Treating Chronic Pain: Residents' Attitudes and Behavior toward Managing Patients on Chronic Opiate Therapy

Jana K. Zaudke, M.D., M.A.[1], Edward F. Ellerbeck, M.D., M.P.H.[2]
University of Kansas Medical Center, School of Medicine-Kansas City
[1]Department of Family Medicine
[2]Department of Preventive Medicine and Public Health

Abstract

Background. Primary care physicians care for many chronic non-cancer pain (CNCP) patients, yet rarely utilize the Pain Medication Agreement (PMA) and the random Urine Drug Screen (UDS) as tools to monitor for adherence to therapy. We surveyed family medicine residents to describe their preparation for CNCP management, characterize their clinical encounters with CNCP patients, and document their current management practices.

Methods. Family Medicine residents in a large academic medical center were surveyed about CNCP management using a 30-item instrument. This instrument was modified from previously conducted surveys. Univariate data were characterized by response rate.

Results. Of the 24 residents who completed the survey, 54% perceived their residency training in CNCP management to be good and 96% of them rated patient care as a useful modality for preparation for CNCP management. When asked to characterize their encounters with CNCP patients, 59% of resident physicians perceived that visits with CNCP patients take longer. Only 25% found the care of CNCP patients rewarding and only a third of residents were as confident managing CNCP as diabetes. While all residents reported that the PMA was helpful when managing CNCP, only two residents reported having ordered a random UDS on all of their patients within the last six months.

Conclusions. Although residents perceive the management of CNCP negatively, they reported good preparation for CNCP management. In addition, residents reported high utilization of the PMA. Use of the random UDS was surprisingly low. Further study is warranted to determine which educational modalities are linked to utilization of CNCP management strategies and what barriers and biases prevent adoption of the random UDS.

KJM 2011; 4(1):1-5.

Introduction

Approximately 70 million Americans currently have chronic non-cancer pain (CNCP) defined as persistent pain lasting for more than three months.[1] Primary care physicians care for a significant proportion of these patients. As physicians have grown more comfortable treating CNCP with chronic opiate therapy (COT), there has been a concomitant increase in prescription opioid misuse, medication diversion, and medication overdose.[2-3]

Recent consensus guidelines recommended the use of Pain Medication Agreements (PMA) and random Urine Drug Screens (UDS) for monitoring adherence to drug therapy, but primary care physicians rarely use these tools.[4-8] Poor utilization of PMA and UDS may be a product of poor preparation for CNCP management.[9-12] On the other hand, physicians may find these tools to be unhelpful. To better understand the impact of residency training on the util-

ization of the PMA and random UDS, residents were surveyed about their preparation for CNCP management, the quality of their clinical encounters with CNCP patients, and their current management practices.

Methods

Setting and subjects. Thirty residents in a family medicine residency program at a large academic medical center located in the Midwest were surveyed. Residents saw patients at one of two family practice locations between two and four half-days a week. Although a PMA was available for use at both clinical sites at the time of the study, there were no specific guidelines for CNCP management within the resident clinics.

Data collection. A 30-item survey was developed that utilized modified items from previously conducted surveys.[13,14] A draft version of this instrument was pilot tested and items were modified to enhance clarity. The survey was divided into three sections. All items used a 5-point Likert scale for responses. First, resident physicians were surveyed about their preparation for CNCP management. Second, residents were asked to rate their level of agreement with statements about the quality of their clinical encounters with CNCP patients. Third, residents were asked to rate the frequency with which they utilized the PMA and random UDS for CNCP management. In addition, residents were asked to rate the helpfulness of these tools.

In the fall of 2008, the survey was distributed and collected on the same day during a resident didactic session. Participation was voluntary. The project was approved under 'exempt' status by the institutional Human Subjects Committee.

Data analysis. Univariate data were characterized by response rate. For bivariate data, two-by-two tables were constructed to detect factors associated with level of training, level of preparation, and frequency of encounters. Fisher's exact and Chi-square tests were used when appropriate and a p-value of less than or equal to 0.05 was the threshold for statistical significance.

