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Pattern of Clinical Presentations in Immunocompromised Patient

Umezurike Hughes Okafor

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1. Introduction

Immunodeficiency (or immune deficiency) is a state in which the immune system's ability to fight infectious disease is compromised or entirely absent. Most cases of immunodeficiency are acquired (secondary) but some people are born with defects in their immune system (Primary) immunodeficiency.

The following conditions and diseases that are associated with primary immunodeficiency disorder include, Combined variable immunodeficiency disease, Ataxia-telangiectasia, Chediak-Higashi syndrome, Complement deficiencies, DiGeorge syndrome, Hypogammaglobulinemia, Job syndrome, Leukocyte adhesion defects, Bruton disease, Congenital agammaglobulinemia, Selective deficiency of IgA, Wiscott-Aldrich syndrome etc

As for acquired immunodeficiency, in 2006, UNAIDS and the World Health Organization estimated that approximately 39.5 million people were living with HIV. That year alone, there were 4.3 million new infections, with the majority occurring in sub-Saharan Africa. HIV targets T cells, and in particular, T helper cells, which are critical to fighting infections caused by fungi and parasites. This is why people with advanced, untreated AIDS develop unusual infections such as *Pneumocystis carinii* pneumonia and *Toxoplasmosis gondii*.

Since transplanted organs such as kidneys, hearts, livers, and lungs are foreign bodies, recipients' immune systems must be permanently suppressed to prevent them from attacking and destroying the organs. More than 19,000 transplants are performed in the United States each year. Each month, approximately 3,700 people are added to the U.S. national transplant waiting list, and each day, 77 people receive organ transplants. The breakthrough in transplant technology occurred in 1983 when cyclosporine, a powerful immunosuppressive drug, became licensed. However, even with cyclosporine, transplanted organs typically only last around 10 years before needing to be replaced. Research efforts to

induce bodies to tolerate transplanted organs without using immunosuppressive drugs are ongoing. But until a breakthrough in understanding immunologic tolerance or a way to grow replacement organs occurs, newly immunocompromised organ-transplant recipients will occur each year.

In addition, cancer chemotherapies typically cause immunosuppression. Since cancer cells are cells that multiply uncontrollably, the goal of cancer therapy is to kill them without killing too many normal cells. Unfortunately, the cells involved in immunity are frequently adversely affected by chemotherapy, thus rendering the patient vulnerable to infections.

Autoimmune disorders are typically treated with immunosuppressive drugs such as corticosteroids, 6-mercaptopurine, and azathioprine to keep the immune system from attacking the body. For example, Crohn's disease is an autoimmune disease in which the immune system attacks the body's gastrointestinal system, causing intense pain, bleeding, and obstructions. Another treatment is infliximab, which stops the body's inflammatory response. But these treatments only alleviate pain and suffering, they don't cure the underlying immune disorder.

Also splenectomy, diabetes mellitus, cancer, increasing age, chronic diseases and strenuous exercise had been associated with various degrees of impairment in immune functions

The immune System's primary function is to fight off infection. When the immune system is suppressed or dysfunctional the ability to combat infection is reduced. A person who has an immunodeficiency of any kind is said to be immunocompromised. These immunocompromised patients are more vulnerable to infections including infection with organisms that don't normally cause disease. In addition, they are more likely to develop severe and sometimes life-threatening illness following infection.

Many patients admitted into the Medical Unit especially Intensive Care Unit (ICU) have varying degrees of immunosuppression. In some, immunosuppression is easily apparent, especially when caused directly by underlying disease (such as haematological malignancy) or treatment (such as drugs used to prevent organ rejection or as a side effect of cancer chemotherapy). In others, immunosuppression is less apparent and is induced by the underlying disease, for example following traumatic injury or sepsis, or as a response to therapies provided during intensive care such as steroids.

Immunosuppression itself does not cause pathology but does leave the patient prone to infection and other disease conditions. There is no good clinical test to measure the degree of immunosuppression; the clinician must simply maintain a high index of suspicion. The consequences of immune suppression in most patients highlight the importance of infection prevention and control, as well as surveillance measures to ensure that appropriate treatment is implemented safely and quickly. Thus there is need to understand the pattern of clinical presentations of patients with immune dysfunction to avoid delay in making diagnosis and hence intervention.

