DFASM3 – FollowUp 04 *Fever of Unknown Origin* Transcript

Based on *http://www.medscape.org/viewarticle/757309_3*

*Dr. Jonathan Smith, a 1st year **resident** at Mass General Hospital, is reporting a case to the **attending** in charge of teaching him, Dr. Brenda Jenkins.*

BRENDA JENKINS: Ah, Jonathan, hello, what case did you wish to discuss with me?

JONATHAN SMITH: Hello, Dr. Jenkins. I wanted to check with you about a 28-year old patient I just examined, Melany Jones. She was transferred from an outside hospital with a **chief complaint** of fever of unknown origin for the past 3 months. Her fever has been as high as 39°C and has had no **noticeable pattern**.

BRENDA JENKINS: Alright, is there any noticeable **history**?

JONATHAN SMITH: Yes, quite. The patient has a history of bronchial asthma and chronic bronchitis that has not **responded to** multiple **courses** of antimicrobial treatment, including amoxicillin/clavulanic acid, cefotaxime, and levofloxacin. She has a 5-year history of asthma managed with inhaled bronchodilators and an occasional need for aminophylline. She also has a history of allergic rhinitis that precedes her history of asthma. She does not smoke or take other medications, has not traveled, and does not have pets.

BRENDA JENKINS: Are any other symptoms associated with her fever?

JONATHAN SMITH: She has **severe** upper-back pain that limits movement and is associated with **numbness** of the **sole** of her right foot. The pain developed 2 weeks after the fever and **affects** her daily life. She has noted difficulty holding heavy objects with both her right and left hands and difficulty with other upper-extremity tasks, like combing her hair. She also has a **productive cough** (yellowish **sputum**) that is not related to **posture** and has no diurnal variation. She also reports **significant weight loss**. Although she is unable to quantify how much weight she has lost, she noticed that her clothes no longer fit her.

BRENDA JENKINS: Have you tried to estimate how much weight she might have lost?

JONATHAN SMITH: Yes. Miss Jones weighs 85 kg, and **according to** what she reports about her change in clothes size, I would estimate nearly a 20-kg weight loss over the past 5 to 6 months.

BRENDA JENKINS: Well, that's certainly significant. And what did your examination reveal?

JONATHAN SMITH: Throughout the examination, Miss Jones was very uncomfortable and **restless**. Besides the high fever, she had a pulse of 110, blood pressure of 110/70, and a **respiratory rate** of 25. Examination of the chest revealed crepitations and **wheezes** throughout both lung fields, but I found normal heart sounds without **evidence** of cardiac murmur or friction rub. Examination of the back revealed severe **tenderness** of the midline cervical spine, which **broadens** to involve both **shoulders** down the **spine** to the 2nd lumbar vertebra. I noted proximal **weakness** of both **upper limbs**, but the sensory examination of the upper extremities was normal. Lower extremity sensory motor examination was normal and symmetric.
There was no cervical, axillary, or inguinal lymph node enlargement. Abdominal examination revealed no tenderness, rigidity, ascites, organomegaly, or masses. I didn't find any extremity edema, and I felt intact dorsalis pedis, posterior tibialis, and radial pulses.

BRENDA JENKINS: And what did you want to check with me?

JONATHAN SMITH: Well, I thought it would be **appropriate** to run a **CBC**, check her **ESR**, liver enzymes, creatinine, **BUN** and to get an X-ray of her lungs, but I wanted to make sure I was doing the right thing.

BRENDA JENKINS: Those are certainly indicated, but you should also run a **urinalysis** and a CT-scan, given her pain and expectorations. We need to get a good look at what is happening in her chest.

JONATHAN SMITH: Ok, I'll order that and come back to you with the results. Thank you, Dr. Jenkins.

Later that day, Jonathan Smith returns with the results of the tests.

