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Systematic Condition in a NCAA-I Collegiate Soccer Player

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**SYSTEMATIC CONDITION IN A NCAA-I
COLLEGIATE SOCCER PLAYER**

A case study submitted to
the Graduate College of
Marshall University

In partial fulfillment of
the requirements for the degree of
Master of Science
in
Athletic Training

by
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Approved by
Dr. Suzanne Konz
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May 2014

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ABSTRACT

Objective: The purpose of this case study is to inform athletic trainers of a systematic disease not common in our patient population. **Background:** The athlete, a twenty-one YO, 160 lb, 69 inch female NCAA-I collegiate soccer goalie presented with complaint of bilateral elbow and knee joint pain and stiffness along with tender red itchy bumps on the anterior aspect of her shins. The athlete had flu-like symptoms and a URI prior to this complaint. The athlete has a history of anemia, mononucleosis, and streptococcal. **Differential Diagnosis:** Rheumatoid arthritis, lymphoma, HIV/aids, erythema nodosum, lupus, Lyme disease. **Treatment:** The athlete sought out multiple medical evaluations to treat the condition; including the ER. Multiple tests were run to rule out strep among other things. The athlete received various prescriptions to treat fatigue, infection, inflammation, and pain. **Uniqueness:** Erythema nodosum is a rare disorder that affects approximately 1-5 per 100,000 people per year. Typically seen in the female 25-40 year old population, the cause is usually idiopathic; however, the most common cause is streptococcal pharyngitis.¹⁻⁶ **Conclusion:** This case demonstrates the awareness of a systematic condition that could be present within the athletic population. With this information, clinicians can better diagnose and treat erythema nodosum along with awareness of etiologies causing the condition. **Key Words:** Erythema nodosum

CHAPTER 1

INTRODUCTION

Erythema nodosum (EN) is a common type of septal panniculitis that occurs when the hypodermal septa becomes inflamed with neutrophils.¹ Due to a reactive process the septa in subcutaneous fat filters with inflammatory cells and produces reactive oxygen causing localized edema.¹⁻⁶ This hypersensitive response can be caused by varying antigens, but in 1/3 of all cases is reported as idiopathic.^{7,8} Most commonly seen in females, in 83% of cases, during their twenties to forties, EN presents as round red tender nodules bilaterally on the anterior tibia.³ Nodules generally resolve within 4-6 weeks after onset without signs of scarring, atrophy, or ulceration.^{7,8}

Association with infections, drugs, chronic inflammatory diseases, malignancy, and a number of disease processes can cause the sudden acute onset of EN.^{3,6-8} Patients may present with fever, chills, malaise, arthralgia, and arthritis in conjunction with anterior tibia nodules.^{4,6,9} Diagnostic testing can consist of a complete blood count (CBC), erythrocyte sedimentation rate (ESR), throat culture, chest x-ray, tuberculin test, antistreptolysin O (ASO), serum immunoglobulins, and biopsy.^{3,6,7,9-11}

If the cause of outbreak is known, treatment is to remove the underlying trigger. However, in other cases, the use of non-steroidal anti-inflammatories (NSAIDs), potassium iodide (KI), colchicine, corticosteroids, and rest will help alleviate symptoms.^{3,6-9} Recurrences occur more commonly if the etiology is unknown and are estimated in 33-41% of cases.³

CHAPTER 2

CASE REVIEW

A 21 YO female NCAA-I collegiate soccer goalie presented with complaint of bilateral elbow and knee joint pain and stiffness along with tender red itchy bumps on the anterior aspect of her shins that did not follow a dermatome pattern (Figure 1). The previous week, she complained of flu-like symptoms that resolved within three days but did not see a physician for symptoms. The current symptoms began approximately three to four days from the onset of joint pain and swelling. She presented in the athletic training room walking with locked knees and was unable to actively flex her elbows past 90 degrees due to pain; however, passively she had full range of motion with mild pain at the end points. A family history of lipoma and breast cancer exists. Athlete also has a history of anemia diagnosed in 2009, mononucleosis diagnosed in 2009, and multiple diagnosis of streptococcal between 2006 and 2008 that occurred once a year; she is not on any prescription drugs or oral contraceptives at this time.

