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MISSOURI HOSPITALIST

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Hospitalist Update:

Hospital-Acquired Infections

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Hospitals in Missouri perform surveillance and external reporting for a number of hospital-acquired infections (HAI). We are required to do so variously by the state of Missouri, the Centers for Medicare and Medicaid Services (CMS) and for those of us reporting to a Patient Safety Organization (PSO). Hospital-acquired infections are recognized as typically preventable with optimal infection prevention and control practices. In the context of the National Quality Strategy required by the Affordable Care Act, reducing HAI is part of the priority of "Making care safer by reducing harm caused in the delivery of care."[1] As one piece of the growing national strategy linking payment with measures of quality and safety of care, CMS does not pay hospitals for care related to a defined list of hospital acquired conditions, and other payers are following suit in their contracts.

The focus of surveillance and prevention for hospital acquired infections has historically been on device- and procedure-related infections. These include catheter-associated urinary tract infections (CAUTI), ventilator associate pneumonia (VAP), central line-associated bloodstream infections (CLABSI) and surgical site infections (SSI). The Missouri Nosocomial Infection Control Act of 2004 established the requirement for state reporting of HAI. Infections currently reportable to the Department of Health and Senior Services are central line associated bacteremia and SSI for certain surgeries. Additional reporting is required for hospitals participating in the National Healthcare Safety Network of the Centers for Disease Control (NHSN), and includes CLABSI and CAUTI. Reporting definitions often vary from organization to organization, with particular distinction between programs using case definitions based on clinical variables versus those using administrative data with billed diagnoses.

Participation in the NHSN allows comparison of a hospital's infection rates to performance percentiles defined by all reporting hospitals.[2] These benchmarks provide comparisons by facility (acute care hospital, long-term acute care facilities, etc.) and unit (medical ICU, surgical ICU, etc.). NHSN provides detailed criteria for definitions of each condition, with revisions up to twice yearly. The most prominent recent change involves assessment of ventilator associated pneumonia. NHSN has defined a broader category consisting of "ventilator associated events," which then narrow to infections and again to pneumonia. While improving the accuracy of categorization, such definition changes do cause changes to reported rates, limiting the ability to meaningfully compare performance in an individual organization over time.

Participation in the CMS Hospital Inpatient Quality Reporting program for Federal Fiscal Year 2014 requires "Participation in a Systematic Clinical Database Registry for General Surgery." One such database is the American College of Surgeons National Surgical Quality Improvement Program (NSQIP). The database supports reporting, risk adjustment and comparisons of surgical complications based on clinical data entered by a reviewer, with SSI as one such complication.[3]

Hospitals began reporting three new measures to the NHSN as of January 2013, as required by CMS. The first of these is Healthcare Personnel Influenza Vaccination. Healthcare organizations must report the number of healthcare providers working during flu season, as well as the numbers who receive influenza vaccine from the organization or externally, and the numbers who have medical contraindication or who decline vaccination. The second new measure is laboratory identification of Methicillin-Resistant *Staphylococcus aureus* (MRSA) positive blood specimens. The final HAI measure added for reporting in 2013 is laboratory identification of toxin-positive/toxin-producing *Clostridium difficile* stool specimens. Hospital data for these three measures will be found on the public CMS Hospital Compare website in December.

Currently, the Medicare Hospital Compare website[4] presents hospital data on HAI, including CLABSI, CAUTI and SSI with colon surgery and abdominal hysterectomy. Performance is presented as Standardized Infection Ratio (SIR), which is the ratio of observed rate to the expected rate. Expected rate is defined as the NHSN median, with comparisons by unit type and facility type aggregated for a given hospital. Hospitals performing at the median would have SIR of 1. The SIR for each HAI is additionally rated as better, no different, or worse than the U.S. national benchmark based on whether the confidence interval for the SIR is less than, includes or greater than 1.

The CMS Value Based Purchasing program ties a portion of a hospital's payments to outcomes of care. For payments beginning in October 2014, CLABSI reported to NSHSN through 2013 will serve as one such outcome of care, both individually and as part of a composite measure of other indicators of patient safety and quality of care. An additional program defined by the Patient Protection and Affordable Care Act of 2010 outlines a payment adjustment of 1% for hospitals in the top quartile of hospital acquired conditions, beginning in October 2014.[5]

As Hospitalists, we need to be aware of the national focus and payment consequences for hospital acquired infections. More importantly, however, we need to know how to prevent these events in our patients. For all device-related infections, the most important decision is whether the device is truly needed for a patient's care. When it is, the continual review of whether the device is still

needed, or whether care can be provided in a safer way remains essential. The second intervention important for prevention of all HAI is hand hygiene.[6] Using the concept of the "health-care zone" and the "patient zone," performing hand hygiene protects our patients when we move from one zone to the other, as well as before a clean/aseptic procedure and after any bodily fluid exposure risk.

