AUTOIMMUNE DISORDERS IN THE ACUTE SETTING

Diagnosis and Treatment Goals

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Objectives

• Give an update on the causes for admission, clinical features, and outcomes of patients with ADs requiring acute care

• Review variables associated with mortality that could be possible prognostic factors.

• Describe the therapeutic strategies in the ICU to manage life-threatening conditions and manifestations common to all ADs
Autoimmune Disease Update

- **Autoimmune disease** – problems with the acquired immune system’s reactions

- Antibodies and immune cells target the body’s own healthy tissues by mistake.
Autoimmune Diseases

Brain
- Multiple Sclerosis
- Guillain-Barre Syndrome
- Autism

Thyroid
- Thyroiditis
- Hashimoto's Disease
- Graves' Disease

Blood
- Leukemia
- Lupus Erythematosus
- Hemolytic Dysglycemia

GI Tract
- Celiac's Disease
- Crohn's Disease
- Ulcerative Colitis
- Diabetes Type I

Muscles
- Muscular Dystrophy
- Fibromyalgia

Nerves
- Peripheral Neuropathy
- Diabetic Neuropathy

Lung
- Fibromyalgia
- Wegener's Granulomatosis

Skin
- Psoriasis
- Vitiligo
- Eczema
- Scleroderma

Bones
- Rheumatoid Arthritis
- Ankylosing Spondylitis
- Polymyalgia Rheumatica

>100 Autoimmune Diseases

we are 50 million
Autoimmune Disease Update

- Systemic manifestations of autoimmune diseases (ADs), can become so severe that they can cause life threatening illnesses.

- The majority have a rheumatologic AD and up to 25% of them require hospitalization.

- Of these, up to one third will require care and support in an intensive care unit. The reported in-ICU mortality of patients with ADs reaches as high as 55%.
Autoimmune Disease Update

- During the 1990s, the main AD causing ICU admission was RA with 36% of reported cases, followed by SLE accounting for 20% of the admissions.

- Since the year 2000, systemic lupus erythematosus (SLE) has replaced rheumatoid arthritis (RA) as the most frequent AD found in ICU.

- From year 2000 to 2010,
  - SLE (33.5%),
  - rheumatoid arthritis (25%),
  - systemic vasculitis (15%).
Systemic Lupus Erythematosus (SLE)

• Lupus is a chronic inflammatory, rheumatologic disease that occurs when your body's immune system attacks your own tissues and organs.

• Inflammation caused by lupus can affect many different body systems — including joints, skin, kidneys, blood cells, brain, heart and lungs.
SLE

• The most common signs and symptoms include:
  • Fatigue and fever
  • Joint pain, stiffness and swelling
  • Butterfly-shaped rash on the face that covers the cheeks and bridge of the nose
  • Skin lesions that appear or worsen with sun exposure (photosensitivity)
  • Fingers and toes that turn white or blue when exposed to cold or during stressful periods (Raynaud's phenomenon)
  • Shortness of breath
  • Chest pain
  • Dry eyes
  • Headaches, confusion and memory loss
Rheumatoid arthritis affects the lining of your joints, causing a painful swelling that can eventually result in bone erosion and joint deformity.

Signs and symptoms of rheumatoid arthritis may include:

- Tender, warm, swollen joints,
- Joint stiffness that is usually worse in the mornings and after inactivity,
- Fatigue, fever and weight loss
Rheumatoid Arthritis

• Rheumatoid arthritis is a chronic inflammatory autoimmune disorder that can affect more than just your joints.

• In some people, the condition also can damage a wide variety of body systems, including the skin, eyes, lungs, heart and blood vessels.
Systemic Vasculitis

- Inflammation of blood vessels which leads to tissue necrosis
- Blood vessels affected include arteries, veins, and capillaries
- Common (and nonspecific) complaints include fatigue, weakness, fever, arthralgias, abdominal pain, hypertension, renal insufficiency, and neurologic dysfunction.
Myasthenia Gravis

- The immune system produces antibodies that block or destroy many of your muscles' receptor sites for a neurotransmitter called acetylcholine.