Results

Of the 30 eligible residents, 24 (80%) completed the survey. Of these, 21 respondents (88%) reported that medical school provided poor to fair preparation for management of CNCP and 13 (54%) reported that residency provided good preparation for management of CNCP. During residency training, 20 respondents (83%) rated patient care as excellent to outstanding in terms of CNCP management training. Only 11 residents (46%) rated time spent with a preceptor as excellent to outstanding for preparation. Response ratings for the usefulness of educational modalities in preparing residents for CNCP management are shown in Table 1.

When asked about the quality of their clinical encounters with CNCP patients, 14 residents (58%) agreed that visits with CNCP patients take longer. Only six residents (25%) agreed that they find care of CNCP patients rewarding. When asked about confidence, 13 (54%) disagreed with the statement that they are just as confident managing CNCP as diabetes.

When asked about current management practices, all residents, except one, reported some degree of utilization of the PMA. When asked about utilization of the random UDS, 15 (63%) reported that they had ordered few to none for their CNCP patients within the six months prior. Of note, only two residents reported having ordered a random UDS on all of their patients within the last six months.

All residents reported that the PMA was helpful in preventing early and after-hours refill requests (see Table 2). All residents

reported that PMA was helpful in providing rules that can be enforced. When asked about PMA violations, nine residents (38%) reported that they had fired a patient from the clinic within the last six months. Of concern, eight residents (33%) reported having been verbally or physically threatened over a conflict born out of violation of a patient's PMA.

Two-by-two tables were constructed to detect factors associated with level of training, level of preparation, and frequency of encounters. No significant associations were found.

Discussion

Although consensus guidelines recommended the use of the PMA and random UDS to monitor for adherence to therapy, primary care physicians rarely use these tools.[4-8] In this study, the impact of residency training on utilization of these

Table 1. Usefulness of educational modalities for preparation for CNCP management.

Educational Modality, n (%)	N/A	Poor	Fair	Good	Excellent	Outstanding
Standardized patients	8 (33)	4 (17)	3 (13)	7 (29)	2 (8)	0 (0)
Time spent with preceptor	1 (4)	2 (8)	5 (21)	5 (21)	11 (46)	0 (0)
Case-based presentations	0 (0)	3 (13)	3 (13)	12 (50)	6 (25)	0 (0)
Lectures	2 (8)	1 (4)	4 (17)	13 (54)	3 (13)	1 (4)
Self-study	0 (0)	0 (0)	6 (25)	10 (42)	8 (33)	0 (0)
Patient care	0 (0)	1 (4)	0 (0)	3 (13)	15 (63)	5 (21)
Personal experience with CNCP	8 (33)	2 (8)	3 (13)	6 (25)	5 (21)	0 (0)

Table 2. Helpfulness of Pain Medication Agreement for CNCP management.

	Not Helpful	Somewhat Helpful	Helpful	Very Helpful	Extremely Helpful
Prevention of, n (%)*					
Early refill requests	0 (0)	1 (4)	6 (27)	6 (27)	9 (41)
After-hours refill requests	0 (0)	1 (4)	4 (18)	6 (27)	11 (50)
Requests for refills after medications are lost or stolen	1 (4)	2 (9)	3 (14)	7 (32)	10 (45)
Monitoring for, n (%)*					
Abuse	2 (9)	2 (9)	4 (18)	8 (36)	6 (27)
Addiction	4 (18)	4 (18)	2 (9)	8 (36)	4 (18)
Diversion	2 (9)	3 (14)	4 (18)	7 (32)	6 (27)
Providing for, n (%)**					
Rules that can be enforced	0 (0)	0 (0)	3 (13)	7 (30)	13 (57)
Grounds for termination from clinic	0 (0)	1 (4)	2 (9)	6 (26)	14 (61)

*n = 22. **n = 23.

tools was investigated. Residents rated their preparation for CNCP management to be good and reported high utilization of the PMA. Use of the random UDS, however, was low.