Specific for prevention of CLABSI, the preferred site is subclavian.[7] Skin preparation with chlorhexidine with alcohol is to be used in adults. Sterile gloves should be worn during placement, and either clean or sterile gloves should be worn during dressing changes. Full sterile barrier precautions are recommended during placement and guidewire exchange, including cap and mask, as well as sterile gown, gloves and full body drape. If catheters are expected to remain in place more than five days, use of an antimicrobial/antiseptic impregnated catheter may further contribute to CLABSI reduction when added to recommended skin preparation and use of full sterile barrier precautions.

The "ventilator bundle" is well-established in prevention of VAP.[8] Elements of this bundle have been studied in isolation and in a grouping, with the essential elements of head of bed elevation to 30 degrees or greater, breaks in sedation, peptic ulcer prophylaxis and venous thromboembolism prophylaxis. ICU teams focused on bundle adherence reported a 45% reduction in VAP.[9]

Hospitalist can have significant impact on CAUTI reduction with rigor in requiring clinical indications for catheter placement and regular review of ongoing or unresolved indications to continue bladder catheterization. As electronic health records develop to standardize optimal care, structural support to review ongoing catheter use can range from daily reminders to pre-set discontinuation orders.[10] Optimal placement techniques should be part of a hospital's nursing education. Antimicrobial/antiseptic-coated catheters may be helpful, particularly if catheterization is expected to be prolonged.

In summary, it is clear that hospital acquired infections, amongst other complications, are no longer accepted as a normal part of care. To the extent that we can reduce or prevent these infections, we must do so for our patients. There are well-established ways to do so for many of these infections, and hospitals will see reductions in infection rates with consistent adoption of practices presented in the medical literature. Hospitals face increasing financial accountability to reduce or eliminate HAI, and will look to Hospitalists for participation, expertise and leadership in initiatives to do so.

REFERENCES

1. Goodrich K, Garcia E, Conway PH. A history of and a vision for CMS quality measurement programs. Jt Comm J Qual Patient Saf. 2012 Oct;38(10):465-70.
2. Dudeck MA, Horan TC, Peterson KD, Allen-Bridson K, Morrell G, Anttila A,Pollock DA, Edwards JR. National Healthcare Safety Network report, data summary for 2011, device-associated module. Am J Infect Control. 2013 Apr;41(4):286-300.
3. http://site.acsnsqip.org/about/
4. http://medicare.gov/HospitalCompare/about/hosinfo/rcd.aspx
5. http://www.gpo.gov/fdsys/pkg/PLAW-111publ148/pdf/PLAW-111publ148.pdf

6. WHO guidelines on hand hygiene in health care: first global patient safety challenge. Clean care is safer care. World Health Organization - 2009
7. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, Lipsett PA, Masur H, Mermel LA, Pearson ML, Raad II, Randolph AG, Rupp ME, Saint S; Healthcare Infection Control Practices Advisory Committee (HICPAC). Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis. 2011 May;52(9):e162-93.
8. Tablan OC, Anderson LJ, Besser R, Bridges C, Hajjeh R; CDC; Healthcare Infection Control Practices Advisory Committee. Guidelines for preventing health-care--associated pneumonia, 2003: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. MMWR Recomm Rep. 2004 Mar 26;53(RR-3):1-36.
9. Resar R, Pronovost P, Haraden C, Simmonds T, Rainey T, Nolan T. Using a bundle approach to improve ventilator care processes and reduce ventilator-associated pneumonia. Jt Comm J Qual Patient Saf. 2005 May;31(5):243-8.
10. Hooton TM, Bradley SF, Cardenas DD, Colgan R, Geerlings SE, Rice JC, Saint S, Schaeffer AJ, Tambayh PA, Tenke P, Nicolle LE; Infectious Diseases Society of America. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. Clin Infect Dis. 2010 Mar 1;50(5):625-63.

A CASE OF DRESS SYNDROME DUE TO VANCOMYCIN

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BACKGROUND

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a severe systemic reaction that usually begins 2-6 weeks after the introduction of the inciting agent. It is most commonly characterized by fever, rash, hematologic abnormalities (eosinophilia, atypical lymphocytosis), lymphadenopathy, HHV-6 reactivation and internal organ involvement. At least 10% of the cases are fatal. Treatment includes withdrawal of the offending medication and administration of corticosteroids, though the efficacy of the latter has not been fully evaluated.