Immunocompromised patients are prone to various infectious and non infectious disorders. The infectious disease is the commonest presentations of these patients because of the weakening of the patient's immune state. The severity of the infection depends on the degree of the immunosuppression. Some organs like respiratory pathways are more liable to infections in these patients for obvious anatomical reasons; however all organs are at risk of developing infection.

Also there are various non infectious manifestation in patients with immunosuppression. These may be directly or indirectly related to the degree of immune suppression in the patient. Patients have presented with various degrees of impaired kidney function, liver disease, cardiorespiratory dysfunction, psychosocial, dermatological and neurological disorders that are not directly related to infections.

Immunocompromised patients also can present with features not directly related to immunosuppression. For example obesity in patients on steroid therapy, and hepatic disease associated with severe combined immunodeficiency disease.

Clinical presentations in immunocompromised differs among patients. The presentations are determined by the severity of the immunosuppression, the severity of the infection and other comorbid condition. Furthermore the organ involved and the type of the associated clinical state play important role in determining the presentation of the patient. There are many uncommon presentations that have been reported in these patients. However poor response to treatment of infection, incomplete recovery from illness, certain types of infections and malignancies are common presentations seen in immunocompromised patients.

The clinical setting is extremely important in recognizing immunosuppression. Immune dysfunction induced by therapeutic intervention will be evident from the history, but immune impairment due to underlying disease may be more difficult to recognize. Inherited immune deficiencies often have characteristic patterns of disease distribution and may be associated with other clinical abnormalities (such as cardiac anomalies).

The various organs/systems in the body have differing impact by the resultant effect of immunosuppression. This results from either the direct impact of the immunosuppression or diseases resulting from the immunosuppression.

These manifestations will be discussed according to the impact on various systems and organs..

2. Gastrointestinal tract in immunocompromised

The primary function of the gastrointestinal tract is digestive, absorption and assimilation of nutrients. It has the largest surface area among all organs. With such large surface area and its close proximity to the external environment it necessitates that it evolved a large compliment of both innate and acquired immune mechanism. The gastrointestinal associated lymphoid tissue constitutes the largest immune compartment in the body. It is

estimated that the GIT contains about 60% of the total body lymphocyte. The immune cells in the GIT are organized into distinct anatomic and functional sub compartments..

The gastrointestinal tract associated lymphoid tissue, can be divided into three sectors. The first is represented by the pharyngeal tonsils, the appendix, and the large aggregates of nodules known as Peyer patches located at intervals throughout the small intestine. The second sector includes the lymphocytes and plasma cells that populate the basement membrane (lamina propria) of the small intestine, the area of loose connective tissue above the supporting tissue of the mucosal lining extending into the villi. The third sector comprises lymphocytes that lie between the epithelial cells in the mucosa. The interaction between these cells of the lymphatic system and the threatening agent is the basis of defense in the gastrointestinal tract. The gastrointestinal tract also possesses other protective measures which include tight epithelial junctions, the digestive enzymes, the acidic gastric fluid, the lysozyme and the high flow of the gastrointestinal fluid.

However the gastrointestinal tract is particularly at risk of infectious and non infectious injuries because of the following reasons – because of their close proximity to the external environment and continuous exposure to myriad of food and other infectious and non infectious antigens, the mucosa is maintained in physiologic inflammatory state characterized by presence of proinflammatory cytokines, marked expression of CCR5 and CXCR4 chemokine receptor that promotes HIV entry into the mucosa cells.

In immunocompromised patients the normal defenses are disrupted, leading to a wide range of clinical and pathogenic consequences. This usually leads to various disease conditions that can be classified into one of several general categories: infections, mucosal injury and ulceration, biliary tract diseases, diverticular disease, pancreatitis, and malignancy

The infections may be bacterial, viral, fungal, or parasitic and may infect one or more gut segments between the mouth and anus. The viral infections that had been reported in these patients include cytomegalovirus, herpes simplex, human papilloma virus, ebstein barr virus and rota virus. The bacterial infections include clostridium difficile, salmonella spp, shigella spp, *H. pylori*, eiserichia coli, campylobacter spp, *Yersinia enterocolitica*, mycobacterium tuberculosis, mycobacterium avium intracellulare complex. The parasitic infections include cryptosporidium, microsporidium, entamoeba histolytica, giardia lamblia, *Strongyloides stercoralis*. *The fungal infections include histoplasma capsulatum, candida albicans, candida tropicalis, mucormyces spp. The gastrointestinal infections have varying presentations but the commonest presentation is diarrhea.*

Mucosal injuries and ulceration of the gastrointestinal tract has been reported in patients with immunodeficiency. Many factors had been associated with ulcer formation and propagation in these patients. Some of these factors include stress, impairment of native cytoprotection of the gastrointestinal mucosa, drugs and infections especially helicobacter pylori. Complications that had resulted from gastrointestinal mucosa injury and ulceration include perforation, penetration, peritonitis and gastrointestinal bleeding.