Our first objective was to describe residents' preparation for CNCP management. The majority of residents perceived their preparation to be good. Of note, patient care was rated as the most useful modality for preparation. Patient care is not a traditional educational modality like lectures, case-based presentations, and time spent with a preceptor. In addition, patient care is highly variable within and between residency programs. Further study is warranted to determine which educational modalities are linked to utilization of CNCP management strategies.

Our second objective was to characterize the quality of clinical encounters with CNCP patients. Previous studies with internal medicine residents found CNCP visits to be less satisfying than visits for general medical problems.[13] In our study, residents reported seeing CNCP patients often, and, like their internal medicine colleagues, they perceived these visits negatively. The majority of residents perceived that visits take longer, that care is not rewarding, and that they lack confidence for caring for CNCP patients compared to patients with diabetes. In addition, a third of the residents reported having been verbally or physically threatened in the context of CNCP management.

Our third objective was to describe current management practices. A previous study with internal medicine residents found the PMA to be useful when managing CNCP.[14] Yet, in the same study, only 37% of internal medicine residents reported that the majority of their CNCP patients had a PMA in the chart. In our study, 19 residents (79%) reported that their CNCP patients have a PMA in the chart often or always. Residents perceived the PMA to be helpful for preventing inappropriate refills and monitoring for abuse, addiction, and diversion. While managing CNCP, residents have to be aware of signs of misuse, abuse, addiction, and diversion. Our study underscores how important the PMA is to residents in this regard.

Interestingly, our study revealed that residents are not monitoring for adherence with the random UDS regularly. To our knowledge, this was the only study to date addressing resident use of the random UDS in managing CNCP. Residents were either not aware that they can order a random UDS for their CNCP patients or they were unwilling to do so. Asking a patient for a random UDS may precipitate threatening patient behavior. Over a third of surveyed residents reported being verbally or physically threatened over a conflict related to pain medication. Residents need to be taught not only how to use the random UDS to confirm compliance, but how to do so safely within the clinical setting. Further study is warranted to understand the barriers and biases preventing use of this tool.

Our study had a number of limitations. First, we surveyed family medicine residents in one training program. Our response rate was high, but our sample size was small. In addition, our findings may be unique to our training site and biased by self-report. Last, our findings do not address patient-important outcomes.

Conclusions

Residents reported high utilization of the PMA while use of the random UDS was low. Further study is warranted to determine which educational modalities are linked to utilization of these management tools and what barriers and biases prevent adoption of the random UDS.

References

[1] Brunk D. Chronic pain is public health problem. Family Practice News 2009; 39(21):7.

[2] Hall AJ, Logan JE, Toblin RL, et al. Patterns of abuse among unintentional pharmaceutical overdose fatalities. JAMA 2008; 300(22):2613-2620.

[3] Harris G. FDA to place new limits on prescriptions of narcotics**.** February 9, 2009. Accessed at: www.nytimes.com.

[4] McLellan AT, Turner B. Prescription opioids, overdose deaths, and physician responsibility. JAMA 2008; 300(22): 2672-2673.

[5] Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. J Pain 2009; 10(2):113-130.

[6] Bhamb B, Brown D, Hariharan J, Anderson J, Balousek S, Fleming MF. Survey of select practice behaviors by primary care physicians on the use of opioids for chronic pain. Curr Med Res Opin 2006; 22(9):1859-1865.

[7] American Academy of Pain Medicine and American Pain Society. The use of opioids for the treatment of chronic pain: A consensus statement from the American Academy of Pain Medicine and the American Pain Society. Clin J Pain 1997; 13(1):6-8.

[8] Sinatra R. Opioid analgesics in primary care: Challenges and new advances in management of noncancer pain. J Am Board Fam Med 2006; 19(2):165-177.

[9] Darer, JD, Hwang W, Pham HH, Bass EB, Anderson G. More training needed in chronic care: A survey of US physicians. Acad Med 2004; 79:541-548.

[10] Blumenthal D, Gokhale M, Campbell EG, Weissman JS. Preparedness for clinic practice: Reports of graduating residents at academic health centers. JAMA 2001; 286(9):1027-1034.

[11] Cohen AJ. Caring for the chronically ill: A vital subject for medical education. Acad Med 1998; 73(12):1261-1266.