CASE REPORT

A 64 year-old white male with past medical history of type 2 diabetes mellitus, hypertension, hyperlipidemia, COPD, coronary artery disease, gout, and a fifteen pack-year smoking history presented with complaints of fever, rash and abdominal discomfort. Patient developed a new pruritic, nontender rash on back, chest, arms associated with bilateral arm swelling and shortness of breath. Eight months prior to the admission, he had an open reduction for fracture of the left distal femur after a motor vehicle accident. He had two admissions related to this. One month previously, he was admitted with left septic knee, which was treated by arthrocentesis, screw removal, irrigation and drainage. Intravenous vancomycin was given and vancomyin beads were placed in the knee joint space. Eight days prior to the arrival, the patient was readmitted with complaints of fever, chills, left knee pain and the X-ray of the left knee was suggestive of septic arthritis, which was subsequently managed with irrigation and drainage. Vancomycin was continued and the patient was discharged two days prior to the current admission. The patient hadn't had any recent medication changes and denied any exposure to exotic pets, molds, dusts, chemicals, and drugs.

On physical exam, his temperature was 37.8 °C with a blood pressure of 98/64mmHg. The exam

was remarkable for bilateral upper extremity edema and limited range of motion in the left knee secondary to mild swelling, without erythema or tenderness to palpation or movement. The skin exam revealed a very subtle, erythematous, papular, non-tender and non-confluent pruritic rash on chest and abdomen, more prominent on back and arms. Nikolsky sign was negative.

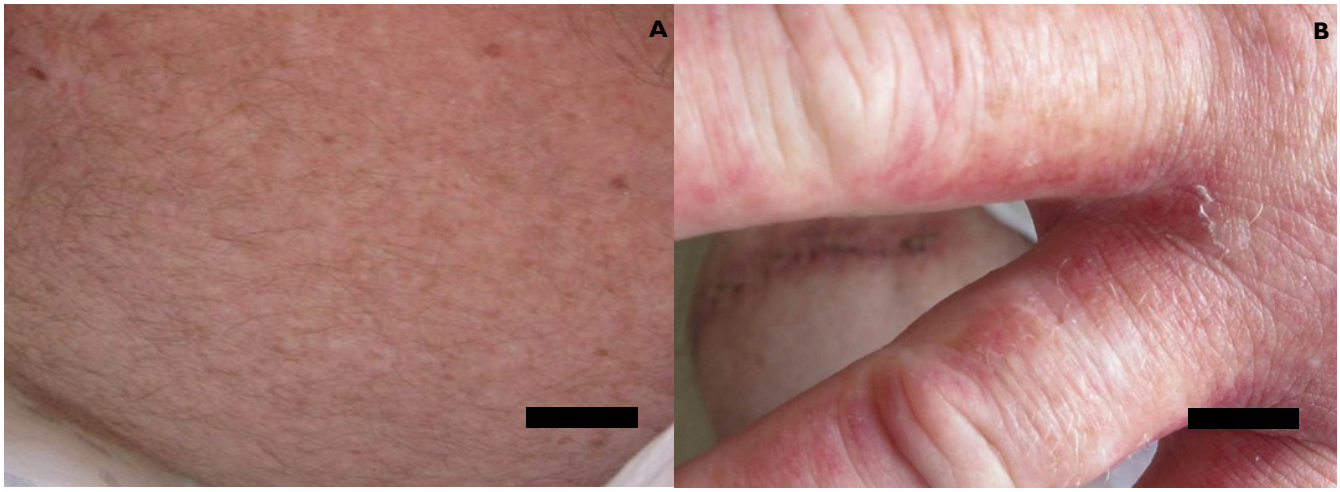

Figure A: Back showing rash with hyperemia and blanching; hospital day 6
Figure B: Edematous fingers and rash, left knee s/p ORIF in background; hospital day 6

Laboratory results on admission revealed white blood cell count of 10,300/μL, with 16.5% eosinophil's (normal 0-10%), and platelet count of 390,000 /μL. Other labs included alkaline phosphatase of 332 U/L, AST of 225 U/L, and ALT of 413 U/L compared to previous normal LFT's. Urinalysis was unremarkable and opacities, likely due to atelectasis. Peripheral smear from later hospital course showed large atypical eosinophil's and no toxic granulations in neutrophils. Blood culture remained negative during the hospital stay. Chest x-ray and abdominal ultrasound were unremarkable.

Given the cutaneous changes, eosinophilia and other systemic signs, a presumptive diagnosis of DRESS syndrome was made. Vancomycin was discontinued and patient was switchd to Daptomycin. Prednisone 60 mg daily was initiated for treatment of DRESS syndrome. The white counts increased to 18,800/μL on day 2, so steroids were held with concern regarding its immunosuppressive effects. Allopurinol was discontinued on hospital day 3, given its reported association with DRESS syndrome. However, as shown in the table over the next several days the white blood cell count escalated dramatically with accompanying eosinophilia. Without further signs of infection in the left knee, prednisone 60 mg was restarted on hospital day 7 to treat presumptive DRESS syndrome.

