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AUTOIMMUNE CONDITIONS PROTOCOL

PRELIMINARIES

a. Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease of unknown cause. The hallmark feature of this condition is persistent symmetric polyarthritis (synovitis) that affects the hands and feet, although any joint lined by a synovial membrane may be involved. CD4 T cells, mononuclear phagocytes, fibroblasts, osteoclasts, and neutrophils play major cellular roles in the pathophysiology of RA, while B lymphocytes produce autoantibodies (ie, rheumatoid factors).

Abnormal production of numerous cytokines, chemokines, and other inflammatory mediators has been demonstrated in patients with RA. Ultimately, inflammation and exuberant proliferation of synovium leads to destruction of various tissues, including cartilage, bone, tendons, ligaments, and blood vessels. Extra-articular involvement of organs such as the skin, heart, lungs, and eyes can be significant.

b. Treatment Options: The American College of Rheumatology developed recommendations and algorithms for the use of non-biologic and biologic DMARDs for patients with rheumatoid arthritis.

DMARDs can be classified into xenobiotic and biologic agents. These treatments represent the most important measure in the successful treatment of rheumatoid arthritis. These agents can delay or prevent disease progression and ultimately decrease destruction of joints and subsequent loss of function. The Xenobiotic DMARDs: Gold salts (aurothiomalate, auranofin), D-penicillamine.

Immunodulators: Immunomodulators are biologic agents which include Anakinra (IL-1 receptor antagonist [IL-1ra]), Abatacept (inhibitor of T-cell activation), Tocilizumab (IL-6 receptor inibitor)

Glucocorticoids are potent anti-inflammatory drugs and are commonly used in patients with RA to bridge the time until DMARDs are effective.

NSAIDs interfere with prostaglandin synthesis through inhibition of the enzyme cyclooxygenase (COX), thus reducing swelling and pain. NSAIDS do not delay joint destruction and, therefore, when used alone, are not sufficient to treat RA.

Surgery in patients with RA can relieve pain, correct deformities and improve joint function.

MONONUCLEAR LAYER CORD BLOOD PRODUCT TREATMENT OPTION :

Concentrated human stem cell product comprised of donated cord blood, that has been processed to remove excess plasma, red blood cells, vascular material and tissue solids leaving stem cells and other cellular components, which are then concentrated and banked through a validated process.

A. **Objective:** To provide the patient with a treatment that stimulates his / her immune system, promote cellular regeneration and improve symptoms associated with Rheumatoid Arthritis. The endovascular/intravenous Mononuclear Layer UCB product should serve to compliment the patient's current treatment regimen or to promote healing when current treatment is not responding.

B. **Patient management:**

- *Initial patient evaluation:* Reviews the medical information, lab work, and diagnostic imaging provided by the patient in order to determine the stage of the medical condition and any other secondary conditions.

- *Patient consultation:* Informed consent is obtained from all patients and medical records are updated, including patient's most recent physical exam, medication history, most up-to-date lab results and imaging studies to include:
  - X-rays of affected joints
  - Serum rheumatoid factor
  - Anti-cyclic citrullinated peptide antibody (Anti-CCP)
  - Erythrosedimentation rate (ESR)
  - C-reactive Protein (CRP)
  - Anti-RA33 assay
  - Antinuclear antibody assay (ANA)

- *Treatment Day*:
  - Premedication infusion protocol is started one hour before product application.
  - Benadryl 25mg IM, Zantac 200mg IV, Solumedrol 125mg IV. Single Dose.
  - Attach certificate of analysis to patient's chart.
  - Place the bottle in the palm of your hand until product is in a complete liquid form which can take about 3-5 min.
  - Swab the outside of the vial with alcohol, then remove the sterile cover and draw the contents into a syringe using aseptic technique.
  - Sample should be injected within 2 hours of thawing.
  - Product should not be mixed with any other biologic compound.

- Autoimmune conditions require a single dose of 2 million cells per kg of body weight administered via IV push.

c. Risks:

There are possibilities for unwanted effects related to the injection of stem cells. Even with the most established protocol, adequate technique, and careful administration; a medical team may encounter uncontrollable events. Although there is no guarantee of perfect results, excellent results can be attained. The risks of complications with the administration of cord blood products are very low. Possible risks include but are not limited to:

- Pain at site of injections
- Malaise
- Fever
- Allergic reaction

d. Outcomes :

Clinical response: Clinical response demonstrates a decrease in progression of disease and evidence of an improved repair process. In addition to physical examinations prior to stem cell graft and 6 months post-procedure, laboratory test results serve as evidence of repair process.

e. Follow Up Plan:

- Pre treatment: Clinical evaluation of RA symptoms, taking note of any changes in flare-up frequency. Review & record current laboratory results specific to RA.

- 3 months after implant: Clinical evaluation of RA symptoms, taking note of any changes in flare-up frequency. Review & record current laboratory results specific to RA.

- 6 months after implant: Clinical evaluation of RA symptoms, takingnote of any changes in flare-up frequency. Review & record currentlaboratory results specific to RA and X-ray report. Review of criteria from American College of Rheumatology.

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