[12] Olsen Y, Daumit GL. Opioid prescribing for chronic nonmalignant pain in primary care: Challenges and solutions. Adv Psychosom Med 2004; 25:138-150.

[13] Chen JT, Fagan MJ, Diaz JA, Reinert SE. Is treating chronic pain torture? Internal medicine residents' experience with patients with chronic nonmaligant pain. Teach Learn Med 2007; 19(2):101-105.

[14] Fagan MJ, Chen JT, Diaz JA, Reinert SE, Stein MD. Do internal medicine residents find pain medication agreements useful? Clin J Pain 2008; 24(1):35-38.

Acknowledgements

We thank Daniel Alford M.D., M.P.H. for his guidance during the 2008 Chief Resident Immersion Training (CRIT) Program sponsored by the National Institute of Drug Abuse. We are grateful to Dr. Joyce Chen and Dr. Mark Fagan at Brown Medical School for the use of their survey which was modified for this project. We also thank Dr. John Delzell and Dr. Heidi Chumley for help with editing. And last, we are grateful for the students who helped modify and pilot test the survey: Thomas Champion, Joseph Gillespie, and Phat Long.

Keywords: pain management, health knowledge, attitudes, practice, opioid analgesics, medical residency, family practice

Severe Nitrofurantoin-Induced Lung Toxicity

Rami Jambeih, M.D.[1], John Flesher, M.D.[1,3], Joe J. Lin, M.D.[2,4]
University of Kansas
School of Medicine – Wichita
[1]Department of Internal Medicine
[2]Department of Pathology
[3]PMA Pulmonology, Wichita, KS
[4]Southcentral Pathology Laboratory, Wichita, KS

Introduction

Nitrofurantoin is a frequently used antibiotic for treatment and prophylaxis against urinary tract infections. It is a relatively safe medication with rare side effects, however, cases of severe pulmonary injury secondary to its use have been reported.[1] We report a patient with pulmonary infiltrates with eosinophilia, pleural effusion, and interstitial lung disease induced by the chronic use of nitrofurantoin. The association of severe eosinophilic bronchopneumopathy with interstitial fibrosis makes this case rare and shows the possible deleterious effect of chronic nitrofurantoin use.

Case Report

An 83-year-old male with a two-year history of chronic cough and shortness of breath presented with progressive worsening of symptoms over the two months prior to presentation. He denied hemoptysis, fever, chills, or sick contacts. He was a non-smoker and denied any occupational exposures.

The patient was taking nitrofurantoin 100 mg daily for recurrent urinary tract infections. It was started two years ago before his symptoms began. His past medical history was significant for coronary artery disease and diabetes mellitus II treated with insulin.

On physical examination, he had no fever. Oxygen saturation by pulse oximetry was 61% on room air and increased to 90% on four liters of oxygen. Bilateral coarse crackles were noted on both lung fields, more prominent on the right side with decreased air entry at the bases. Laboratory workup revealed a normal blood count, chemistry, and liver panel. Arterial blood gas analysis revealed hypoxemia with a PaO2 of 66 mmHg on 6 liters oxygen, PCO2 was normal.

A chest radiograph showed diffuse, bilateral infiltrates most concentrated in the right upper lobe, and a small right pleural effusion. A review of previous chest x-rays over the prior two years revealed the same findings with temporal progression (see Figure 1). High resolution CT scan of the chest showed diffuse fibrosis, right upper lobe and lingular consolidation, and small right pleural effusion (see Figure 2).