The prednisone was tapered from 60mg to 30mg daily on hospital day 9. (The patient's white cell count peaked at 44,000/μL on hospital day 10, and then decreased substantially by the day of discharge). Improvement of the patient's rash and edema was noted starting on hospital day 3 and continued until discharge, when the rash was no longer visible. However, bilateral axillary lymphadenopathy persisted. (HHV-6 titer drawn on hospital day 2 were negative; however, a repeat HHV-6 titer drawn on hospital day 8 came back positive). Due to absence of left shift and

Progression of WBC Count				
Date	**Hospital Day**	**WBC X 10^3/ µL**	**% Eosinophils**	**Treatment Notes**
8/13	2	10.3	16	Daptomycin begun One dose prednisone given
8/14	3	18.8	5	Daptomycin increased Allopurinol discontinued
8/15	4	19.9	26	
8/16	5	22.7	20	
8/17	6	29.1	21	
8/18	7	29.9	18	Prednisone restarted 60 mg
8/19	8	29.9	22	Prednisone 60 mg
8/20	9	36.5	22	Prednisone 30 mg
8/21	10	44.0	10	Prednisone 30 mg
8/22	11	38.7	32	Prednisone 30 mg
8/23	12	33.3	41	Prednisone 30 mg
8/24	13	22.1	39	Prednisone 30 mg
8/25	14	15.6	31	Prednisone 30 mg

toxic granulations in the neutrophils the infection and steroid response were less likely. Clonal hypereosinophilic disorder was also deemed unlikely because the eosinophils had been normal within the month. Because the patient continued to have complaints of left knee pain and given the leukocytosis, daptomycin was continued during this hospitalization. Patient was discharged on Prednisone 30mg for total of ten days, and then tapered down to 10 mg every 10 days.

DISCUSSION

DRESS syndrome was originally identified as a hypersensitivity reaction to certain anticonvulsants, including carbamazepine, lamotrigine, and phenobarbital, but a number of other medications with aromatic groups have been reported to cause the syndrome (1, 2, 3, and 5), including about 18 cases reported with allopurinol and four with vancomycin (2). Our patient had been on allopurinol for several years and he had started vancomycin about four weeks prior to the onset of symptoms, which makes vancomycin the most likely causative agent. More support for this conclusion includes the score of 4 which is a "possible adverse drug reaction" according to Naranjo Adverse drug Reaction Scale (1) and a "definite" case of DRESS syndrome per the criteria described by Kardaun et. al (6). Our patient also met all criteria for DRESS syndrome using the diagnostic criteria established by a Japanese consensus group (7).

This case illustrates the challenge in making a definitive diagnosis of DRESS syndrome. As most of the clinical features of DRESS syndrome are non-specific, it may be difficult to exclude other conditions. In this case, our patient's history of recent surgery and infection, leukocytosis, and leg pain made it difficult to rule out re-infection of the knee. Though infection of the knee remained a concern, DRESS syndrome was considered as highly probable because of the patient's multiple negative blood cultures and absence of other signs of infection other than knee pain. The most common manifestations of DRESS syndrome include fever, rash, and systemic symptoms, including lymphadenopathy, leukocytosis, and organ damage. Our patient had elevated liver enzymes, axillary adenopathy and bilateral arm edema.

RegiSCAR Diagnostic Criteria (6)	Naranjo Adverse Drug Reaction Scale
Hospitalization Reaction suspected to be drug-related Acute rash Fever > 38 °C* Enlarged lymph nodes at a minimum of two sites* Involvement of at least one internal organ* Blood count abnormalities* Lymphocytes above or below normal limits Eosinophils above the laboratory limits Platelets below the laboratory limits *3/4 of these are required to make the diagnosis	1. Are there previous conclusive reports on this reaction? *Yes (+1) No (0) Do not know or not done (0)* 2. Did the adverse event appear after the suspected drug was given? *Yes (+2) No (-1) Do not know or not done (0)* 3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given? *Yes (+1) No (0) Do not know or not done (0)* 4. Did the adverse reaction appear when the drug was readministered? *Yes (+2) No (-1) Do not know or not done (0)* 5. Are there alternative causes that could have caused the reaction? *Yes (-1) No (+2) Do not know or not done (0)* 6. Did the reaction reappear when a placebo was given? *Yes (-1) No (+1) Do not know or not done (0)* 7. Was the drug detected in any body fluid in toxic concentrations? *Yes (+1) No (0) Do not know or not done (0)* 8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased? *Yes (+1) No (0) Do not know or not done (0)* 9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure? *Yes (+1) No (0) Do not know or not done (0)* 10. Was the adverse event confirmed by any objective evidence? *Yes (+1) No (0) Do not know or not done (0)* **Scoring** > 9 = definite ADR 5-8 = probable ADR 1-4 = possible ADR 0 = doubtful ADR

The pathogenesis of DRESS syndrome is complex and has yet to be completely elucidated. Both drug metabolism and genetic susceptibility have been implicated. Hapten-carrier adduct formation, by either the drugs themselves or their metabolites, and nonconvalent drug presentation (8) may lead to T cell activation with an overrepresentation of $CD8^+$ cells. It has been hypothesized that the increased risk for DRESS syndrome and other drug reactions among patients with certain HLA variants is due to the affinity of certain drugs, their metabolites, or hapten-carrier adducts for specific HLA binding sites.

