# Autoimmune Dysfunction and Subsequent Renal Insufficiency in a Collegiate Female Athlete: A Case Report

# James E. Leone, PhD, ATC, CSCS\*D, CHES\*; Amie Kern, MS, ATC†; Joshua D. Williamson, MS, ATC, CSCS‡; Robert M. Colandreo, DPT, ATC, CSCS\*

\*Department of Movement Arts, Health Promotion, and Leisure Studies, Bridgewater State University, MA; †University of Colorado at Colorado Springs; ‡Washington and Lee University, Lexington, VA. Ms Kern is now at Lake Forest College, IL.

**Objective:** To present the case of a female collegiate basketball player who was diagnosed with Wegener granulomatosis of the eyes and immunoglobulin A (IgA) nephropathy.

**Background:** A 19-year-old female collegiate basketball player presented to a rheumatologist, urologist, and nephrologist with severe eye pain and was diagnosed with Wegener granulomatosis and IgA nephropathy. At age 20, during routine follow-up testing, urine protein levels were found to be 3 times normal values (0–8 mg/dL), prompting the need for a kidney biopsy, which showed IgA nephropathy, another autoimmune disorder.

**Differential Diagnosis:** Sinus infection, scleritis, lymphomatoid granulomatosis, Churg-Strauss syndrome, lupus erythematosus, general granulomatosis.

**Treatment:** Initial assessment revealed signs and symptoms, particularly in the patient's eyes, consistent with a sinus infection and scleritis. Her corneas were examined by a specialist, who prescribed various medications, including prednisone, for the relief of symptoms. When the dosage of prednisone was reduced, symptoms returned. Further tests revealed the presence of anti-neutrophil cytoplasmic antibody, a protein associated with Wegener granulomatosis, which helped confirm the diagnosis. The following year, a routine urinalysis showed abnormal levels of protein in her urine. A kidney biopsy

revealed that IgA nephropathy also was present. At the time of this case report, the athlete continues to be monitored by an ophthalmologist who specializes in Wegener granulomatosis, a rheumatologist, and a nephrologist.

**Uniqueness:** This athlete presented with 2 rare autoimmune disorders at an early stage of life. The medications used to treat the disorders left the athlete fatigued on a daily basis. Additionally, she was placed on 3 immunosuppressant drugs, which increased her risk for further health complications, yet she was able to successfully compete in athletics at the collegiate level. No family history of renal disease or other autoimmune disorders was discovered, further adding to the complexity and uniqueness of this case.

**Conclusions:** Autoimmune disorders, such as Wegener granulomatosis, can present with a variety of common signs and symptoms. As athletic trainers, we encounter a host of unusual signs and symptoms; however, in cases such as this, further investigation into the cause of the chief complaints can go a long way toward restoring or managing an athlete's health. Excellent communication among the sports medicine team helped this athlete manage her potentially life-threatening condition while allowing her to remain active in her sport.

Key Words: Wegener granulomatosis, nephropathy, prednisone, immunosuppressants, autoimmune disorders

omplications from autoimmune disorders can greatly affect a patient's daily activity, including sport participation, and may require treatment with various medications that place additional strain on the body and leave the patient susceptible to other illnesses.<sup>1</sup> Autoimmune disorders can present during many stages of life. Some autoimmune disorders, such as diabetes mellitus type I and celiac disease, are more common and recognizable in high school and collegiate populations. Others are rare and more difficult to recognize and diagnose. Wegener granulomatosis is one of these disorders. Classified as an illness associated with antibodymediated injury, it most often affects the lungs, respiratory tract, kidneys, sinus and nasal passages, blood vessels, and eves.<sup>2–4</sup> Approximately 90% of patients who present with symptoms have sinus or lung (or both) involvement. Most patients with this disorder also develop renal failure.<sup>3,5,6</sup> Although rare, eye symptoms can include pain, pressure,

vision loss, and protrusion of the globe from the orbit<sup>5</sup>; these symptoms indicate the presence of Wegener granulomatosis.