- With fewer receptor sites available, muscles receive fewer nerve signals, resulting in weakness.
Myasthenia Gravis

- Symptoms can include:
  - Breathing difficulty
  - Blurry or double vision
  - Swallowing difficulty
  - Chewing problems
  - Weakness in arms and legs
  - Weakness in neck muscles

- **Myasthenic crisis** is a life-threatening condition that occurs when the muscles that control breathing become too weak, which can cause respiratory failure.
Guillain-Barre Syndrome

- Rapid-onset muscle weakness caused by immune system damaging the peripheral nervous system. The initial symptoms include numbness and weakness beginning in the feet/hands which often spreads to the arms and legs.

- The symptoms develop over hours to a few weeks.

- During the acute phase, the disorder can be life-threatening with about 15% developing respiratory failure.
Cause and Symptoms of Guillain-Barre

Guillain-Barré syndrome is caused by the destruction of myelin, known as demyelination. Symptoms include:

- Paralysis, including loss of breath
- Prickly, tingling sensations, in the arms and legs (paresthesias)
- Muscle weakness
- Loss of reflexes

Damage to the myelin sheath, which is a protective layer around nerves, results in communication issues between the brain and the rest of the body.
Autoimmune Disease Update

• In recent case series reports, ADs were diagnosed for the first time in the ICU in up to 42% of admitted patients.

• This increase in the rate of in-ICU diagnosis might be due to an increasing awareness of ADs in the ICU.
Autoimmune Disease Update

- Causes of ICU admission in case series reports published since the year 2000 were grouped into 10 categories.

- Respiratory involvement was the leading cause of admission to the ICU followed by infection and AD flare up with 51 (35.4%), 42 (29.2%) and 37 (25.7%) respectively out of a total of 144 admissions.

- The most frequent cause of ICU admission for SLE was infection (34%), followed by respiratory compromise (26%) and cardiovascular/hemodynamic involvement (19.8%)
Autoimmune Disease Update

- Systemic vasculitis, leading causes of admission were respiratory compromise (32.4%), followed by flare up of the disease (29.8%), and infection (23.4%).

- Mortality ranges for specific ADs:
  - SLE from 28% to 79%
  - Systemic vasculitis from 10% to 33%
  - Neuromuscular disorder from 5% to 27%.
Autoimmune Disease Update

- The variables most frequently reported that were associated with mortality were multi-organ dysfunction, cytopenia, and old age.
Autoimmune diseases in the intensive care unit. Case-report actualization.

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Autoimmune Disease Update

• In the case of infection, SLE patients are the most frequently affected, indicating that SLE patients might be more susceptible to infection than patients with other ADs due to the disease itself, the immunosuppressive treatment or both.

• Respiratory causes of admissions are significantly more prevalent in neuromuscular diseases.
Autoimmune Disease Update

• Patients with ADs are in a state of immunosuppression, which is due to both the disease itself and the treatment. This puts them at high risk for severe systemic infections and which ultimately may lead to death.

• Although in-ICU mortality can be as high as 79% when all reports on ADs are considered, it always tends to be higher if the cause for admission is infection compared to other reasons for admission.
Autoimmune Disease Update

• Measurement of procalcitonin levels is an approach which could be useful for differentiating between infection and exacerbation of the disease.

• Procalcitonin is the precursor of the hormone calcitonin and has emerged as a new parameter of inflammation.

• This acute phase hormokine seems to be more accurate for differentiating between bacterial infections and viral or non-infective causes of inflammation than other serological markers.
Comorbidities have also been shown to be more important than the severity of the disease itself in increasing the risk of long-term mortality.

Up to 92% of patients with an AD may have coexisting diseases, therefore, managing comorbidities is just as important as managing the condition that led the patient to the ICU.
Autoimmune Disease Update

- The majority of clinical manifestations that renders patients with ADs in the ICU are systemic.

- Even though ADs can result in many clinical features that lead patients to ICU admission, infection secondary to the immunosuppressive state of these patients remains the main cause of in-ICU mortality.
Clinical Management

• Therapeutic strategies for ADs are based in general on suppressive measures that down regulate an over-reactive immune system and control the clinical manifestations of this phenomenon.

• Among the classical drugs used to do such thing are steroids, disease-modifying drugs, and non-steroidal anti-inflammatory drugs.