The athlete was referred to her family physician for evaluation the day she presented to the athletic training room. A complete blood count (CBC), metabolic panel, erythrocyte sedimentation rate (ESR), and antistreptolysin O (ASO) test performed did not show abnormalities. She was prescribed 200 mg of Celebrex for pain and arthralgia taken once daily for six days and told the symptoms should resolve in 24-48 hours. HIV/aids were ruled out at this time due to lack of risky history, Lyme disease because of the rash appearance, and lymphoma due to normal WBC count. Two days later, the athlete was treated at the emergency room due to worsening symptoms. She admitted symptoms related to an upper respiratory infection (URI) two weeks prior to the flu-like symptoms but denied continuing symptoms. She did not see a physician for any of these symptoms she experienced. Athlete reported stiffness and decreased

range of motion in both knees and elbows. No signs of joint erythema, warmth, or swelling were noted at the ER.

An ECG, urine culture, ASO test, and another CBC/ESR were ordered. The ECG showed normal clear lungs and normal heart size, cloudiness of urine, and a negative strep test was concluded. The CBC showed low hemoglobin and her ESR was high (Table 1). She was diagnosed with erythema nodosum, prescribed 800 mg ibuprofen TID PRN for pain and follow up with her primary physician in one week. At the follow-up, the athlete's labs revealed a trace of ketone and increased ESR. The blood culture, urine culture, ANA, rheumatoid arthritis factor, and strep tests were all within normal limits. Negative RAF ruled out rheumatoid arthritis and normal ANA tests suggested she did not have lupus.

Test	Norms		First Visit (2-4-13)	ER Visit (2-6-13)	Follow-Up (2-11-13)
CBC	WBC	4.5 - 10 x10E3/uL	6.7	6.2	-
	RBC	3.7 - 5.2 x10E6/uL	4.38	4.08	-
	Hg	12 - 16 g/dL	12.4	11.9	-
	Hct	35 - 47 %	36.60%	35.30%	-
Metabolic Panel	Glucose	65 - 99 mg/dL	85	92	-
	Albumin	3.5 - 5.5 g/dL	4.1	4.2	-
	Globulin	1.5 - 4.5 g/dL	3	3.2	-
ESR	0 - 32 mm/hr		9	36	53
ASO	Negative		Negative	Negative	Negative
Urinalysis	Clarity	Clear	-	Cloudy	Clear
	Color	Yellow	-	Dark Yellow	Yellow
	Specific Gravity	1.005 - 1.030	-	1.032	1.025
	pH	4.5 - 8	-	6.5	6
	Occult Blood	Negative	-	Negative	Negative
	Glucose	Negative	-	Negative	Negative
	Ketones	Negative	-	Trace	Trace
	Protein	40 - 80	-	30	Negative
Leukocytes	Negative	-	Moderate	Negative	
ECG	Heart Size	WNL	-	WNL	-
	Lungs	Clear	-	Clear	-
	Spine Curvature	WNL	-	Scoliosis	-
RAF	.0 - 13.9		-	-	11.5
ANA	Negative		-	-	Negative

Table 1. Diagnostic Testing

Despite medications prescribed, the athlete's pain continued to worsen and she was unable to walk without pain. Swelling appeared around her knees and elbows; however, she no longer has range of motion limitations. Her family physician diagnosed her with erythema nodosum and pyrexia; she was prescribed 500 mg of penicillin QID for ten days and 10 mg of prednisone for 30 days to treat infection and inflammation. Diagnosis of pyrexia could be caused by the amount of inflammation she presented with and as a side effect of EN. Although the diagnosis did not change, her treatment plan was altered due to worsening symptoms and no alleviation of pain. At the fourteen-day follow-up after diagnosis, the athlete complained of fatigue and joint stiffness; however, the lesions disappeared and left mild scarring (Figure 2). Lastly, she was prescribed vitamin D for fatigue and advised to follow-up as needed.