Diverticular disease had been reported in immunocompromised patients especially in post transplant patients on immunosuppressive therapy. The clinical presentation varies from asymptomatic to peritonitis. Complicated diverticulitis which was reported in 1.1% of renal transplant patients can presents as intestinal perforation, abscess, phlegmon or fistula.

Acute pancreatitis in immunocompromised patients are not common. It has been associated with alcohol ingestion, billiary stones, malignancy, hepatitis B and cytomegalovirus infection. Acute pancreatitis markedly increase the morbidity and mortality associated with immunodeficiency. The clinical presentation is usually atypical.

There is increase in prevalence of both common and uncommon gastrointestinal malignancies in patients with immune deficiency. Decreased immune surveillance, continuous mucosa inflammation, gastrointestinal infections, ingestion of carcinogens including medications are some of the factors suspected to be responsible for the heightened prevalence of malignancy in these patients. Also cigarette smoking, sclerosing cholangitis, crohns syndrome and splenectomy had been reported as risk factor for the development of gastrointestinal malignancy in these patients. The gastrointestinal malignancies that have been associated with immunosuppression include Kaposi sarcoma, colorectal carcinoma, post transplant lymphoproliferative lymphoma, gastric mucosa associated lymphoma. The malignancies are initially asymptomatic however acute abdomen from perforation or obstruction and gastrointestinal bleeding are the usual though late presentations.

The commonly experienced gastrointestinal (digestive) complications; include oral lesions, esophageal lesions, diarrhea, and anorectal diseases (disease that affects the anus and/or rectum). The oral lesions are aphthous ulcer, oral thrush (candidiasis), oral wart, oral hairy leukoplakia, Kaposi sarcoma.

The oesophageal lesions include oesophageal candidiasis, oesophageal herpes simplex, cytomegalovirus, aphthous ulcer, malignancy, and reflux oesophagitis manifesting as dysphagia, odynophagia, and sensation of food sticking in the throat.

The anorectal lesions which are usually seen in immunocompromised patients with AIDS include herpes simplex infection, gonorrhoea, syphilis, anal wart(condylomata) and Chlamydia.

Diarhoea is a common clinical presentation in immunocompromised patients independent of the cause. This has been attributed to gastrointestinal infections, malabsorption, medications etc.

3. Hepato billiary system in immunocompromised

The hepatobilliary system is usually considered part of the digestive system however they have both digestive and non digestive functions. The liver acts as a detoxifier by processing potentially harmful agents into safe chemicals. It is also responsible for metabolism of glucose, fat and protein. It manufactures and controls the release of bile.

The bile plays an important role in breaking down of fats, the source of cellular energy. It is necessary for the absorption of many vitamins and other fat related substances. It also participates in the excretion of many product of metabolism including bilirubin, bile acid and medications.

The hepatobiliary system receives dual blood supply, from the portal and systemic circulation. Hence in immunocompromised patient the hepatobiliary system is exposed to many infectious and non infectious antigens. This predisposes the patient to many disease conditions relating/affecting the system.

Immunodeficiency states resulting from AIDS, cytotoxic chemotherapy, radiation, organ transplantation and common variable immunodeficiency disorders have been associated with hepatobiliary disease. These disorders that have been reported in immunocompromised patients include infectious hepatitis, granulomatous hepatitis, alcoholic liver disease, cholangiopathy, hepatocellular carcinoma, schistosomiasis, haemangioma and hepatic adenoma. Nodular regenerative hyperplasia of the liver has also been reported in patients with combined variable immunodeficiency syndrome.