Typically, Wegener granulomatosis affects people in their 40s and 50s, although approximately 15% of cases are seen in people younger than 20 years of age. The mean age of diagnosis is 55 years.<sup>5,6</sup> Wegener granulomatosis can occur in both sexes but is most commonly seen in males.<sup>3</sup> In many patients, 2 types of antibodies have been identified. This means that Wegener granulomatosis could be genetically linked, but studies<sup>3</sup> have been inconclusive.

What makes Wegener granulomatosis a devastating disorder is that the signs and symptoms may not be true indicators of disease severity; progression to the deadly form may occur over years<sup>2</sup> and may include pulmonary hemorrhages and fibrosis of the lungs or kidneys (or both), which can cause blockages and leave the organs function-ally insufficient.<sup>3,6</sup> Treatments are aggressive, often requir-

ing the use of corticosteroids, such as prednisone, and chemotherapy drugs (cyclophosphamides) to fight the various antibodies attacking the patient's cells.<sup>1–3,5</sup> The first stage of treatment attempts to control the disease and put it into a stage of remission. The second stage focuses on controlling the remission, which calls for progressing from one type of medication to another in various dosages to prevent complications and relapse.<sup>2,4,6</sup> If left untreated, the disease may be fatal.<sup>7</sup> However, treatment is generally successful, and the prognosis is positive, with more than 75% of patients going into complete remission. Moreover, survival rates have increased to greater than 20 years after diagnosis for younger patients, although in older patients, the average survival rate is lower.<sup>2,4,5</sup> Survival rates in elderly people are generally only a few years.<sup>2,4,5</sup>

Another autoimmune disorder, immunoglobulin A (IgA) nephropathy, is the result of abnormal accumulation of the IgA protein in the kidneys, causing renal blockages and damage and ultimately leading to renal insufficiency. Also known as Berger disease, IgA nephropathy is the most common form of glomerulonephritis in the world.<sup>3,8,9</sup> Glomerulonephritis is the inflammation of tissues (glomeruli) that filter blood in the kidney.8 This disease is more common in males, with higher incidence rates in Japan, Australia, and southern Europe and lower rates throughout North America and the United Kingdom.3,8 Because of strong familial patterns, current research<sup>10</sup> points to environmental or genetic factors as causes of the mutations that result in IgA nephropathy. A link also seems to exist between IgA nephropathy and hypertension in families, making the latter a potential predisposing factor.<sup>11</sup>

As is the case with Wegener granulomatosis, the diagnosis of IgA nephropathy is difficult, because it is often accompanied by few signs and symptoms. Renal failure from IgA often occurs in combination with vascular deterioration, which may result from Wegener granulomatosis.<sup>3</sup> The main sign is hematuria, but sometimes the amount of hematuria may be so negligible that it only can be detected by advanced testing procedures. Thus, early detection and identification can be a challenge. Another discrete sign is excess protein in the urine, which indicates that the kidneys are not properly filtering waste products.<sup>5</sup> As the kidneys begin to fail, the patient may develop referred pain in the back below the ribs, an increased need to urinate, fatigue, nausea, swelling of the hands and feet, and increased blood pressure.3,8,12 A total of 20% to 40% of those with a definitive diagnosis develop endstage renal failure.<sup>6,13</sup> If the disease is suspected, the patient needs to undergo a kidney biopsy to search for the presence of IgA deposits.12

Treatment involves immunosuppressant medications, which help the patient feel better but do not preserve renal function.<sup>3</sup> Other medications, such as diuretics, are used to regulate blood pressure and to try to protect the kidneys by using hormones and steroids to reduce the immune response. Medications may be added or changed post-diagnosis.<sup>1,9</sup> Some researchers<sup>13–15</sup> have examined the efficacy of fish oils and increased vitamin E intake to help control symptoms of IgA nephropathy, especially in the early stages or with unconfirmed test results. Cardiovascular complications are more common in patients who are smokers or who have hypertension. Wegener granulomatosis and IgA neuropathy should be treated independently.<sup>15</sup>