Figure 1. Lesions of bilateral anterior tibia two days after formation



Figure 2. Resolution of lesions two weeks after diagnosis

Since recovering from diagnosis, athlete has no signs or symptoms of further illnesses. A follow-up appointment was not needed due to alleviation of symptoms. Lesions resolved two

weeks and arthralgia persisted for two months after diagnosis. She was back to feeling normal ten weeks after diagnosis but chose not to return to activity such as leisure running and intermural soccer until four months after diagnosis (Table 2).

Timeline	Events
1/21/2013	Experienced flu-like and URI symptoms - did not seek medical attention
2/1/2013	Joint pain and swelling
2/4/2013	Noticed tender red itchy bumps on bilateral anterior shins with symptoms of bilateral knee and elbow arthralgia, presented to the ATR and referred to family physician - CBC, metabolic panel, ESR, and ASO WNL. Prescribed 200 mg Celebrex; ruled out lymphoma, HIV/aids, and Lyme disease.
2/6/2013	ER visit due to worsening symptoms - urinalysis, ASO, CBC, ESR, and ECG ordered. Low hemoglobin showed in CBC, high ESR, and all other tests WNL. Prescribed 800 mg ibuprofen.
2/11/2013	Follow-up with PCP - urinalysis showed trace of ketones, elevated ESR, and negative RAF, blood culture, ANA, and ASO. Prescribed 500 mg Penicillin and 10mg Prednisone; ruled out RA and Lupus.
2/25/2013	Follow-up with PCP - complaints of fatigue and joint stiffness, lesions resolved leaving mild scarring. Prescribed Vitamin D, follow-up as needed.
4/1/2013	Arthralgia symptoms resolved
4/15/2013	Began feeling "normal"
5/27/2013	Returned to activity

Table 2. Timeline of Events

CHAPTER 3

DIFFERENTIAL DIAGNOSIS

The following is a list of the possible diagnosis and their key symptoms (Refer to Table 3):

Rheumatoid Arthritis¹²

- Joint Pain/Stiffness/Inflammation
- Decreased Range of Motion
- Fever
- Tenderness
- Rash
- Fatigue
- Loss of Appetite
- Pain Over Several Joints – Symmetrical Pattern

Rheumatoid arthritis was ruled out to do a negative rheumatoid factor and ANA.

Lymphoma¹³

- Fever
- Night Chills
- Weight Loss
- Rash/Itching
- Chest/Lower Back Pain

Lymphoma was ruled out due to lack of symptoms that coincided with the illness.

HIV/aids¹⁴

- Fatigue
- Fever

- Sore Throat
- Swollen Glands
- Headache
- Muscle/Joint Aches and Pains
- Red or Brown Blotches Under Skin

HIV/aids were ruled out due to lack of risky history such as blood transfusion and sexual behavior.

Erythema nodosum^{4,6,9}

- Malaise
- Flu-like Symptoms
- Joint Pain
- Red Tender Bumps on Anterior Tibia (Bilateral)

Erythema nodosum was diagnosis due to symptoms; especially that of the bilateral anterior shin lesions.

Lupus¹⁵

- Extreme Fatigue
- Headache
- Fever
- Photosensitivity
- Painful/Swollen Joints
- Abnormal Blood Clotting
- Anemia
- Pleurisy

Lupus was ruled out after a negative ANA test as well as symptoms did not correspond with athlete's complaints.

Lyme disease¹⁶ (Figure 3)

- Flu-like Symptoms
- Joint Pain
- Fatigue
- Rash (“Bulls-eye” Appearance)

Lyme disease ruled out because athlete does not live in an area of high risk, no history of tick bite, and her rash does not have the “bulls-eye” appearance.



Figure 3. Lyme disease “Bulls-eye” rash.¹⁶

	Joint Pain	Decreased ROM	Inflammation	Fever	Rash/Lesions	Flu-like Symptoms	Anemia
Rheumatoid Arthritis	X	X	X	X	X	X	
Lymphoma				X	X	X	
HIV/Aids	X			X	X		
Erythema Nodosum	X		X	X	X	X	
Lupus	X			X			X
Lyme Disease	X				X	X	

Table 3. Differential Diagnosis

CHAPTER 4

DISCUSSION

Based on the individual's previous history of an upper respiratory infection and flu-like symptoms prior to being diagnosed with EN, these are assumed to be the underlying trigger. However, due to worsening of symptoms after the athlete was prescribed penicillin, the drug could also be a possible cause. The athlete states her lesions resolved within two weeks and symptoms within six weeks of diagnosis. The condition typically resolves on its own in 3-6 weeks. Patients are treated symptomatically with NSAIDs, rest, and elevation.^{3,7} She was able to discontinue the prednisone after the first dose. She does not report complications after being asymptomatic nor has EN recurred.