The patient underwent a bronchoscopy with bronchoalveolar lavage and trans-bronchial biopsies. The bronchoalveolar lavage was obtained from the right upper lobe and revealed numerous white blood cells with significant eosinophilia (25%). Fungal and bacterial cultures were negative as well as viral PCR, pneumocystis carinii pneumonia (PCP) stain, and acid fast bacilli

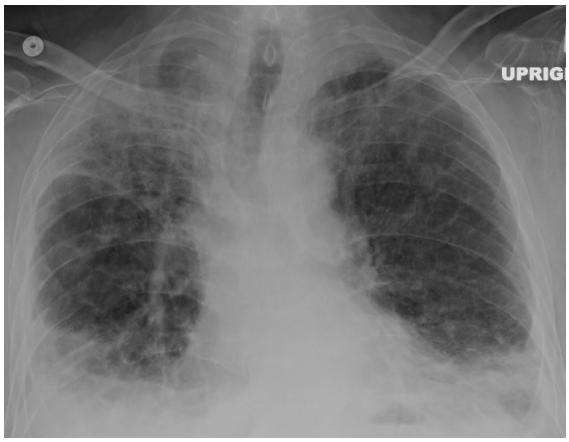


Figure 1. A chest x-ray revealed bilateral interstitial infiltrates more prominent in the right upper and lower lung and at the periphery. Also, a small right pleural effusion is noted.

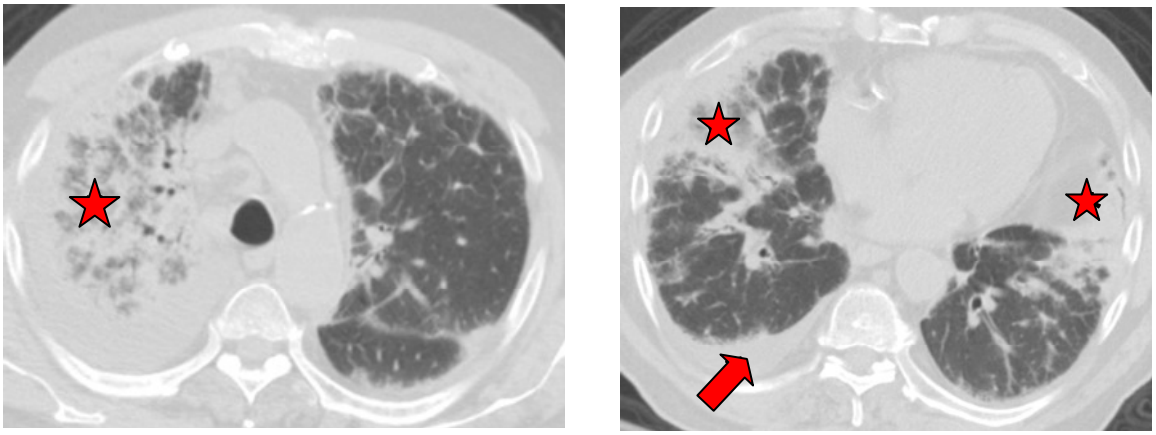


Figure 2. A high resolution CT scan of the lung showed mild right pleural effusion (arrow) and right upper lobe, right lower lobe, and lingular infiltrate (stars).

