

What's Wrong with Me?

Easy and Hard Diagnoses in Immunology

by

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Part I – Meet Claudia

Brief History of Symptoms

Claudia is a 34-year-old research scientist at Evermore University who used to really enjoy her work. However, for the past two years, she has noticed that she no longer has the energy to spend long hours running experiments in the lab. She is generally fatigued despite getting a good night's rest. She has also noticed that her right leg is very restless. Within the past three months, she has had recurrent arm pain, leaving her unable to lift her arms over her head. Recently, the pain has spread to the wrist and knee, with swelling in the joints and tenderness. She is unable to close her hands and cannot perform basic functions like pipetting in the lab. She has also noticed that her fingertips are often tingling, numb and have turned a ghostly shade of white. She has seen her primary care doctor but has been unable to find any relief to her symptoms after multiple visits. Her doctor has given her a referral to a rheumatologist as she suspects that it may be an immunological disorder.

**** You and your team will be in charge of her case. ****

Medical History

Aside from her current symptoms, Claudia is in good health. Her mother, 62, has signs of arthritis. Her father, 67, has high blood pressure and is currently taking medications. Claudia has two siblings, both in perfect health. Her pulse is 80 beats per minute with good volume and is normal in radial and pedal regions. Her blood pressure is normal at 120/70 mm of Hg and her systemic examinations are normal.

Claudia's symptoms seem to be recurrent but scattered over a long time. She is taking ibuprofen for the pain and doing light physical exercise such as yoga to help stretch her muscles as recommended by her primary care physician.

Your Initial Plan of Action

Claudia's initial visit with you leads you to suspect that she may have an autoimmune disease. Her symptoms suggest that she may have Raynaud's syndrome in association with an autoimmune disease. You propose an initial round of biochemical tests, X-rays of her hands and knees, and a follow-up visit in two weeks. You recommend that Claudia get a referral for the following blood work: complete blood cell counts, basic metabolic panel, erythrocyte sedimentation rate (ESR), C3, C4, C-reactive protein (CRP), and ANA. Additional tests include presence of antibodies against rheumatoid factor (RF), RNP, CCP, dsDNA, and Smith (Sm).

To help alleviate her current symptoms, you suggest she use compression gloves a few hours a day.

Objectives for Your Team

Answer the questions below so that you are able to provide information to your patient about the current battery of tests that were ordered. Make sure to identify the sources you consulted. Upon completion, your team will receive Claudia's results.

1. What is restless leg syndrome?
2. What are ESR, C3, C4, and CRP tests? Are they similar?
3. What is the RF test?
4. Describe Sjögren's syndrome.
5. Describe Raynaud's syndrome.
6. What is the ANA test? What information do tests like dsDNA, CCP, and RNP provide?
7. How do some of these tests relate back to autoimmune diseases that you learned in class?
8. Based on the questions you have answered above, what are the potential autoimmune diseases that may match Claudia's symptoms?

Part II – Claudia’s Test Results

Complete Blood Cell Counts

<i>Component</i>	<i>Value</i>	<i>Reference range</i>
WBC	5.8 × K/ μ L	3.4–10.8 × K/ μ L
RBC	4.71 × M/ μ L	3.77–5.28 × M/ μ L
Hgb	12.5 g/dL	11.1–15.9 g/dL
Hct	39.2 %	34.0–46.6 %
MCV	83 fL	79–97 fL
MCH	29.7 pg	26.6–33.0 pg
RDW	14.0 %	12.3–15.4 %
Plts	280 K/ μ L	150–379 K/ μ L
C3	171 mg/dL	82–167 mg/dL
C4	33 mg/dL	14–44 mg/dL
ESR	19 mm/hr	0–15 mm/hr
CRP	6.7 mg/L	0.0–4.9 mg/L

Basic Metabolic Panel

<i>Component</i>	<i>Value</i>	<i>Reference range</i>
Glucose, serum	66 mg/dL	65–99 mg/dL
Bun	11 mg/dL	6–20 mg/dL
Creatinine, serum	0.73 mg/dL	0.57–1.00 mg/dL
eGFR if Non-African Am	107 mL/min/1.73	>59 mL/min/1.73
eGFR if African Am	123 mL/min/1.73	>59 mL/min/1.73
Sodium, serum	137 mmol/L	124–144 mmol/L
Potassium, serum	4.3 mmol/L	3.5–5.2 mmol/L
Chloride, serum	101 mmol/L	96–106 mmol/L
Carbon dioxide, total	23 mmol/L	18–29 mmol/L
Calcium, serum	9.8 mg/dL	8.7–10.2 mg/dL
Protein, total, serum	6.7 g/dL	6.0–8.5 g/dL
Albumin, serum	4.2 g/dL	3.5–5.5 g/dL
Globulin, total	2.9 g/dL	1.5–4.5 g/dL
Bilirubin, total	0.5 mg/dL	0.0–1.2 mg/dL
Alkaline phosphatase	94 IU/L	39–117 IU/L

Antibody Tests

<i>Test</i>	<i>Result</i>	<i>Range</i>
ANA	Above High Normal	
ANA titer and pattern	1:1280, speckled pattern	N/A
Sjogren's	<0.2 ai	0.0–0.9 ai
Smith's	0.6 ai	0.0–0.9 ai
CCP	3 units	0–19 units
RNP	6.3 ai	0.0–0.9 ai
dsDNA	1 IU/mL	0–9 IU/mL
RF	<20 IU/mL	<20 IU/mL

Hand X-ray Results

No evidence of abnormality in either of the hands or wrists.