# CASE REPORT

A 19-year-old female collegiate basketball player presented to the athletic trainer with complaints of ocular pain, redness, and irritation in mid-December of her freshman year (Table). Initially, she treated her symptoms with an over-the-counter anti-inflammatory medication (ibuprofen) in an attempt to resolve her symptoms. A month after the self-treatment, her eyes remained bloodshot and the pain persisted. The patient was referred by her athletic trainer to the emergency department, where she was diagnosed with a sinus infection and referred to an ophthalmologist. After seeing various doctors without diagnosis or resolution of symptoms, she was placed on Tobradex (Alcon Inc, Hunenberg, Switzerland), a corticosteroid in ocular form, by her ophthalmologist. Her eyes began to improve, and she was able to complete the basketball season without incidence. However, within weeks of completing the season, she reported to the athletic training department with a return of her symptoms at a more intense and persistent level. At this point, she was referred to another physician, who referred her to a cornea specialist, who diagnosed her with scleritis. After consulting 2 other eye specialists, she was placed on prednisone (dosage unknown) and found immediate relief of all signs and symptoms.<sup>1</sup>

After successful treatment with prednisone, the patient's dosage was decreased. Shortly thereafter, symptoms of intense ocular pain and a bloodshot appearance of the sclera returned; she also complained of headaches. Her physician ordered blood tests, which were positive for antineutrophil cytoplasmic antibodies, commonly associated with various immunologic disorders.<sup>1,5</sup> The physicians suspected Wegener granulomatosis and referred her to a rheumatologist. He concurred with the diagnosis and prescribed Imuran (dosage unknown; Prometheus Laboratories Inc, San Diego, CA), a chemotherapeutic drug that is used as an immunosuppressent.<sup>1,4</sup> The patient remained on this medication regimen for approximately 9 months.

Symptoms attenuated, and the patient continued regular follow-up visits with her cornea specialist and rheumatologist. Routine tests in September 2006 showed that more than 3 g of protein was detected in her urine. Again, Wegener granulomatosis was suspected, and she was referred to a nephrologist, who ordered a kidney biopsy. The biopsy was positive for IgA nephropathy. She was placed on Lisinopril (dosage unknown; Lupin Pharmaceuticals, Inc, Baltimore, MD), which is commonly prescribed to treat hypertension and congestive heart failure. Because of the side effects of the medications, wound healing at the biopsy site was prolonged, and she was medically restricted from participation in basketball for more than 2 weeks. Once medically cleared, she was able to complete the basketball season without further complication. With close communication among her physicians and athletic trainer, she successfully began decreasing her prednisone dosage. She continued follow-up visits with the cornea specialist and nephrologist, who took over her testing and medical care. She discontinued care with her rheumatologist for personal reasons.

In June 2007, the patient developed conjunctivitis and had a relapse of symptoms but was able to continue activity. Upon returning to school in September 2007, she consulted the cornea specialist and was informed that her