These activated T cells produce the cytokines TNF α, IFN γ, and IL-2 that mediate the "cytokine storm," which may be responsible for the wide constellation of symptoms seen in DRESS syndrome (8, 9). The expansion and activation of $CD8^+$ cells may cause the reactivation of latent human herpes viruses seen at the onset of DRESS syndrome, typically HHV-6, but also HHV-7, CMV, EBV, and VZV (9). The broad inflammatory response in DRESS syndrome encourages expansion of regulatory T cells, which are susceptible to infection by viruses such as HHV-6. The infection and compromise of regulatory T cells may mediate the abnormal immunological function observed in this condition. While it has been proposed that polymorphisms in genes for detoxification enzymes may also contribute to DRESS syndrome by increasing the concentration of immunologically active or toxic metabolites, no such polymorphisms have yet been found (8).

Detection of HHV-6 DNA and anti-HHV-6 IgG by PCR analysis is considered sensitive and specific for the diagnosis of DRESS syndrome outside of the United States (10). Thymus and activation-regulated Chemokine (TARC/CCL17), a chemokine, has recently been proposed as an early marker for DRESS syndrome in a study of 29 patients, due to its role in T_H2 type immunity (11).

Current therapy is limited to withdrawal of the offending agent and initiation of corticosteroids to temper the immune response. Our patient received oral prednisone, and the extreme leukocytosis began to subside four days after continuous therapy. Furthermore, his rash and edema had dissipated by the time of discharge. However, it should be noted that there have been no controlled trials validating steroid therapy for this condition (1, 2, and 4). There are several case reports of DRESS syndrome which showed improvement with IVIG, but given the expense and lack of evidence, it is used on an experimental basis only (12, 13). While there are not yet any definitive indicators of mortality, a recent publication showed that an erythema multiforme-like rash, as opposed to the other cutaneous phenotypes possible with DRESS syndrome, may be prognostic for worse hepatic function during the course of illness (14). Sequelae may include end-organ dysfunction (13) and autoimmune disease (15, 16). The latter may be due to viral reactivation and deregulated immune response (16).

Physicians should maintain a low threshold of suspicion for DRESS syndrome when their patients present with a fever, rash, leukocytosis and eosinophilia and a history of new medication use. Further study of documented cases of DRESS syndrome would be helpful in gaining a better understanding of the pathophysiology and optimal therapy for this potentially life threatening disorder.