There are various clinical manifestations relating to this system in these patients. In a study of patients with common variable immunodeficiency syndrome with nodular regenerative hyperplasia 39% of the patients were asymptomatic but had deranged liver functions, 46% had jaundice, 46% had hepatomegaly, 23% had pruritus, 15% had ascitis, 15% had oesophageal varices. Also jaundice and hepatomegaly is a common presentation in immunocompromised patients resulting from opportunistic and conventional infections of either hepatobiliary or other systems. Other manifestations include portal hypertension, cirrhosis, primary and secondary malignancies of the liver and biliary tree, and hepatic failure.

4. Respiratory system in immunocompromised

The immune system in the airways consists of both innate and specific immunity. Innate immunity consists of mechanical defenses, antimicrobial molecules generated in the airways, and phagocytic defenses provided by the resident alveolar macrophages and the polymorphonuclear leukocytes (PMNs) that are recruited into the lung in response to infection. The specific immunity are usually initiated by the dendritic cell that act as the antigen presenting cell. They migrate to the regional lymphoid tissue to initiate the primary response with generation of memory B and T cells.

This sophisticated immune defense system effectively protects the host from infections and other immunodeficiency related diseases of the respiratory tract. However this function is impaired in immunocompromised individuals thus exposing them to many diseases of the airways.

Patients with compromised immune function suffer from a wide variety of infectious and non infectious lung insults. Infections are the most common cause of both acute and chronic

lung diseases in immunocompromised patients however noninfectious diseases are not uncommon.

Pulmonary infections decisively contribute to morbidity and mortality in immunocompromised patients. The prevalence of both the common infections implicated in community acquired pneumonia and some uncommon infections including opportunistic infections are increased in immunocompromised patients. Among the infections encountered are streptococcus pneumoniae, klebsiella pneumonia, haemophilus influenza, pseudomonas aeruginosa, actinobacter spp, fusobacterium nucleatum, bacteroids melaninogenicus, bacteroids fragilis, mycobacterium tuberculi, mycobacterium avium intracellulare, pneumocystis carinii (jirovecii), norcadia spp, coccidomyces spp, aspergillus spp, *Rhodococcus equi* etc. The infections usually present as pneumonia, suppurative lung disease, interstitial lung disease and obstructive lung diseases

The spectrum of noninfectious lung injury and response in the immunosuppressed host includes interstitial edema, interstitial fibrosis, diffuse idiopathic pneumonia, acute respiratory distress syndrome, obliterative bronchiolitis, alveolar hemorrhage, pulmonary embolism, radiation pneumonitis, drug toxicity, progression or recurrence of neoplastic disorders, chemotherapy, transfusion and transplant related lung injuries. The clinical manifestations of various non infectious complications in immunocompromised patients are non specific and may mimic infections.

Clinical approach to respiratory tract diseases in immunocompromised patients are classified into five categories. The first situation is defined by a slow progression of the disease, the absence of fever (or mild fever), and diffuse opacities. Pulmonary oedema, pulmonary localisation of the underlying disease, or toxic treatment induced pneumonitis are usually the cause. Non-specific pneumonitis may also be responsible, particularly in bone marrow transplant recipients.

The second situation, defined by a rapid progression of the condition, fever, and diffuse opacities, usually indicates an opportunistic pneumonia but, in a few cases, a hypersensitivity drug induced pneumonitis (for example, to methotrexate) or a localisation of the underlying disease—for example, in cases of vasculitis or collagen vascular disease—may be the cause. In the absence of new extrapulmonary symptoms, *Pneumocystis carinii* must be considered. In contrast, the presence of new extrapulmonary symptoms or signs suggests an association or another opportunistic infection such as cytomegalovirus, cryptococcosis, toxoplasmosis, or tuberculosis.

In the third situation the clinical feature is that of bacterial pneumonia or sepsis with ARDS. The pathogens responsible are usually *Streptococcus pneumoniae* or *Haemophilus influenzae* and, to a lesser degree, *Legionella* spp.

The fourth situation with rapid to moderate progression of the condition, fever, nodules or round infiltrates evolving towards dissemination and/or cavitation is highly suggestive of fungal pneumonia. However, legionellosis, tuberculosis and even pulmonary infarction or specific localisation of vasculitis may also result in similar manifestations.

The last situation is certainly the most complex. The clinician is confronted with focal pulmonary infiltrates which do not respond to antibiotics. Opportunistic agents such as *Mycobacteria* spp, *Nocardia* spp, or *Rhodococcus equi*, organising pneumonia or tumour may be the cause.