#### Table. Athlete's Medical Timeline

Date	Age, y	Signs and Symptoms	Treatment and Medications	Comments
Mid-December 2005	19	<ul><li>Ocular pain</li><li>Acute iritis</li></ul>	Ibuprofen	
January 2006	19	<ul><li>Persistent eye pain</li><li>Ocular pressure</li><li>Bloodshot eyes</li></ul>	<ul> <li>Emergency room visit</li> <li>Diagnosed with sinus infection</li> <li>Referred to ophthalmologist</li> <li>Prescribed Tobradex<sup>a</sup></li> </ul>	Symptoms resolved with medication
March–April 2006	19	<ul> <li>Increasing eye pain and sensitivity</li> </ul>	Referred to cornea specialist	
April 2006	19	Intense eye pain	<ul><li>Diagnosed with scleritis</li><li>Prescribed prednisone</li></ul>	Symptoms nearly resolved
August 2006	20	<ul> <li>Persistent eye pain</li> <li>Headaches</li> <li>Acute iritis reappeared after prednisone dose decreased</li> </ul>	<ul> <li>Physicians began to suspect Wegener granulomatosis</li> <li>Sent for blood panel</li> <li>Referred to rheumatologist</li> </ul>	
September 2006	20	<ul><li>Eye pain</li><li>Iritis</li></ul>	<ul> <li>Began Imuran<sup>b</sup></li> <li>Blood panel showed increase in ANCA levels</li> <li>Referred to nephrologist</li> <li>Obtained kidney biopsy</li> <li>Prescribed Lisinopril<sup>c</sup></li> </ul>	Blood tests confirmed presence of Wegener granulomatosis Symptoms stabilized and eventually resolved IgA nephropathy suspected and confirmed
June 2007	21	<ul> <li>Contracted conjunctivitis</li> <li>Experienced relapse of Wegener symptoms</li> </ul>	Continued medications     (Tobradex, Imuran, Lisinopril)	Symptoms attenuated after medication dose adjustment Lisinopril added to help address IgA nephropathy
September 2007	21	Deteriorating vision	<ul> <li>Consulted cornea/retina specialist</li> <li>Prednisone increased</li> <li>Methotrexate replaced Imuran</li> </ul>	Methotrexate added to protect kidney function
October 2007	21	<ul> <li>Developed unrelated staphylococcal infection</li> </ul>	Continued on methotrexate	Lost 3 wk of competition because of slow healing rate
December 2007	21	Eye issues resurfaced	Prednisone injected into right eye	
Late-December 2007	21	<ul> <li>Developed foot pain (fifth metatarsal)</li> </ul>	<ul> <li>Referred to orthopaedist for foot pain</li> <li>Radiographs, bone density tests conducted</li> <li>Bone scan indicated stress reaction</li> <li>Prescribed orthotics, supportive modalities, rehabilitation</li> </ul>	
January–April 2008	21	None	<ul> <li>Continues to do well</li> <li>Follows up regularly with ophthalmologist, rheumatologist, nephrologist</li> </ul>	Wegener granulomatosis, kidney function stabilized

Abbreviations: ANCA, anti-neutrophil cytoplasmic antibody; IgA, immunoglobulin A.

<sup>a</sup> Alcon, Inc, Hunenberg, Switzerland.

<sup>b</sup> Prometheus Laboratories, Inc, San Diego, CA.

<sup>c</sup> Lupin Pharmaceuticals, Inc, Baltimore, MD.

vision had decreased markedly since the previous spring. She was then referred to a retinal specialist, who found that both the retina and optic nerve were swollen and increased her prednisone to 20 mg from the progressively reduced dosage. Her dosage of prednisone was increased significantly, and she was referred to a rheumatologist who specialized in Wegener disease. The rheumatologist determined that she needed a lower dosage of prednisone and discontinued the Imuran because he believed it was ineffective at this stage. He prescribed methotrexate (dosage unknown), which is similar in function to Imuran and prednisone but helps to protect kidney function.<sup>1,4</sup>

After starting methotrexate, she again developed inflammation in her right eye, which required an intraocular injection of prednisone in December 2007.

The following month, while taking 3 drugs (Tobradex, Lisinopril, and methotrexate), the athlete developed a staphylococcal infection (unrelated to her conditions) that required surgical intervention. Again, as with the kidney biopsy, the immunosuppressant drugs hindered healing, and she was unable to return to play for approximately 3 weeks. Upon return to play after the injection and surgery, she dealt with extreme fatigue and developed foot pain in the fifth metatarsal. The athletic trainer referred her to the team orthopaedic physician because of concern that taking such high doses of prednisone while participating in basketball could lead to bone deterioration. The orthopaedic physician ordered radiographs and a bone scan and prescribed orthotics to help reduce stress on the foot. The radiographs were negative; the bone scan showed an uptake in contrast, indicating a stress reaction. However, the physician did not recommend discontinuing participation in basketball. The patient's treatment plan, which was coordinated by her athletic trainer, included ice-cup massage and orthotic therapy for the rest of the season to reduce symptoms. Arch taping was used to relieve pressure on the foot until the orthotics were delivered.