JONATHAN SMITH: So Miss Jones's hemoglobin is at 12.9, she has a **platelet** count of 350,000, and a white blood cell count of 25,000, with 12% eosinophils. Her ESR is elevated at 65 in the 1st hour. Liver enzyme findings are unremarkable, with an **AST** of 35, **ALT** of 25, and a serum bilirubin of 0.7. Creatinine is normal at 0.5, with a BUN of 35. The rheumatoid factor finding is positive. The urinalysis shows no evidence of infection or proteinuria.

BRENDA JENKINS: And what of her lungs?

JONATHAN SMITH: The plain chest radiograph revealed multiple **scattered** infiltrates in both lungs, and the high-resolution CT scan showed interstitial lung fibrosis.

BRENDA JENKINS: What are your hypotheses for a diagnosis?

JONATHAN SMITH: It could be an eosinophilic disorder: the pulmonary infiltrates can indicate **Löffler syndrome** and the peripheral infiltrates can suggest **chronic eosinophilic pneumonia**. Or it could be a vasculitic condition like **Wegener granulomatosis** or **Goodpasture syndrome**. But I'm thinking **Churg-Strauss syndrome**. Miss Jones's history and physical examination seem consistent with CSS, including allergic rhinitis and asthma, myalgias, elevated ESR, eosinophilia, transient interstitial lung fibrosis, positive rheumatoid factor, and mononeuritis.

BRENDA JENKINS: I would agree that her symptoms, history and lab results are most suggestive of CSS. What would you say if the antineutrophil cytoplasmic antibodies (c-ANCA and p-ANCA) were negative?

JONATHAN SMITH: I'm not sure. Would that exclude CSS?

BRENDA JENKINS: No, negative antibodies are found in approximately 50% of CSS patients. But we do need to confirm the **diagnosis**. What can you tell me about CSS?

JONATHAN SMITH: Well, it is a granulomatous small-vessel vasculitis. The cause is unknown. The incidence of CSS is rather low, I think, but it affects men and women **roughly** equally.

BRENDA JENKINS: That's right, the incidence is approximately 2.5 cases per hundred thousand individuals. Do you know the 1990 American College of Rheumatology criteria for diagnosis of Churg-Strauss Syndrome?

JONATHAN SMITH: If I **recall** correctly, they include asthma, which I think almost always precedes the systemic manifestations, eosinophilia **greater than** 10% in the peripheral blood, evidence of a mononeuropathy in a vasculitic pattern or polyneuropathy, non-fixed pulmonary infiltrates, presence of paranasal sinus abnormalities, and histological evidence of extravascular eosinophils.

BRENDA JENKINS: That's correct. For classification purposes, a patient is said to have Churg-Strauss syndrome if at least 4 of these 6 criteria are positive. The presence of any 4 or more of the 6 criteria **yields** a sensitivity of 85% and a specificity of 99.7%. Now, what would be most **worrying** in patients with CSS?

JONATHAN SMITH: Don't most deaths **occur due to** cardiac involvement?

BRENDA JENKINS: Yes, exactly. So it is important to **keep an eye on** Miss Jones's heart. Cerebral hemorrhage or infarction is the second most common cause of death and is often associated with cerebral vasculitis or hypertension. Now, what treatment would you recommend for this patient?

JONATHAN SMITH: I think we should hospitalize her. We first need to **induce** remission with prednisolone and cyclophosphamide, and then we will be able to reduce the prednisolone rapidly and replace the cyclophosphamide with azathioprine.

BRENDA JENKINS: That sounds good to me. Let me know how it all progresses.

A week later, Jonathan Smith reports to Dr. Jones.

BRENDA JENKINS: Hello Jonathan, how is our CSS patient doing?

JONATHAN SMITH: As you know, Miss Jones was hospitalized and treated with prednisolone 45 mg for remission induction, with a dramatic response. Two days after the start of therapy, she was able to sleep normally and serve herself. Her back pain, respiratory symptoms, and numbness also disappeared. Miss Jones's ESR returned to normal in a few days. For remission maintenance, we added azathioprine in a dose of 200 mg daily commencing with the reduction of the prednisolone therapy.

BRENDA JENKINS: That's very good news. Thank you, Jonathan and good work.