• However, in the ICU there are often times when it becomes necessary to use other strategies if the patient is not responding to the usual treatment or if a more immediate response is needed in order to preserve the patient's life.
Clinical Management

- Since the 1970s, TPE techniques have become a well-known first-line or second-line therapy for multiple illnesses, either as a primary standalone treatment or in conjunction with other modalities of treatment.

- To date, a significant amount of evidence has been accumulated on its utility in ADs.
Therapeutic Plasma Exchange (TPE)

- TPE removes large-molecular-weight substances such as harmful antibodies from the plasma. Gets replaced with plasma from a donor or with a plasma substitute.
Clinical Management

- Side effects of TPE include fever, chills, urticaria, muscle cramps, or paresthesias; these reactions were encountered more frequently when plasma was used in the replacement fluid.

- Severe reactions are rare, but can include cardiac arrest, blood clots, respiratory arrests.
Clinical Management

- Besides TPE, other strategies have emerged in the field of autoimmunity in the ICU setting with the use of IVIg for the management of clinical manifestations of ADs being one of the most notable.

- The use of IVIg in the ICU is a therapeutic approach that has become more important over time in the management of systemic ADs, especially in cases of non-responsiveness to conventional immunosuppressive therapy.
IV Immunoglobulin (IVIg)

- Immunoglobulin is part of your blood’s plasma. It has antibodies in it to fight infections/disease. When people donate blood, this part can be separate out.

- Liquid immunoglobulin is taken from the blood plasma of donors who are screened to make sure they are healthy. The plasma is tested for serious infections like hepatitis and AIDS. The plasma is purified before it's used for IVIg therapy.
Clinical Management

- As of today, the United States Food and Drug Administration approved the use of IVIg in specific cases:
  - 1. treatment of primary immunodeficiency disorders associated with defects in humoral immunity
  - 2. prevention of bacterial infections in patients with hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell chronic lymphocytic leukemia
  - 3. Chronic immune thrombocytopenic purpura
  - 4. Immune-mediated thrombocytopenic purpura
  - 5. Kawasaki disease
  - 6. Chronic inflammatory demyelinating polyneuropathy
  - 7. Pediatric HIV-1
Clinical Management

• IVIg therapy is primarily used for off-label indications.

• Some of these include severe sepsis and septic shock, etc.

• Since their appearance, IVIg therapy has been used extensively for some systemic manifestations of ADs such as severe compromise of SLE.
IVIg for Guillain-Barre Treatment

• Since 1980, TPE has been the gold-standard for treatment. Nevertheless, the use of immunoglobulins in clinical practice to treat this syndrome has not resulted in any significant differences in patient outcomes.

• Therefore, IVIg is being used more frequently as an alternative therapy in place of TPE, especially in patients with GBS who are unable to undergo plasmapheresis.
IVIg for Myasthenia Gravis

- Myasthenic crisis
  - Increased pulse and respirations
  - Rise in BP
  - Anoxia
  - Cyanosis
  - Bowel and bladder incontinence
  - Absence of cough and swallowing reflex

- IVIg has been used in cases of crises that are resistant to treatment and have proven to be as effective as TPE.
IVIg for SLE treatment

- There are no randomized clinical trials that evaluate if IVIg are indicated in SLE patients.

- Nevertheless, there are case series and case reports that describe the successful use of IVIg in these patients, especially in cases of severe neurological compromise or in cases of infection concomitant with lupus flare-up.
What is the number one cause of death in patients with autoimmune diseases admitted to the ICU?

• A. Respiratory failure
• B. Cardiac arrest
• C. Infection
• D. Drug side effects
Conclusion

• ADs generate significant mortality according to one of the latest case series which showed an overall in-ICU mortality of up to 55%.

• The most frequent autoimmune diseases (ADs) found in an intensive care unit (ICU) in the last decade are systemic lupus erythematosus, rheumatoid arthritis and systemic vasculitis.

• Efforts should be concentrated mainly on preventing ICU admission of patients with ADs by an early diagnosis and treatment.

• Since infection is one of the most common causes of ICU admission for this group of patients, and one that markedly increased mortality rates, it should be promptly identified and treated in an aggressive and appropriate manner.
35th Annual Barrow Neuroscience Nursing Symposium:
Looking Back: Nursing Forward