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LRA by ELISA/ACT®

CLINICAL PEARLS UPDATE#36

Connective tissue syndromes

July 30, 2004

Dear Colleague,

Autoimmune conditions often occur together. This is particularly true in the immune aspect of the human surveillance system where **impaired dendritic cell function systemically, Connective tissue syndromes, periodic antioxidant deficits with intermittent free radical bursts, scleral status as a window on the body, and mineral status for nutritional and toxic metals form a clinically integrated way of managing these issues.** Mineral status can be checked using the d-penicillamine protocol. Repair deficits in distressed individuals may promote the concurrent autoimmunity and toxic mineral effects. The cumulative repair deficit is clinically often described as an inflammatory syndrome. Inflammatory markers increase. Examples are **hsCRP, mastocytosis, eosinophilic basic protein, fibrinogen, insulin and related growth factors, free cortisol, sed rate, and anti-collagen antibodies.** LRA by ELISA/ACT® tests and plans determine each individual's delayed allergic reactions or mystery hypersensitivities. Our LRA tests are **functional, ex vivo, and comprehensive assays.** Substitution for reactive items is blended into an alkaline way repair diet. Targeted supplementation aims to correct antioxidant deficits and enhance detoxification ability. Healing actions engage the mind and body in an integrated direction. Go by results. Several retest cycles will be routinely needed in complex cases. The sequential improvement in health quotient speaks clearly about how effective are LRA by ELISA/ACT interpretation plans in integrating health fundamentals.

We encourage you to share this valuable clinical update newsletter with your colleagues and staff so they can learn more about how our comprehensive approach can be applied to their practice with beneficial results. Please also let us know if any of your colleagues or staff would like to be added to our email distribution list. We are grateful for the opportunities to be of service to you and your patients.

Sincerely,

Russ Jaffe, MD, Ph.D., CCN, NACB
Lab Director

Watson PG, Young RD. Scleral structure, organization and disease. A review. *Exp Eye Res* 2004;78(3):609-623.

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Although disease of the sclera is unusual, when it occurs it can rapidly destroy both the eye and vision. However, normally the sclera provides an opaque protective coat for the intraocular tissues and a stable support during variations in internal pressure and eye movements, which would otherwise perturb the visual process through distortion of the retina and the lens/iris diaphragm. This stability, which is vital for clear vision is made possible by the organisation and viscoelastic properties of scleral connective tissue. Microscopically, the sclera displays distinct concentric layers including, from outside, Tenon's capsule, episclera, the scleral stroma proper and lamina fusca, melding into underlying choroid. Two sites exhibit specialised structure and function: the perilimbal trabecular meshwork, through which aqueous filters into Schlemm's canal, and the lamina cribrosa, which permits axons of the optic nerve to exit the posterior sclera. Throughout, sclera is densely collagenous, the stroma consisting of fibrils with various diameters combining into either interlacing fibre bundles or defined lamellae in outer zones. Scleral fibrils are heterotypic structures made of collagen types I and III, with small amounts of types V and VI also present. Scleral elastic fibres are especially abundant in lamina fusca and trabecular meshwork. The interfibrillar matrix is occupied by small leucine-rich proteoglycans, decorin and biglycan, containing dermatan and dermatan/chondroitin sulphate glycosaminoglycans, together with the large proteoglycan, aggrecan, which also carries keratan sulphate sidechains. Decorin is closely associated with the collagen fibrils at specific binding sites\ situated close to the C-terminus of the collagen molecules. Proteoglycans influence hydration, solute diffusion and fluid movement through the sclera, both from the uvea and via the trabecular meshwork. As the sclera is avascular, nutrients come from the choroid and vascular plexi in Tenon's capsule and episclera, where there is an artery to artery anastomosis in which blood oscillates, rather than flows rapidly. This predisposes to the development of vasculitis causing a spectrum of inflammatory conditions of varying intensity which, in the most severe form, necrotising scleritis, may destroy all of the structural and cellular components of the sclera. Scleral cells become fibroblastic and the stroma is infiltrated with inflammatory cells dominated by macrophages and T-lymphocytes. This process resembles, and may be concurrent with, systemic disease affecting other connective tissues, particularly the synovial joints in rheumatoid arthritis. Current views support an autoimmune aetiology for scleritis. Whilst the role of immune complexes and the nature of initial pro-inflammatory antigen(s) remain unknown, the latter may reside in scleral tissue components which are released or modified by viral infection, injury or surgical trauma.

Saif MW, Hopkins JL, Gore SD. Autoimmune phenomena in patients with myelodysplastic syndromes and chronic myelomonocytic leukemia. *Leuk Lymphoma* 2002 Nov;43(11):2083-92.

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Autoimmune paraneoplastic syndromes are commonly encountered in patients with myelodysplastic syndromes (MDS). A review of case reports and small series suggest as many as 10% of MDS patients may experience various autoimmune syndromes. Clinical manifestations of such phenomena may include an acute systemic vasculitic syndrome, skin vasculitis, fever, arthritis, pulmonary infiltrates, peripheral polyneuropathy, inflammatory bowel disease, glomerulonephritis, and even classical connective tissue disorders, such as relapsing polychondritis. On the other hand, asymptomatic immunologic abnormalities have also been reported in these patients. These autoimmune manifestations frequently respond to immunosuppressive agents including steroids and occasional hematologic responses to steroid therapy have also been reported.

We report five patients with history of MDS who manifested different spectrums of autoimmune phenomena including: pyoderma gangrenosum (PG), vasculitis, Coombs negative hemolytic anemia, idiopathic thrombocytopenia, and chronic inflammatory demyelinating polyneuropathy (CIDP). We also review the incidence, nature, course and response to therapy of these manifestations and discuss potential pathogenic mechanisms.