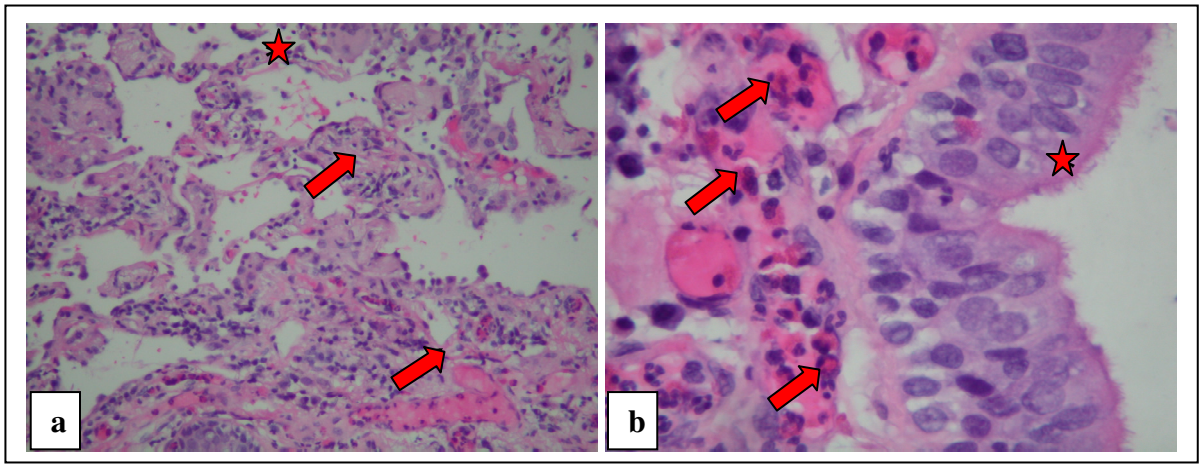


Figure 3. A transbronchial biopsy showing: (a) a normal alveoli (star) compared to thickened alveoli with fibrosis (arrows) and (b) of normal bronchial epithelium (star) with numerous eosinophils (arrows) involving the adjacent connective tissue.

(AFB) stain. Transbronchial biopsies from the right upper lobe showed fibrosis and eosinophilic infiltrates without evidence of malignancy (see Figure 3).

Drug-induced lung toxicity was suspected and nitrofurantoin was stopped. The patient was treated with prednisone 20 mg daily. There was marked clinical and radiologic improvement in a follow-up examination one month later.

Discussion

Based on World Health Organization criteria[2], nitrofurantoin was the "probable" cause of the lung toxicity. There was a reasonable time sequence of the lung toxicity to administration of the drug. It was unlikely to be attributed to concurrent disease or other drugs or chemicals, and followed a clinically reasonable response on withdrawal of nitrofurantoin.

Nitrofurantoin has been associated with several lung diseases. The first pulmonary reaction to nitrofurantoin was described in 1957.[2] Subsequently, cases of bronchiolitis obliterans with organizing pneumonia (BOOP),[3] pulmonary infiltrates with eosinophilia (PIE) syndrome,[4] diffuse alveolar hemorrhage,[5] diffuse alveolar damage (DAD),[6] and acute, subacute, and chronic interstitial lung disease have been reported.[7]

Two forms of nitrofurantoin-induced lung injury have been described: acute and chronic. The acute form is a hypersensitivity reaction (type I or III),[8] clinically characterized by fever (82%), dyspnea (60%), cough (43%), rash (20%), chest pain, and cyanosis.[9,10] On the other hand, the chronic form may be either an allergic or a toxic response,[8] and usually presents with nonspecific symptoms including dyspnea (73%), dry cough (63%), and fatigue (37%). Fever might also occur in chronic forms but it is unusual.[10] Oxidative stress also has been implicated in lung injury as reported by in vivo studies conducted on rats.[11] Symptoms usually start within a few days in acute forms, while chronic forms manifest after 1 to 6 months of treatment.[10]

Among the pulmonary toxicity of nitrofurantoin, PIE syndrome rarely has been reported.[12] It was first described after the use of sulfonamide, however, currently more than 100 drugs can cause this disease. The most common medications causing PIE syndromes include antibiotics (e.g., minocycline, sulfasalazine, sulfamethoxy-pyridazine, sulfamethoxazole), angiotensin-converting enzyme inhibitors, nonsteroidal anti-inflammatory drugs, imipramine, and carbamazepine.

The diagnosis of PIE syndrome is established by the presence of pulmonary infiltrates and eosinophilia, detected in blood, bone marrow, bronchoalveolar lavage, or lung tissue.[13] Marked peripheral eosinophilia may not be present primarily because of the sequestration of eosinophils in the lung tissue or secondary to previous use of steroids.

The cause of PIE syndrome is not only limited to drugs. It includes infectious causes (e.g., fungi or parasites), and idiopathic and autoimmune diseases.[14] It also was reported in patients with AIDS, lymphoma, a variety of inflammatory lung diseases, and collagen vascular diseases.[15]

Treatment of PIE syndrome varies depending on the etiology.[16] In case of drug-induced syndrome, the treatment consists of withdrawal of the offending agents. The same applies for the other drug-induced infiltrative lung diseases. Patients with mild-to-moderate inflammatory interstitial lung diseases (ILD) will respond quickly, whereas drugs that cause acute interstitial reactions or pulmonary fibrosis may not. In this situation, corticosteroids often are used in conjunction with drug discontinuation. Discontinuation is more complex in patients on multiple drugs. In

this case, sequential discontinuation sometimes is performed beginning with the drug most likely to have caused the syndrome, then withdrawing the others until improvement occurs.[16]

