DRUG RELATED LUPUS

Drug Induced Lupus and Its Causes

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This article describes drug-related lupus (DRL) and explains how it is differentiated from systemic lupus erythematosus (SLE).

What is Drug Related Lupus?

Drug-related lupus (DRL) is an autoimmune disease variant with symptoms similar to those of systemic lupus erythematosus (SLE). However, in drug-related or drug-induced lupus, the syndrome resolves quickly (within a few days) after the offending drug is withdrawn. Usually, the medication has been used for many months to many years before it triggers DRL although rarely DRL can develop shortly after starting a new drug. DRL affects men and women equally, whereas 80 percent of patients with SLE are women. Because the medications most likely to cause DRL are used in conditions that primarily affect men older than 50 years, DRL is sometimes reported to occur most often in this population.

Signs and Symptoms

Usually, symptoms in DRL develop and anti-nuclear antibodies (ANA) develop around the same time. After the causative drug is stopped, symptoms resolve quickly and the ANA titer slowly begins to fall. Because the positive ANA in DRL can persist for months after the medication is stopped, it can be difficult to distinguish DRL from SLE without more specific blood tests.

Symptoms in DRL are usually characterized by arthralgia and may closely resemble those seen in SLE. Multiple organ systems can be affected in both disorders. Symptoms that occur in both disorders include: muscle and joint pain and swelling; flu-like symptoms such as fatigue and fever; serositis (inflammation around the lungs or heart that causes pain or discomfort); skin rash, Raynaud's phenomenon, and positive ANA test results. Although kidney involvement is rarely seen in DRL, the rate of glomerulonephritis in hydralazine-induced DRL is 5-10 percent.

Raynaud phenomenon is seen in about 25 percent of patients with DRL compared to about 50 percent of patients with SLE. Cutaneous (skin) changes are seen in about 25 percent of patients with DRL compared to more than 75 percent of patients with SLE. Patients with DRL typically develop symptoms of arthritis and usually do not develop kidney or central nervous system impairment. Symptoms do not recur after the offending drug is withdrawn, and people with DRL do not have a higher risk for developing systemic lupus erythematosus than other people.
Diagnosis

DRL is diagnosed in patients with one or more symptoms of SLE such as arthralgia and swollen lymph glands who have positive ANA titers and no symptoms before starting the suspected drug. Patients with DRL rarely have antibodies to double-stranded (ds) DNA, whereas in SLE, antibodies to ds-DNA are common. Both patients with drug-related lupus and patients with SLE typically have anti-histone antibodies and single-stranded (ss) DNA antibodies. Complement levels are typically normal in DRL, whereas in SLE complement levels are low.

Causes

People known to metabolize drugs slowly (slow acetylators) have a higher risk for DRL. Slow acetylators are seen in about 50 percent of whites and blacks. All drugs associated with DRL have metabolites that are subjected to oxidative metabolism. The same drugs suspected of triggering DRL after long-term use are suspected of causing flares of disease activity after short-term use in people with SLE.

Certain drugs are definitely known to cause DRL, and other drugs are suspected of possibly being a cause. Some drugs are considered to have an unlikely or very low association with DRL.

Although as many as 100 drugs have been reported to cause DRL, most cases are caused by the following 4 drugs: procainamide (Pronestyl), hydralazine (Apresoline), minocycline, and quinidine (Quinaglute). With these 4 drugs, the risk of developing DRL after 2 years of drug use is 5-20 percent. With the other drugs reported to cause DRL, the risk is less than 1 percent.

Drugs with a definite association to DRL include: chlorpromazine (Thorazine), hydralazine, isoniazid (used for tuberculosis), minocycline, methyldopa, and the heart medications procainamide and quinidine.

Drugs reported to have a possible association with DRL include: the beta-blockers propranolol, metoprolol, and atenolol; captopril; the anticonvulsants carbamazepine (Tegretol), primidone (Mysoline), ethosuximide (Zarontin), valproic acid (Depakene, Depakote), trimethadione (Tridone), and phenytoin (Dilantin); hydralazines; interleukins; interferons; levodopa, tumor necrosis factor (TNF), tiotropium bromide inhaler, ophthalmic timolol, lithium; the anti-thyroid drugs methimazole and propylthiouracil (PTU); the chelating agent penicillamine; the antibiotics nitrofurantoin, sulfasalazine, and sulphonamides.

Drugs reported to have an unlikely or very low association with DRL include: allopurinol (used for gout), chlorthalidone and hydrochlorothiazide (diuretics), gold salts, griseofulvin, methylsergide, oral contraceptives, lovastatin, minoxidil, perphenazine, penicillin, phenylbutazone, reserpine, streptomycin, and tetracyclines.
Drugs that cause flares of systemic lupus erythematosus after periods as short as several hours include: hydralazine, sulfonamides, penicillin, P-aminobenzoic acid (PABA), hydrochlorothiazide, cimetidine, phenylbutazone, and mesantoin.

**Treatment**

Besides stopping the offending drug, non-steroidal anti-inflammatory drugs (NSAIDs) may be used to help symptoms resolve faster. In patients with severe symptoms of DRL, corticosteroids may be used to help reduce inflammation.

**Resources:**

David Lamont, Systemic Lupus Erythematosus, eMedicine, Jan 17, 2006.


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