At the time of this case report, the patient's treatment has remained consistent and successful. The coordination of care by the athletic trainer and the close communication among the various physicians and the athletic trainer have kept all parties well informed and have maintained effective lines of communication. Her physicians continue to work to reduce medication levels and to maintain normal levels of protein in her urine as well as normal kidney function. She resumed care with a rheumatologist every 6 weeks and was able to consistently reduce her prednisone dosage. She continues follow-up visits with her ophthalmologist every 2 months and with her nephrologist every 4 months. The eye pain, fatigue, and general symptoms have, for the most part, resolved. Minor relapses of all of her aforementioned physical ailments, such as eye pain, fatigue, and others, have been controlled with medication. She has been able to fully participate in all training activities.

## CONCLUSIONS

Although Wegener granulomatosis and IgA nephropathy have been independently documented in collegiate athletes, we are unaware of any documented cases of the conditions occurring simultaneously in otherwise healthy elite National Collegiate Athletic Association Division I collegiate athletes. Although they share the similar characteristics of autoimmune disorders affecting the kidneys, with the potential for renal failure, Wegener granulomatosis and IgA nephropathy are not commonly seen together. This athlete originally presented with signs and symptoms that could be identified as a sinus infection but instead resulted in a life-altering diagnosis of 2 autoimmune disorders, which, if not recognized and managed early, could have required a kidney transplant or led to death.<sup>1,3,12</sup> With its trademark vague signs and symptoms consistent with other medical conditions, as well as signs and symptoms that do not appear clinically for years, Wegener granulomatosis poses a particular challenge for the athletic trainer and the sports medicine team.<sup>2,5</sup> As previously mentioned, the elderly can be particularly adversely affected because they may not be able to tolerate the dosages of medications used to treat this disorder. Age may have been a relative advantage for this athlete, as is evident based on her success thus far in her sport performance. Although the cause of Wegener granulomatosis remains uncertain, both genetic mutations and environmental factors, such as exposures to heavy metals (eg, mercury, lead), silica, and aromatic hydrocarbons,

possibly through contaminated water sources, may contribute to the development of this disorder.<sup>5,11</sup>

Autoimmune disorders, such as Wegener granulomatosis, can present with a variety of common signs and symptoms. Athletic trainers may encounter a host of unusual signs and symptoms in their athletes; however, in cases such as this, further investigation into the chief complaint(s) can go a long way to restoring or managing an athlete's health. In younger patients with Wegener granulomatosis, the prognosis is usually positive, yet complications such as vision loss and kidney dysfunction can arise unexpectedly. Thus, regular monitoring is very important. Our patient was a well-conditioned athlete, so exercise may have moderated her recovery, although this factor has not been examined in younger, physically active athletes.<sup>1–4</sup>

Athletic trainers are often the first professionals to assess these types of conditions, however common or rare. Being aware of the diverse presentation of various autoimmune diseases and disorders is an essential skill for any athletic trainer and will help facilitate optimal care for patients. Even though the combined occurrence of Wegener granulomatosis and IgA nephropathy is relatively uncommon in younger athletic populations, this case documents the possibility of encountering less well-known autoimmune issues in athletes. Athletic trainers have the professional responsibility to stay abreast of all types of issues that may afflict their athletes and patients. Lastly, excellent communication among and utilization of the sports medicine team helped this athlete manage her potentially life-threatening situation while at the same time allowing her to remain active in her sport. Challenging our paradigm of skills and training with new and unique cases will allow for better clinical diagnosis, management, and follow-up care for those we serve.

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Address correspondence to James E. Leone, PhD, ATC, CSCS\*D, CHES, Department of Movement Arts, Health Promotion, and Leisure Studies, Bridgewater State University, Bridgewater, MA 02325. Address e-mail to jleoneatc@yahoo.com or james.leone@bridgew.edu.