopsy, urine, and blood studies. The classification scheme used to stage and type the severity of LN is comprised of six classifications. The mildest form of renal involvement, class I minimal mesangial lupus nephritis, is rarely diagnosed as the urinalysis remains normal, showing minimal if any protein. Biopsy is not warranted at this stage as serum creatinine also remains normal. Class II mesangial proliferative lupus nephritis is characterized by microscopic hematuria or proteinuria without renal insufficiency. Subendothelial deposits or glomerular scarring noted on light microscopy, are hallmarks of class III focal lupus nephritis and class IV diffuse lupus nephritis. Hematuria and proteinuria, decreased glomerular filtration rate and hypertension are often seen with class III, while the class IV patient will exhibit hematuria, proteinuria, reduce glomerular filtration rate, hypertension and nephrotic syndrome. The differentiation between class III and class IV is made through the determination of the percentage of glomeruli affected. If involvement of glomeruli tops 50%, class IV LN is diagnosed, while less than 50% involvement is consistent with class III. Class V, lupus membranous nephropathy, is characterized by glomerular capillary wall thickening and subepithelial immune complex deposits on light and electron microscopy. Class V patients
present with hypertension and microscopic hematuria without significant serum creatinine elevation. Class VI, advanced sclerosing lupus nephritis, is characterized by the sclerosis of at least 90% of glomeruli on biopsy. Glomerular sclerosis is indicative of previously injury. However, no active glomerulonephritis will be seen. Patients exhibit proteinuria without active urine sediment (Bomback & Appel, 2016).

TABLE: INTERNATIONAL SOCIETY OF NEPHROLOGY/RENAL PATHOLOGY SOCIETY (ISN/RPS) 2003 CLASSIFICATION OF LUPUS NEPHRITIS (CLASSES II-V)

Class II	Class III	Class IV	Class V
Mesangial proliferative LN	Focal LN	Diffuse LN	Membranous LN
		 IV-G	
		 IV-S	
The glomeruli show mesangial proliferation with mesangial immune deposits by IF (lower panel) and EM. Isolated subepithelial or subendothelial deposits may be present by IF or EM.	Active or inactive segmental or global endocapillary or crescentic GN involving less than 50% of all glomeruli. Segmental is defined as a lesion that involves less than half of the glomerular tuft.	Active or inactive segmental or global lesions in > 50% of all glomeruli. The glomerular lesions are classified as global (G) when > 50% of the involved glomeruli have global lesions (upper panel), and as segmental (S) when > 50% of the involved glomeruli have segmental lesions (lower panel).	Global or segmental subepithelial immune deposits, usually with mesangial alterations. Class V LN may occur in combination with Class III or IV LN.

LN = Lupus Nephritis; IF = Immunofluorescence; EM = Electron Microscopy

Figure 3: This table displays renal biopsy findings consistent with the different classifications of lupus nephritis (Lager, 2011).

Implications and Conclusion

Understanding the pathophysiology of LN is paramount to early diagnosis and treatment. Following a diagnosis of LN associated end stage renal disease, patients and providers face a three-year mortality rate of roughly 27% (Gomez-Puerta et al, 2015). Given the autoimmunity and inflammation which contribute to renal damage, induction and maintenance therapies aim to immunosuppress and reduce inflammation. Cyclophosphamide, mycofenolate mofetil, and prednisone are commonly used medications for both induction and maintenance. The objective of induction, or initiation of therapy, is to quickly halt renal inflammation related to immune complexes in order to allow for tissue healing (Pons-Estel et al., 2011). This is accomplished through the use of potent immunosuppressants and corticosteroids over a course of three to six months. Complete remission occurs in a small number of patients, with the majority of LN patients relapsing. The goal of maintenance therapy is to limit relapses through continued use of drugs, all the while minimizing the toxicity, metabolic dysfunction, and other complications associated with such medications. While the most advantageous length of maintenance therapy time remains ambiguous, 12 – 36 month long courses have been studied (Parikh & Rovin, 2016).

It is of note to recognize the disproportionate number of non-white women of lower socioeconomic status diagnosed with LN. Furthermore, SLE related end stage renal disease is linked to lower socioeconomic status (B. Rovin, personal communication, July 12, 2016). This highlights the importance of patient education and health literacy. Discussions regarding disease progression and renal replacement associated with both non-compliance and treatment failure should be apart of education once a LN diagnosis is suspected. Additional considerations as identified by Rovin (personal communication, July 12, 2016) include:

- Management of hyperlipidemia and hyperglycemia, with goal low density lipoprotein (LDL) < 100 and goal hemoglobin A1c < 6.5
- Administration of angiotensin converting enzyme (ACE) inhibitors, and angiotensin II receptor blockers (ARBs) for those with glomerular disease and proteinuria > 3 months
- Use of prophylactic antibiotics for pneumocystis pneumonia (PCP) prevention in the immunocompromised patient
- Prophylactic proton pump inhibitor administration for ulcer prevention in those receive long term corticosteroid therapy
- Provision of appropriate medication education, including side effects and risks associated with use of immunosuppressants and corticosteroids
- The importance of the LN patient avoiding nephrotoxic substances such as non-steroidal anti-inflammatories and intravenous iodinated contrast dye
- Dietary modifications for renal protection, including the need to choose foods low in sodium, potassium, protein, and phosphorus
- Screening for malignancy and infection related to immunosuppression

Routine care of the SLE patient should be completed every three to six months, with urine studies completed at every office visit to assess for the presence of protein, blood cells, and casts. Serologic work up should include complete blood cell count, comprehensive metabolic screening, complement, immunoglobulin, and antiDNA antibody testing. Careful attention should be paid to the physical assessment as well. Aside from the obtainment of vital signs, visual inspection of the face and extremities for evidence of edema, and the skin for dermatologic signs of renal disease such as thickening and pigmentary alterations, thorough evaluation of respiratory status should also occur. Information gained from inquiries regarding urinary habits can be crucial for early diagnosis of LN. For patients with suspicion for LN, prompt renal biopsy should be completed to determine the extent of kidney involvement (Hahn, et al, 2012). If medication is indicated for LN, patients should be seen every two weeks for follow up. Anticipation of complications should guide the provider's use of prophylactic medications and utilization of multi-disciplinary team members such as dieticians, endocrinologists, hepatologists and hematologists.

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