5. Skin in immunocompromised

Skin, once thought to be an inert structure, plays a vital role in protecting the individual from the external environment. The epidermis impedes penetration of microbial organisms, chemical irritation, and toxins, absorbs and blocks solar and ionized radiation, and inhibits water loss.

The stratum corneum, the outermost layer of the epidermis that results from the terminal differentiation of the keratinocytes, forms the primary layer of protection from the external environment. This layer of anucleated keratinocytes is composed of highly cross-linked proteinaceous cellular envelopes with extracellular lipid lamellae consisting of ceramides, free fatty acids, and cholesterol. The free fatty acids create an acidic environment that inhibits colonization by certain bacteria such as *Staphylococcus aureus*, providing further protection.

Apart from the physical barriers the skin also contain other innate immunomodulating substances and cells. This include cathelicidins, cytokines, neuropeptides, eicosanoids, reactive oxygen species and langerhans cell which has phagocytic properties, and act as antigen presenting cell. The skin is consistently exposed to host of injuries because of their size and exposure to the environment. These coordinated protective barriers, cells and substances maintain the integrity of the skin.

In immunodeficiency state there is alteration in this innate immune state in the skin. This thus predisposes the skin to many injuries – infectious and non infectious. Dermatological manifestations are important healthcare concerns in patients with immunodeficiency state. About 25% of patients with immunodeficiency had been reported with dermatological injuries.

Subsequent invasion of the skin by various bacterial, viral, fungal, and parasitic agents spur infectious skin lesions, whereas non-infectious skin conditions mainly emerge from adverse drug reactions or certain inflammatory or malignant aetiologies. Thus microbial infections, inflammatory conditions, and neoplasms are the three main causes for the development of dermatological findings in immunocompromised patients.

There have been several reports detailing the high frequency of dermatological manifestations in HIV infected patients, 96% in India, 70% in Taiwan, 65.3% in France, 65.3% in Tanzania, 34% in Thailand, 32.6% in Iran. The dermatological manifestations in these patients may be as a result of primary dermatological infection, metastatic infection with primary in another organ or systemic infection.

There are many organisms that are associated with infection of or manifestations in the skin in patients with immunodeficiency. The infections could be as a result of conventional or opportunistic infection. These infections include viral, bacterial, fungal and parasitic. The organisms that have been associated with dermatological infections or manifestation in immunocompromised patients are herpes simplex virus, varicella zoster virus, cytomegalovirus and papilloma virus, staphylococcus spp, streptococcus spp, pseudomonas spp, atypical mycobacterium spp, the fungal infections including malassezia furfur, candidiasis, norcadia spp, Cryptococcus neoformans, Aspergillus species, Paecilomyces, Rhizopus species, Candida tropicalis, and scabies.

The commonly reported dermatological lesions in immunocompromised patients include dermatitis, seborrheic dermatitis, folliculitis, dermatophytes including pityriasis versicolor, wart, Kaposi sarcoma, herpes zoster, acne vulgaris, urticaria, pruritus, psoriasis, malasma and erythema multiforme. Other Skin lesions including pustules, gangrenous cellulitis, erythematous subcutaneous nodules, hemorrhagic bullae, petechiae, ecchymoses, and ecthyma gangrenosum had also been reported in immunocompromised patients.

Cutaneous manifestations often are accompanied by fever, defined as an isolated temperature of 38.3°C (101°F), that cannot be attributed to exogenous causes, such as blood products, or a temperature above 38°C (100.4°F) that persists for more than 1 hour.

6. Central nervous system in immunocompromised

Immune responses in the CNS are common, despite its perception as a site of immune privilege. These responses can be mediated by resident microglia and astrocytes, which are innate immune cells without direct counterparts in the periphery. Furthermore, CNS immune reactions often take place in virtual isolation from the innate/adaptive immune interplay that characterizes peripheral immunity. However, microglia and astrocytes also engage in significant cross-talk with CNS-infiltrating T cells and other components of the innate immune system.