The athlete's symptoms were concurrent with those associated with erythema nodosum including flu-like symptoms, fatigue, arthralgia, and nodules on bilateral anterior tibia. An extensive history of streptococcal and recent URI along with her demographics predisposed her to an occurrence of EN. Streptococcal and upper respiratory infections can account for 28-44% of EN cases with a female to male ratio of 4-5:1 in all cases.³

Several diagnostic tests such as CBC, ANA, urinalysis, and ESR should be performed to help rule out other possible diagnosis and/or causes of EN (Table 3). A CBC test is a generalized test of a patient's health status that can be used to diagnose varying conditions and diseases such as anemia, infection, leukemia, bone marrow disorders, and lymphoma, to name a few. White blood cells (WBC), red blood cells (RBC), and platelets are evaluated in a blood sample. Any elevation or depression of data outside the norm is considered a red flag.¹⁷ Antinuclear antibodies (ANA) test was performed under the suspicion of inflammation that may be due to an autoimmune illness such as Raynaud's phenomenon, rheumatoid arthritis, and lupus. ANAs can

inhibit the body to attack itself mistaking normal proteins as dangerous.¹⁸ More commonly used to screen for lupus, if ANAs are present this may suggest a diagnosis of the disease.¹⁹ Physical features as well as contents of a urinalysis can be evaluated for diagnosis of infection or inflammation of the kidneys. The specimen shows levels of pH, glucose, ketones, protein, nitrite, WBC, RBC, bacteria, and concentration. Abnormalities suggested an infection, dehydration, hematuria (red blood in urine), liver disease, or breakdown of muscle.²⁰ ESR is evaluated with a blood sample that will indirectly measure the amount of inflammation in the body. This test, if abnormal, can diagnose some illnesses such as: anemia, lymphoma, lupus, rheumatoid arthritis, kidney disease, pregnancy, and thyroid disease. However, other testing is advised for abnormal findings.²¹

If symptoms do not resolve in 4-6 weeks, other testing may be performed to further diagnose the cause of EN. Tests should be conducted to rule out sarcoidosis, tuberculosis, Behcet's disease, Leprosy, several types of STIs, and other systematic diseases that may lead to EN. Other causes can be excluded after collecting a biopsy of the infected area; however, a biopsy is not commonly performed unless the lesions do not regress.^{3,6,7,9-11} In this case a further testing was not performed because symptoms were alleviated. The etiology of EN is ruled uncertain in 37-60% of cases despite medical testing and labs.⁷

In 15-40% of all cases, EN presents as an early sign of infection, connective tissue disease and/or inflammatory disorder.⁶ Of these cases, patients typically present with an elevated ESR and C-reactive protein levels seen by CBC testing.^{3,6} The athlete in this case study did not report development of these conditions after diagnosis of EN; however, she presented with an elevated ESR that increased from her ER visit to the fourteen-day follow-up. An elevated ESR and cloudiness of urine sample shows presence of inflammation in the body.^{20,21} Labs may show

leukocytosis by a WBC count generally greater than 10,000 per mm.³ Leukocytosis can be present due to an increase in neutrophil count, lymphocyte count, eosinophilic granulocyte count, basophilic granulocyte count, or immature cells.²² In this case, the athlete's WBC count was below 10,000 per mm, therefore she did not present with leukocytosis.

