Renal Causes of Elevated Sedimentation Rate in Suspected Temporal Arteritis

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The erythrocyte sedimentation rate (ESR) is a frequently used but nonspecific indicator of inflammation or infection. Clinicians often check an ESR in patients with symptoms of headache, facial or jaw pain, and visual loss, as an aid in the diagnosis of temporal arteritis. We present two patients with these complaints, who did not have temporal arteritis, nor any other inflammatory condition or infection, but had ESRs near or above 100 mm/h, leading to diagnostic confusion. An occult nephrotic syndrome, with or without renal insufficiency, can cause such a highly elevated ESR, and was discovered in these patients.

Key Words: Sedimentation rate—Temporal arteritis.

CASE REPORTS

Patient 1

A 62-year-old woman was hospitalized for acute throat pain and dyspnea, presumably from angina. She had a 2-hour episode of bifrontal headache, similar to prior headaches, but now followed by an several minute episode of transient left monocular blindness. There were no arthralgias, jaw claudication, rash, or febrile illnesses. She was a diabetic with retinopathy and renal insufficiency, and had a left inferior frontal cerebral infarction 5 months ago. There was a history of coronary artery disease with myocardial infarction and ventricular tachycardia, amputation of the left leg due to ischemia 2 years previously, and hyperlipidemia.

Visual fields were normal, with an acuity of 20/200 OS, 20/100 OD, reactive pupils without a relative afferent pupillary defect (RAPD), and normal optic discs with small retinal hemorrhages and microaneurysms. The rest of the cranial nerves were normal and her temporal arteries were not tender. There was a mild right hemiparesis with diminished sensation in the distal foot, and generalized hyporeflexia. Minimal pedal edema was found.

The erythrocyte sedimentation rate (Westergren) was 114 mm/h, having been 139 mm/h 3 months ago. Pertinent laboratory results included hemoglobin, 10.2 g/dl; BUN, 17 mg/dl; serum creatinine, 2.2 mg/dl; serum albumin, 2.1 g/dl; and 3 to 4+ protein on random urine samples. Fasting blood glucose were 95 and 220 mg/dl. A creatinine clearance of 8 ml/min, and significant proteinuria, 4.83 g over 24 hours, was later demonstrated.

A left temporal artery biopsy was performed to exclude temporal arteritis as the cause of her temporary blindness, and was normal. She had no further neurological symptoms, and her headaches subsequently resolved, but she died 1 year later from septicemia.

Patient 2

A 54-year-old woman had a 2-year history of "stabbing" right-sided headaches and was hospitalized for a severe one. Pain involved the right temple, cheek, and jaw, lasting hours to days, and was worsened by chewing or touching the right face. There were no arthralgias, rash, or febrile illnesses. She was hypertensive, and had diabetes mellitus with retinopathy.

The right temple was diffusely tender, with normal jaw motion. Her funduscopic examination demonstrated a proliferative diabetic retinopathy with fibrous proliferation along the arcades OD and bilateral peripheral laser photocoagulation.

Neovascularization of both discs was also seen. Her pupils were 3 mm bilaterally with a normal reaction to light and no RAPD. Visual acuity was 20/400 OD, 20/50 OS. The remainder of her cranial nerves were normal, including facial and corneal sensation. No peripheral edema was evident.
The erythrocyte sedimentation rate was 82–90 mm/h (Westergren), with normal ANA and DNA titers as well as rheumatoid factor. The hemoglobin was 11.1 g/dl, with BUN, 12 mg/dl; serum creatinine, 1.3 mg/dl; serum albumin, 3.1 g/dl; and 3+ protein on urinalysis. Fasting blood glucose were 180 and 281 mg/dl. Later, a creatinine clearance of 94 mL/min with an increased 24-hour urinary protein of 8.42 g was demonstrated.

A right temporal artery biopsy was performed and was normal. Her headaches ceased after 2 weeks of indomethacin, 25 mg t.i.d. Renal function remained stable.

**DISCUSSION**

The ESR reflects red blood cell (RBC) aggregation, and is the measured fall or settling of a vertical column of erythrocytes within 1 hour when held vibration-free and at room temperature. For uncertain reasons it does increase slightly with age, but in patients over the age of 50 the suggested upper limits of normal are 30 mm/h in women and 20 mm/h in men (1).