Objectives for Your Team

1. Identify the abnormal or out of range test results. Using the information collected from Part I, brainstorm with your teammates about what the above results may indicate.
2. After consulting with your teammates, propose an initial diagnosis for Claudia. Explain your diagnosis and treatment based on the test results.
3. Based on her test results, determine whether Claudia is in early or late stages of the disease.
4. Propose and explain potential treatments. Select a traditional treatment (e.g., methotrexate) and an immunotherapy treatment (e.g., Humira, Xeljanz). When should Claudia visit your office again and what would you discuss with her?

Part III – Class Presentations

Claudia's follow-up visit and your explanation of test results will be presented to the class. You may use PowerPoint slides or simply an oral presentation. Keep in mind that other groups may have arrived at different diagnoses. Be prepared to defend your group's conclusion.

Objectives for Your Team

1. Discuss the initial diagnosis and provide information about the disease.
2. Compare early and late stages of the disease.
3. What test results led your team to arrive at this conclusion?
4. Why did you choose the proposed treatments?
5. What are the points to discuss at your next meeting with Claudia?

Open-Ended Questions and Team Discussion

1. Did other teams reach a different conclusion than your own?
2. Do you feel their diagnoses are valid as well?
3. Compare and contrast common and differential diagnoses between the various groups.
4. Do you agree with their diagnoses?

Part IV – Personal Reflections

Please write an individual reflection to submit after case study discussion that covers the following questions:

1. Among the topics discussed, what topics were integral to your group discussion and diagnosis?
2. Identify (if possible) the types of hypersensitivity reactions that may be associated with the autoimmune diseases discussed by you and your fellow students. You may use more than one.
3. Did you have a prior understanding of the tests used in the case study? If yes, please share where you came across these tests, for example, another course, shadowing, etc.
4. Did you have prior knowledge regarding the treatments proposed in the case study? If yes, explain where.
5. How helpful was it to have a real patient interaction to develop:
 - a desire to provide the closest diagnosis and treatment possible?
 - a relationship with future jobs and real world experiences?
6. Was this case study helpful in expanding your understanding of the medical profession?

Abbreviations

ANA: antinuclear antibody

C3: complement component 3

C4: complement component 4

CCP: cyclic citrullinated peptide

CRP: C-reactive protein

dsDNA: double stranded deoxyribonucleic acid

eGFR: estimated glomerular filtration rate

ESR: erythrocyte sedimentation rate

Hct: hematocrit

Hgb: hemoglobin

MCH: mean corpuscular hemoglobin

MCTD: mixed connective tissue disease

MCV: mean corpuscular volume

Plt: platelets

RBC: red blood cells

RDW: red cell distribution width

RA: rheumatoid arthritis

RF: rheumatoid factor

RLS: restless leg syndrome

RNP: ribonucleoprotein

SEG: segmented neutrophil

SLE: systemic lupus erythematosus

Sm: Smith; RNA-binding proteins

WBC: white blood cells

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Part I – Meet Anita

Brief History of Patient's Symptoms

Anita is a 20-year-old undergraduate student at Whitmore University. She is a student athlete and is part of the track and field team at her school. Anita tends to get hurt at practice or at competition events. She always feels sore or remains bruised for a few days. Over the past two years, she has also noticed that she occasionally has swollen hands or painful joints on non-practice days. Her teammates recommend that she visit the primary care doctor to get medical attention. However, the last three visits to her primary care doctor resulted in a prescription for ibuprofen or hydrocodone for severe pain. Anita decided not to go anymore and save herself the insurance co-payment.

A couple of days ago, she had swollen hands and arms that were warm and tender to touch. She was unable to close her fist or raise her arms over her shoulders. She got very worried and went to her primary care doctor. Her doctor prescribed an anti-inflammatory and analgesic medication along with a referral to a rheumatologist.

**** You and your team will be in charge of her case. ****

Patient's Medical History

Anita has always been in excellent health, with occasional flu-like symptoms in winter. Her parents are in good health and she has no siblings. Other than her grandmother, no one in her family has similar symptoms.

Anita has had a few sport-related injuries including a broken toe a few years prior and a broken wrist about a year ago. Everything healed fine and she has not felt any pain at the site of the fractures.