Microglia are key players of the immune response in the central nervous system (CNS) and being the resident innate immune cells, they are responsible for the early control of infections and for the recruitment of cells of the adaptive immune system required for pathogen clearance. The innate and adaptive immune responses triggered by microglia include the release of proinflammatory mediators. Although an efficient immune response is required for the defense against invading pathogens, an inflammatory response in the CNS may also lead to tissue injury and neurodegeneration. Engagement of Toll-like receptors (TLRs), a major family of pattern recognition receptors that mediate innate immunity but also link with the adaptive immune response, provides an important mechanism by which microglia are able to sense both pathogen and host derived ligands within the CNS.

Patients with immunodeficiency are at risk of a wide range of neurologic diseases including infections, neoplasms, and drug-related complications of therapy

CNS infections caused by infective agents are rare in immunocompetent host, but more frequent in immunocompromised patients. The spectrum of causative organisms may vary greatly, depending on the underlying malignancy, its treatment and various other factors. Infections that had been reported to cause neurological diseases in immunocompromised patients are as detailed below;

Viral – herpes simplex virus, JC virus, cytomegalovirus, varicella zoster virus.

Bacterial – staphylococcus spp, pneumococcus, haemophilus spp, mycobacterium tuberculosis, mycobacterium Avium/ Intracellulare Complex, Listeria spp, norcadia spp.

fungal – *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Zygomycetes* (*Mucor and Rhizopus*), *Candida albicans*, *Coccidioides* spp

Parasitic - toxoplasmosis, strongyloides.

Development of neurologic manifestations depends on a variety of factors, including therapy with drugs like antiretroviral drugs and the patient's overall degree of immunosuppression. Heavily immunocompromised patients like those after allogeneic stem cell transplantation (SCT) or previous T cell depleting treatment regimens (e.g. with fludarabine or alemtuzumab) are at highest risk for cerebral infections. . The infections can cause global or focal cerebral dysfunction, subhemispheric impairment, spinal cord injury and occasionally, peripheral nerve injury.

Thus, in the immunosuppressed patient with neurological involvement there are three inter-related areas to consider. First, has whatever caused the immunosuppression either directly or indirectly affected the nervous system? Second, are such problems due to an infection of the nervous system? And last, are there any medical complications that might produce a neurological disturbance? In assessing immunosuppressed patients, the clinician must remember that more than one of these factors may be involved in the neurological presentation.

Clinical presentations in these patients may include headache, signs and symptoms of increased intracranial pressure, and lateralizing signs appropriate to the area(s) of involvement. These symptoms can include behavioral, cognitive, and personality changes. Focal symptoms include hemiparesis, aphasia, and visual field defects. Ataxia, seizures, and cranial nerve palsies can also occur but are not as common.

Meningoencephalitis is a common presentation however the classical symptoms and signs may be absent in these patients.. Also cerebral toxoplasmosis, cerebral lymphoma and cerebral vascular accident in immunocompromised patients may have similarities in their clinical presentations. The nature of neurological manifestation in patients with impaired immune state also varies with the cause and the degree of the immunosuppression. There is need for high index of suspicion to avoid delay or misdiagnosis that may lead to delay in intervention.

7. Musculoskeletal system in immunocompromised

The immune cells and mediators had been implicated in some musculoskeletal diseases. The bone marrow is the source of various haematological cells including the primordial immune

cells. The bone marrow also harbours matured and maturing immune cells. However the physiological activities of both innate and acquired immunity in the musculoskeletal system are poorly documented.

There is increased prevalence of musculoskeletal diseases especially infections in immunocompromised patients. Musculoskeletal syndromes that occur in HIV-infected patients include manifestations of drug toxicity, reactive arthritis, Reiter's syndrome, infectious arthritis, and myositis. Post transplant patients have developed myopathies and various bony and joint disorders. Myopathy and myositis have been reported in patients with diabetes mellitus and some primary immune deficiency disorders.

Some other musculoskeletal disorders in patients with immunodeficiency include some syndromes with arthritis or myositis as one of the components eg Reiters syndrome, Dermatomyositis, Sjogrens syndrome, Polyomyositis and Psoriasis.

The hallmark of the presentation is pain in the muscle, swelling of muscle, occasionally associated with fever and muscle atrophy. Arthralgia, swelling of the joint and when intervention is delayed distortion of the joint. Patient may develop cellulitis with or without abscess formation and osteomyelitis. There is need for prompt diagnosis and intervention as delay may lead to rapid spread of the infection in these patients.