REFERENCES

1. Ganeva M, Gancheva T, Lazarova R, Troeva J, Baldaranov I, Vassilev I, Hristakieva E, Tzaneva V. "Carbamazepine-induced drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome: report of four cases and brief review." *Int J Dermatol*. 2008 Aug; 47(8):853-60.
2. Cacoub P, Musette P, Descamps V, Meyer O, Speirs C, Finzi L, Roujeau JC. "The DRESS syndrome: a literature review." *Am J Med*. 2011 Jul; 124(7):588-97. Epub 2011 May 17.
3. Fleming P, Marik PE. "The DRESS syndrome: the great clinical mimicker." *Pharmacotherapy*. 2011 Mar; 31(3):332.
4. Walsh SA, Creamer D. "Drug reaction with eosinophilia and systemic symptoms (DRESS): a clinical update and review of current thinking." *Clin Exp Dermatol*. 2011 Jan; 36(1):6-11. doi: 10.1111/j.1365-2230.2010.03967.x.
5. Michel F, Navellou JC, Ferraud D, Toussirot E, Wendling D. "DRESS syndrome in a patient on sulfasalazine for rheumatoid arthritis." *Joint Bone Spine.* 2005 Jan; 72(1):82-5.
6. Kardaun SH, Sidoroff A, Valeyrie-Allanore L, et al. "Variability in the clinical pattern of cutaneous side-effects of drugs with systemic symptoms: does a DRESS syndrome really exist?" *Br J Dermatol*. 2007; 156:609-611.
7. Shiohara T, Inaoka M, Kano Y. "Drug-induced hypersensitivity syndrome (DIHS): a reaction induced by a complex interplay among herpesviruses and antiviral and antidrug immune responses." *Allergol Int*. 2006; 55:1–8.
8. Camous X, Calbo S, Picard D, Musette P. ""Drug Reaction with Eosinophilia and Systemic Symptoms: an update on pathogenesis. *Curr Opin Immunol.* 2012 Dec; 24(6):730-5.
9. Picard D, Janela B, Descamps V, D'Incan M, Courville P, Jacquot S, Rogez S, Mardivirin L, Moins-Teisserenc H, Toubert A, Benichou J, Joly P, Musette P. "Drug reaction with eosinophilia and systemic symptoms (DRESS): a multiorgan antiviral T cell response." *Sci Transl Med*. 2010 Aug 25; 2(46):46ra62.
10. Fields KS, Petersen MJ, Chiao E, Tristani-Firouzi P. "Case reports: treatment of nevirapine-associated dress syndrome with intravenous immune globulin (IVIG)." *J Drugs Dermatol.* 2005 Jul-Aug; 4(4):510-3.
11. Ponnusamy Santhamoorthy, K John Alexander, and Asmahan Alshubaili. "Intravenous immunoglobulin in the treatment of drug rash eosinophilia and systemic symptoms caused by phenytoin." *Ann Indian Acad Neurol*. 2012 Oct-Dec; 15(4): 320–322.
12. Walsh S, Diaz-Cano S, Higgins E, Morris-Jones R, Bashir S, Bernal W, Creamer D. "Drug reaction with eosinophilia and systemic symptoms: is cutaneous phenotype a prognostic marker for outcome? A review of clinicopathological features of 27 cases." *Br J Dermatol*. 2013 Feb; 168(2):391-401.
13. Chen YC, Chang CY, Cho YT, Chiu HC, Chu CY. "Long-term sequelae of drug reaction with eosinophilia and systemic symptoms: A retrospective cohort study from Taiwan." *J Am Acad Dermatol.* 2013 Mar; 68(3):459-65.
14. Ushigome Y, Kano Y, Ishida T, Hirahara K, Shiohara T. "Short- and long-term outcomes of 34 patients with drug-induced hypersensitivity syndrome in a single institution. " *J Am Acad Dermatol.* 2012 Nov 19. pii: S0190-9622(12)01144-9.
15. Criado PR, Avancini J, Santi CG, Medrado AT, Rodrigues CE, de Carvalho JF. "Drug reaction with eosinophilia and systemic symptoms (DRESS): a complex interaction of drugs, viruses and the immune system." *Isr Med Assoc J.* 2012 Sep;14(9):577-82.

16. Ogawa K, Morito H, Hasegawa A, Daikoku N, Miyagawa F, Okazaki A, Fukumoto T, Kobayashi N, Kasai T, Watanabe H, Sueki H, Iijima M, Tohyama M, Hashimoto K, Asada H. "Identification of thymus and activation-regulated chemokine (TARC/CCL17) as a potential marker for early indication of disease and prediction of disease activity in drug-induced hypersensitivity syndrome (DIHS)/drug rash with eosinophilia and systemic symptoms (DRESS)." *J Dermatol Sci*. 2013 Jan; 69(1):38-43.

ASK A PATHOLOGIST

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University of Missouri– Columbia

QUESTION: A 53 years old female receives transfusion of 2 units of PRBCs. One hour later, she develops acute dyspnea with decreased O_2 saturations. Chest x-ray demonstrates new bilateral pulmonary infiltrates. Could this patient have TRALI?

ANSWER: Yes, Transfusion Related Acute Lung Injury (TRALI) is an uncommon but extremely serious complication of blood product transfusion. It can occur with transfusion of any blood products that contains plasma, including RBCs, FFP, whole blood, platelets, and cryoprecipitate. The risk of TRALI is estimated to be between1:2000 and 1:5000 units of blood products; and TRALI is the leading cause of transfusion-related mortality.

TRALI is most commonly caused by donor plasma containing anti-leukocyte antibodies, which react with neutrophils in the pulmonary micro-vasculature of the recipient, leading to increased vascular permeability and a pulmonary capillary leak syndrome resembling ARDS.

By definition, TRALI occurs during or within 6 hours of transfusion of a plasma-containing blood product. Symptoms include sudden onset of respiratory distress with clinical and x-ray evidence of acute bilateral pulmonary edema. Hypotension and fever are often present. TRALI is a diagnosis of exclusion and must be distinguished from the more common Transfusion Associated Circulatory Overload (TACO). BNP and NT-pro-BNP levels can be elevated in both conditions and do not reliably distinguish between the two diagnoses. As opposed to TACO, TRALI does not respond to diuretics. Treatment of TRALI is supportive; symptoms typically resolve within 72 hours. Mortality is 5-10%.

If you suspect a patient may have TRALI, it is extremely important to contact your pathologist or blood bank immediately. Since TRALI is often caused by antibodies in donor plasma, the blood donor center must be contacted to quarantine any remaining products from the suspect donors. Suspect donors are tested for anti-leukocyte antibodies, and donors implicated in an episode of TRALI are evaluated for continued eligibility to donate blood products.