Your Initial Plan of Action

Based on Anita's symptoms, you suggest she could have an autoimmune disease. You provide her with referrals for laboratory work and X-rays of her hands and her arms. You ask that she return in two weeks for a follow-up visit to go over her test results. You also suggest that she continue to take the medication for pain as needed.

Anita's laboratory work includes the following tests: complete blood cell counts, differential white blood cell counts, ESR, and CRP. In addition, she will be tested for the presence of antibodies against RF and CCP.

Objectives for Your Team

Answer the questions below so that you are able to provide information to your patient about the current battery of tests that were ordered. Make sure to identify the sources you consulted. Upon completion, your team will receive Anita's results.

1. Why is it necessary to get X-rays of Anita's hands?
2. What is the purpose of the ESR and CRP tests?
3. What is the RF test?
4. What information do tests like CCP provide? Are there any other antibody tests available?
5. How do some of these tests relate back to the diseases covered in class?
6. Based on the questions you have answered above, what are the potential autoimmune diseases that match Anita's symptoms?

Part II – Anita’s Test Results

Complete Blood Cell Counts

<i>Component</i>	<i>Value</i>	<i>Reference range</i>
WBC	7.0 × K/UL	3.5–10.5 × K/UL
RBC	4.0 × M/UL	3.8–5.2 × M/UL
Hgb	14.0 g/dL	11.0–15.5 g/dL
Hct	40.0 %	34.0–45.0 %
MCV	85.0 FL	80.0–99.0 FL
MCH	33.0 pg	27–34.0 pg
RDW	13.0 %	11.0–15.0 %
Plts	300 K/UL	140–390.0 K/UL

Differential White Blood Cell Counts

<i>Component</i>	<i>Value</i>
SEG	55.0%
Lymphocytes	35.0%
Monocytes	8.0%
Eosinophils	1.0%
Basophils	1.0%

Additional Tests

<i>Test</i>	<i>Result</i>	<i>Range</i>
CCP	110.0 Unit/mL	Less than 5 Unit/mL is negative. Greater than 5 Unit/mL is positive.
RF	205.0 IU/mL	0.0–14.0 IU/mL
ESR	28.0 mm/Hour	2.0–25.0 mm/Hour
CRP	1.3 mg/dL	0.0–0.5 mg/dL

Hand X-Ray Results

No obvious signs of damage.

Objectives for Your Team

1. Identify the abnormal or out of range test results. Using the information collected from Part I, brainstorm with your teammates about what the above results may indicate.
2. After consulting with your teammates, propose an initial diagnosis for Anita. Explain your diagnosis and treatment based on the test results.
3. Based on her test results, determine whether Anita is in early or late stages of the disease.
4. Propose and explain potential treatments. Select a traditional (e.g., methotrexate) and an immunotherapy treatment (e.g., Humira, Xeljanz). When should Anita visit your office again and what would you discuss with her?

Part III – Presenting the Diagnosis

You will present the results of the follow-up visit and explanation of test results to the class. You may use PowerPoint slides or simply an oral presentation. Keep in mind that other groups may have reached a different diagnosis. Be prepared to defend your group's conclusion.

Objectives for Your Team

1. Discuss the initial diagnosis and provide information about the disease.
2. How would you differentiate between early vs late stages of the disease?
3. What were the test results that led your team to this diagnosis?
4. Why did your team choose the proposed treatments?
5. What would you discuss with Anita during her next visit?

Open-ended questions and team discussion

1. Did all the teams arrive at the same diagnosis?
2. If the other teams reached a different diagnosis, was it valid as well?
3. Discuss the similarities and differences in your views.

Part IV – Personal Reflections

Please write an individual reflection to submit after case study discussion that covers the following questions:

1. Among the topics discussed, what topics were integral to your group discussion and diagnosis?
2. Identify (if possible) the types of hypersensitivity reactions that may be associated with the autoimmune diseases discussed by you and your fellow students. You may use more than one.
3. Did you have a prior understanding of the tests used in the case study? If yes, please share where you came across these tests, for example, another course, shadowing, etc.
4. Did you have prior knowledge regarding the treatments proposed in the case study? If yes, explain where.
5. How helpful was it to have a real patient interaction to develop:
 - a desire to provide the closest diagnosis and treatment possible?
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6. Was this case study helpful in expanding your understanding of the medical profession?

Abbreviations

ANA: antinuclear antibody

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CCP: cyclic citrullinated peptide

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eGFR: estimated glomerular filtration rate

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MCV: mean corpuscular volume

Plt: platelets

RBC: red blood cells

RDW: red cell distribution width

RA: rheumatoid arthritis

RF: rheumatoid factor

RLS: restless leg syndrome

RNP: ribonucleoprotein

SEG: segmented neutrophil

SLE: systemic lupus erythematosus

Sm: Smith; RNA-binding proteins

WBC: white blood cells