Patients may also have a higher percentage of reactive oxygen intermediates (ROIs) that are produced by activated neutrophils in peripheral blood. ROIs contribute to the activity of phagocytes, regulation of signal transduction and gene expression, and the oxidative damage to the nucleic acids; proteins; and lipids.²³ ROIs utilize effects of the oxidate and create tissue damage and inflammation. Inflammation is proposed to collect in the anterior shins due to the combination of arterial supply and gravitational effects of the venous system.⁷ This distinguishing location on the shins makes for diagnosis of EN.⁴

The incident rate of EN is 1-5 cases /100,000 per year.^{2,4,5} Diagnosis can be caused by infections such as streptococcal, sarcoidosis, autoimmune disorders, irritable bowel disease, or medications such as oral contraceptives. In some cases, such as sarcoidosis (disease of unknown cause leading to inflammation of organs); the presence of EN shows for an improved prognosis.⁵ Most cases in the United States are diagnosed during the first half of the year when streptococcal is at its highest incident rate.⁷

Erythema nodosum is a form of panniculitis, an inflammation of the subcutaneous fat layer.³⁻⁶ EN can be caused by hypersensitivity to antigens such as beta-haemolytic streptococcal.⁵ Lesions form on the anterior shin and are typically 1-5 cm in diameter. The lesions begin to flatten as the bumps resolve and heal in a bruise-like appearance.^{3,5} Patients may experience new lesions for up to two months, however, they should slowly begin to resolve after two weeks.^{3,7} Symptoms such as arthralgia may last for up to two years after resolution of lesions.³

Treatment of EN is symptomatic usually consisting of rest, elevation, and the use of NSAIDs for alleviation of pain and controlling edema. If caused by a known etiology, such as oral contraceptives or other medications, the patient should discontinue use. For infections, such as streptococcal, medications may be prescribed to treat the illness. Potassium iodide (KI) may be administered if lesions persists longer than six weeks.^{3,7} The mechanism of KI is to cause heparin release, which aids in suppressing hypersensitivity reactions.³ However, KI may also inhibit neutrophil chemotaxis.⁷

Chronic erythema nodosum can progress based on cases presenting with a lesser degree of septa thickening and inflammation compared to acute EN. Chronic EN also exhibits prominent characteristics of phlebitis (inflammation of veins) and extravasated erythrocytes (blood forced out of vessels), not seen in acute EN. However, some cases are misdiagnosed as chronic due to the stage of evolution.¹¹

CHAPTER 5

CONCLUSION

Erythema nodosum is a rare disorder that affects approximately 1-5 per 100,000 people per year. Typically, seen in the female 25-40 year old population, the cause is usually idiopathic; however, the most common cause is streptococcal pharyngitis.^{2-6,11} This case demonstrates the need for the awareness of a systematic condition that could be present within the athletic population. With this information, clinicians can better diagnose and treat erythema nodosum along with an awareness of etiologies causing the condition.

In this case, due to recent diagnosis of URI and flu-like symptoms, they are assumed to be the cause of EN in this athlete. However, it is uncertain and the cause could have been idiopathic. Because symptoms worsened after prescribed penicillin the medication may also be a trigger of the condition. No further investigation was made to determine the actual cause since lesions resolved within two weeks.

Clinicians should keep in mind EN can be easily diagnosed and treated by the sports medicine staff. In some instances, EN can be a sign of a more serious condition such as tuberculosis or sarcoidosis. For this reason it is important for the individual to seek proper medical diagnostic testing.

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APPENDIXES

Appendix A: MU Institutional Review Board Letter



Office of Research Integrity

April 28, 2014

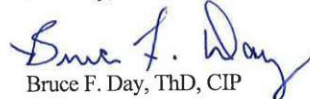
Ashley D. Smith, ATC
Marshall University
Graduate Assistant Athletic Trainer
Women's Soccer and Track & Field

Dear Ms. Smith:

This letter is in response to the submitted thesis abstract of a case study to inform athletic trainers of a systematic disease not common to our patient population. After assessing the abstract it has been deemed not to be human subject research and therefore exempt from oversight of the Marshall University Institutional Review Board (IRB). The Code of Federal Regulations (45CFR46) has set forth the criteria utilized in making this determination. Since the information in this study does not involve human subjects as defined in the above referenced instruction it is not considered human subject research. If there are any changes to the abstract you provided then you would need to resubmit that information to the Office of Research Integrity for review and a determination.

I appreciate your willingness to submit the abstract for determination. Please feel free to contact the Office of Research Integrity if you have any questions regarding future protocols that may require IRB review.

Sincerely,


Bruce F. Day, ThD, CIP
Director

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