Useful References:

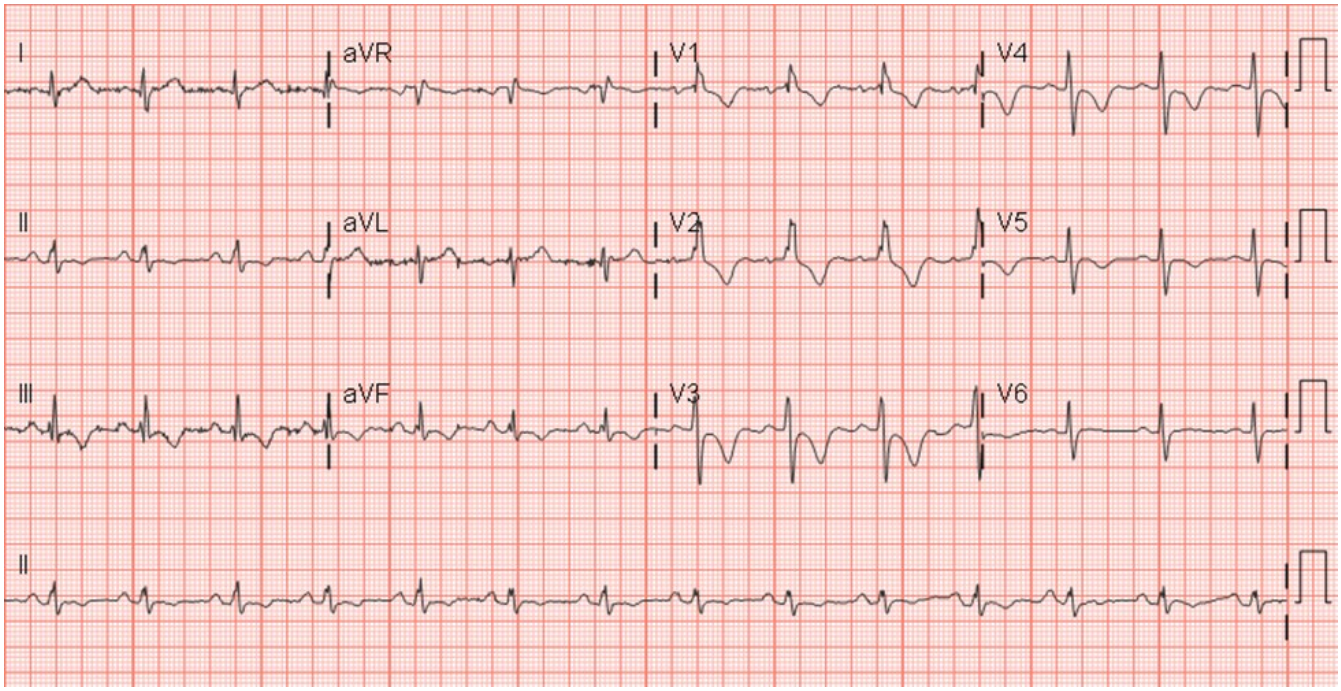
1. Curtis BR, McFarland JG. Mechanisms of Transfusion-Related Acute Lung Injury (TRALI): Anti-Leukocyte Antibodies. Crit Care Med. 2006; 34(5): S118-S123.
2. Guangxi L, Daniels CE, Kojicic M, Krpata T, Wilson GA, Winters JL, Breanndan Moore S, Gajic O. The Accuracy of Natriuretic Peptides (BNP and NT-pro-BNP) in the Differentiation between

Transfusion Related Acute Lung Injury (TRALI) and Transfusion Related Circulatory Overload (TACO) in the Critically Ill. Transfusion. 2009 January; 49(1): 13-20.

3. Petrides M, Stack G, Cooling L, Maes LY. (2007). *Practical Guide to Transfusion Medicine, 2nd Edition*. Bethesda, Maryland: AABB Press.

Send your questions to coberlye@health.missouri.edu to be published in future editions of the Missouri Hospitalist.