8. Urogenital system in immunocompromised

The urogenital tract contain both cellular and non cellular innate immune components. This ensure the sterility of the urinary tract and part of the genital tract. In immunodeficiency state the urogenital tract are exposed to higher prevalence of both common and rare infections. The urogenital diseases that have been reported in immunocompromised patients include urinary tract infection, epididymitis, prostatitis, extensive condylomata of the urethra, renal abscess and other renal related diseases.

The occurrence of urinary tract infection and its clinical impact is determined, as with any infectious disease, by the interaction between the virulence of the infecting organism and the host defense mechanisms that can be mobilized. In the case of urinary tract infections, an anatomically and functionally intact kidney and urinary tract are the primary host defenses, with phagocytic function and immune mechanisms coming into play to limit the consequences of those infections.

Defects in the immune system determine the clinical manifestations and severity of urinary tract infections (UTI) and the rates of complication. However they only have an indirect role in influencing susceptibility to infection. Of all the categories of immunocompromised hosts, the renal transplant patient is the one most susceptible to the direct and indirect consequences of urinary tract infections. The rates of UTI in diabetics, renal transplant, recipients, neutropenic patients, and patients with AIDS are primarily determined by the degree and duration of urinary tract manipulation, and the higher perineal prevalence of potential pathogens that result from frequent hospitalization and antimicrobial use.

Urogenital tract infection has a different clinicoradiological presentation in immunocompromised patients, with predominance of systemic symptoms, multiple parenchymatous renal foci, and lower frequency of lesions of the collecting system. In the context of immunosuppression, Urogenital tract infection behaves as a severe bacterial infection, with bacteremia and visceral metastatic foci.

Many patients are asymptomatic. Symptoms that may occur include dysuria, urinary frequency and incontinence, flank pain, and fever. Confusion and delirium are often attributed to UTI, although without high fever or sepsis. Uncomplicated UTI is unlikely to cause serious central nervous dysfunction. The clinical signs and follow up of these infections were straight forward in half of the cases. However, in some patients, the infection is fulminant with progression to an abscess despite the use of antibiotics or is unusual because of the pathogens isolated.

Mycobacterial agents causing UTIs are less frequent in immunocompetent individuals; they are more common and severe in immunocompromised individuals. Extra pulmonary tuberculosis (EPTB) represents a progressively greater proportion of new cases and the genitourinary tract is the most common site of EPTB. The most common causative organism of kidney and urinary tract tuberculosis is the *Mycobacterium tuberculosis*, and occasionally *Mycobacterium bovis* can also be responsible. *Mycobacterium tuberculosis* (MTB) has an important impact on kidney transplant recipients, particularly during the first year after surgery. Tuberculosis of the urinary tract is easily overlooked. Symptoms that sometimes occur include back, flank and suprapubic pain, hematuria, frequency, and nocturia. These might also suggest conventional bacterial urinary tract infection. Symptoms such as fever, weight loss, and night sweats also are not unusual.

A variety of renal syndromes have been reported in patients with immunosuppression. These can be either acute or chronic kidney disease including electrolyte abnormalities. Renal impairment from opportunistic infections and drugs used in these patients has also been reported. A broad spectrum of renal diseases affecting glomerular, tubular and interstitial tissues had been documented in immunocompromised patients especially HIV infected patients. Most of the renal manifestations represent complications of concurrent infections in a severely immunocompromised host, or side effects of the plethora of treatments required to manage these patients. The renal related presentations except for hypertension and oedema are consistent with clinical presentations in renal disease in immunocompetent patients, however severity varies with the degree of immunosuppression. Hypertension and oedema were reported as not common in immunocompromised patients. The renal disease in these patients deteriorates faster without intervention thus the need for early diagnosis and prompt intervention.

9. Conclusion

Immunocompromised patients are predisposed to a variety of clinical syndromes. The manifestations depend on the cause of immunosuppression, the degree of

immunosuppression, the endemic infections, the system or organ with predominant injury, and other associated diseases like Malignancies and infiltrative diseases. It is noteworthy that these patients may have atypical presentations. Thus there is need for surveillance and high index of suspicion of injuries/diseases in these patients to ensure early diagnosis and intervention.

Author details

Umezurike Hughes Okafor

Enugu State University Teaching Hospital, Parklane, Enugu, Nigeria

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