Usually electrostatic forces cause RBCs to repel each other and inhibit their aggregation. However, increased amounts of plasma fibrinogen or globulins coat the RBCs, fostering their aggregation, and hasten their settling in a glass tube. Thus fibrinogen and globulins as the “acute phase reactants” of inflammatory and infectious states may be responsible for the elevated ESR detected in these cases. Such a mechanism is proposed in the case of polymyalgia rheumatica and temporal arteritis, and an elevated ESR is one of the major clinical criteria which support the diagnosis. In our patients it was this elevation of the ESR, their age, and the complaints of headache and visual symptoms that prompted a tentative diagnosis of temporal arteritis and led to temporal artery biopsy. In each of our cases the biopsy was negative, and subsequent follow-up, without steroid use, did not support this initial clinical diagnosis. While, earlier studies have also suggested that there is an increased incidence of neoplasm in polymyalgia rheumatica. However, epidemiologic data now suggest that, although individuals with malignancy and polymyalgia rheumatica share similar complaints (musculoskeletal pain, malaise, elevated ESR), there is no evidence of an increased rate of malignancy in individuals with polymyalgia rheumatica (2). Despite this assumed relationship, there was no evidence of malignancy discovered on follow-up of our cases, and hence occult neoplasm was not a cause of their elevated ESRs.

Diabetics, without evidence of inflammatory or infectious disease, may also have mildly elevated ESRs. A group of 34 such diabetics were found to have a mean ESR of 32 mm/h, significantly greater than their control group’s mean ESR of 9 mm/h (3). Concentrations of serum proteins, such as fibrinogen and globulins, were no different between these two groups. This moderate ESR elevation was instead attributed to the increased glycosylated hemoglobin (HbA1c) in the diabetics, which facilitates the sedimentation of RBCs (3). Since both of our patients were diabetic, this may partly account for their ESR elevations, but is unlikely to be the primary explanation.

We believe that renal disease, and particularly the nephrotic syndrome, was the cause of the strikingly elevated ESRs in our patients. Both had proteinuria in the nephrotic range, over 3.5 g in 24 hours, but lacked findings of nephritis, such as gross hematuria or urinary RBC casts (4). The creatinine clearance, while decreased in patient 1, was normal in patient 2, which can occur early in the nephrotic syndrome. In 2 studies of patients with stable, chronic renal failure, but no other complicating disease, average ESRs of 56 and 69 mm/h were found (5,6). Markedly elevated ESRs were not uncommon, with ESRs over 60 mm/h in 57% and over 100 mm/h in 20% of one uremic group (6). While most uremic patients are anemic, which itself can raise the ESR since effective RBC repulsion is decreased, the zeta sedimentation ratio, which is independent of hematocrit, was also significantly elevated. This implies that another factor in uremic plasma, most likely fibrinogen or certain globulins, accounts for these elevated ESRs (5). However, the effect of proteinuria itself on ESR elevation in renal disease has not been thoroughly studied. ESR elevation appears unrelated to the etiology of renal failure, duration or type of dialysis, and level of serum creatinine or BUN (6). High ESRs were not due to chronic inflammation in diseased kidneys, since there was no significant difference between nephrectomized patients and those with their own kidneys (7). In a Singapore study of patients with very elevated ESRs of 100 mm/h or more, 5.6% was attributed to the nephrotic syndrome and 4.7% to uremia of various causes (8). Despite this finding, infections (44.2%), connective tissue diseases (24.2%), and neoplasm (11%) remain the most common causes for these markedly elevated ESRs. Therefore, we wonder whether an accelerated, compensatory overproduction of fibrinogen and globulin proteins in nephrotic patients creates these highly elevated ESRs.

Renal failure, or the nephrotic syndrome with or
without renal failure, can result in markedly elevated ESRs, in the absence of infection or inflammation. While there may be few or no clinical clues of renal disease, the discovery of an unexplained 3+ or 4+ proteinuria on a random urinalysis appears to be a helpful screening test. Especially in patients where there is a low clinical suspicion of temporal arteritis, yet a markedly elevated ESR without explanation, renal dysfunction and proteinuria should be excluded prior to urgent steroid therapy and temporal artery biopsy. This possibility should be considered in the clinical evaluation of all patients with suspected temporal arteritis.

REFERENCES