An Electrocardiogram that Tells You All You Need to Know

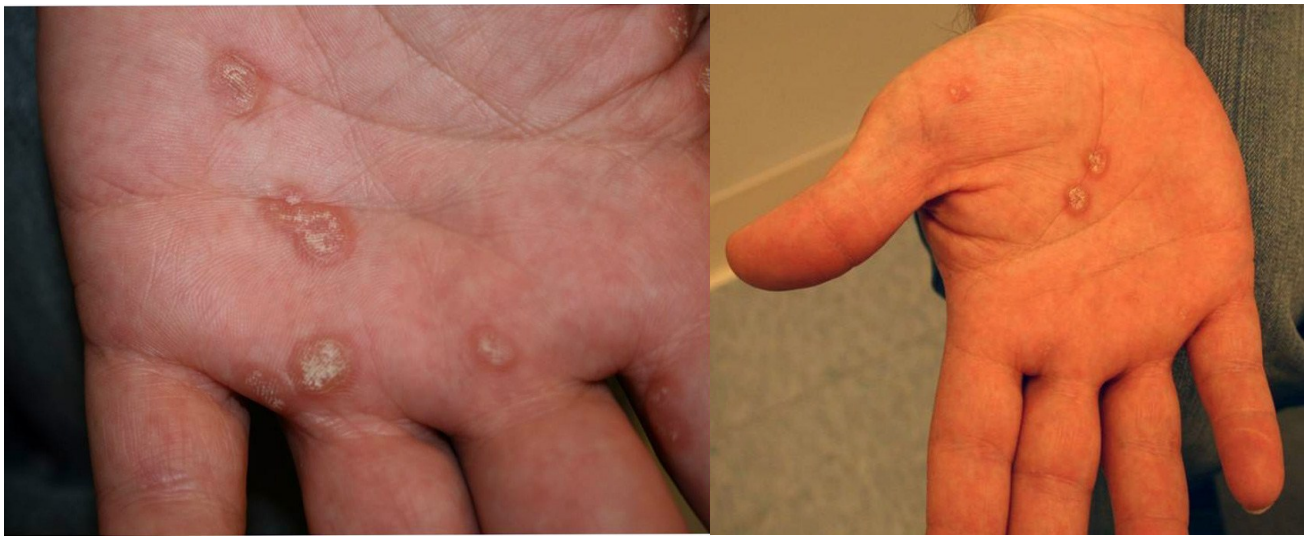


This is a 66 year old woman with progressive dyspnea on exertion for 7 months. Based on the ECG findings, what further evaluation is indicated?

Answer: Page 12

SPOT DIAGNOSIS

Question: A 40 year old male presented with a five week history of rash. His primary physician had initially treated him for eczema, without improvement. What is the diagnosis?



Answer: Page 12

ID Corner

New Sepsis Guidelines

A number of national groups have gotten together and issued new guidelines for the management of severe sepsis and septic shock, led by our former Pulmonary and Critical Care division director Phillip Dellinger. They are available on IDSA practice guidelines web site.

Dellinger RP et al. Surviving sepsis campaign: International guidelines for the management of severe sepsis and septic shock: 2012. Critical Care medicine 2013;41: 580-637. http://www.idsociety.org/uploadedfiles/idsa/guidelines-patient_care/idsa_practice_guidelines/fever_and_infections/2013%20sepsis%20guidelines.pdf

Answers:

ECG:

Mary L. Dohrmann, MD
Professor of Clinical Medicine
Division of Cardiovascular Medicine
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The ECG shows right ventricular hypertrophy with associated ST-T abnormalities. The axis is rightward, and there are both prominent initial forces in V1 and V2 as well as deep narrow S in V5 and V6 greater than 3 mm. The ECG could be mistaken for right bundle branch block; however, the terminal S in lead I and V6 is not wide and the QRS duration is not greater than 120 msec. In a patient with RVH, initial evaluation should include arterial saturation, chest x-ray, and echocardiogram. Physical examination upon presentation in this patient demonstrated an S4 with respiratory variation and a prominent P2 component of the second heart sound, suggesting RV dysfunction and pulmonary hypertension, respectively. A top priority in any patient with pulmonary hypertension, absent evidence of intra-cardiac shunt, is to exclude pulmonary thromboembolic disease. This patient had severe pulmonary hypertension by echocardiogram with an estimated RV pressure of 90 mm Hg. Ventilation-perfusion scan demonstrated multiple segmental mismatches consistent with bilateral pulmonary emboli.

Spot Diagnosis:

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St. Louis, MO

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Secondary syphilis. The image demonstrates the well-circumscribed, scale-covered, erythematous plaques characteristic of secondary syphilis. Rapid plasma regain (RPR) was 1:256. He received a single dose of 2.4 million units of benzathine penicillin G intramuscularly, with resolution of his rash. The patient reported high risk sexual contact and was noted to seroconvert, with a positive HIV test 3 months later. He returned for repeat testing within the year, and had a negative RPR.

MISSOURI HOSPITALIST SOCIETY

CONFERENCE CALENDER

Care of the Hospitalized Patient 2013

Date: April 27, 2013 7:30AM - 5:00 PM
Venue: Eric P. Newman Education Center, Washington University Medical Center, St. Louis, MO

Society of Hospital Medicine, St. Louis Chapter Meeting

Date: May 2, 2013 6:30
Venue: McCormick & Schmicks, West County Center, St. Louis, MO
MRussell@dom.wustl.edu

Missouri ACP 2013 CME Meeting: Updates in Internal Medicine

Dates: September 26 - 29, 2013
Venue: Tan-Tar-A, Osage Beach, MO

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Archived Issues:
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Front page photo: Courtesy of Jami Thompson, Medical Student/Resident Program Specialist, Internal Medicine, University of Missouri- Columbia