In our case, the presence of eosinophils in the lung tissue as well as the significant eosinophilia (25%) in the bronchoalveolar lavage confirmed the diagnosis of pulmonary eosinophilia with infiltrates. Prednisone was initiated because of the severity of symptoms and the presence of fibrosis on the pathology. This case showed the possible deleterious effect of a commonly used medication. It also emphasized the importance of monitoring patients taking nitrofurantoin for prolonged periods, at least by history, and possibly regular chest x-rays and pulmonary function tests.[17]

References

[1] Medsafe. Prescriber update articles. Pulmonary reactions with nitrofurantoin. May 2002. Accessed at: http://www.medsafe.govt.nz/profs/PUarticles/nitrofurant.htm.

[2] The Uppsala Monitoring Centre. Causality assessment of suspected adverse reactions. Accessed at: http://www.who-umc.org/DynPage.aspx?id=22682.

[3] Fisk AA. Brief recording: Anaphylactoid reaction to nitrofurantoin. N Engl J Med 1957; 256:1054.

[4] Fawcett IW, Ibrahim NB. BOOP associated with nitrofurantoin. Thorax 2001; 56:161.

[5] Drug-induced lung disease: The price of progress. Medical Staff Conference, University of California, San Francisco. Calif Med 1973; 119:48-55.

[6] Meyer MM, Meyer RJ. Nitrofurantoin-induced pulmonary hemorrhage in a renal transplant recipient receiving immuno-suppressive therapy: Case report and review of the literature. J Urol 1994; 152: 938-940.

[7] Magee F, Wright JL, Chan N, et al. Two unusual pathological reactions to nitrofurantoin: Case reports. Histo-pathology 1986; 10:701-706.

[8] Qureshi MM. Interstitial lung disease caused by chronic nitrofurantoin reaction; case report. Wis Med J 1984; 83:20-22.

[9] Holmberg L, Boman G, Böttiger LE, Eriksson B, Spross R, Wessling A. Adverse reactions to nitrofurantoin. Analysis of 921 reports. Am J Med 1980; 69**:**733-738.

[10] Holmberg L, Boman G. Pulmonary reactions in nitrofurantoin. 447 cases reported to the Swedish Adverse Drug Reaction Committee 1966-1976. Eur J Respir Dis 1981; 62:180-189.

[11] Sovijärvi AR, Lemola, M, Stenius, B, Idänpään-Heikkilä J. Nitrofurantoin-induced acute, subacute and chronic pulmonary reactions. Scand J Respir Dis 1977; 58:41-50.

[12] Suntres ZE, Shek PN. Nitrofurantoin-induced pulmonary toxicity. In vivo evidence for oxidative stress-mediated mechanisms. Biochem Pharmacol 1992; 43:1127-1135.

[13] Vaughan Jones R, Goldman L. Persistent eosinophilia after nitrofurantoin. Lancet 1968; 291:306.

[14] Benzaquen-Forner H, Dournovo P, Tandjaoui-Lambiotte H, et al. [Hypoxic eosinophilic pneumonia in two patients treated with ACE inhibitors.] (French.) Rev Mal Respir 1998; 15:804-810.

[15] Citro LA, Gordon ME, Miller WT. Eosinophilic lung disease (or how to slice P.I.E.). Am J Roentgenol Radium Ther Nucl Med 1973; 117:787-797.

[16] Saukkonen JJ. Pulmonary Eosinophilia. November 20, 2009. Accessed at: http://emedicine.medscape.com/article/301070-overview.

[17] Schwarz MI, King TE. Interstitial Lung Disease. 4th edition. Hamilton, ON: BC Decker, 2003.
[18] Parker G. Failure to adequately monitor liver and lung function. MDU J 2007; 23: 24-25.

Keywords: nitrofurantoin, interstitial lung disease, drug toxicity, case report

Hemorrhage of Ectopic Deciduosis Necessitating Emergent Surgical Resection

John H. Park, M.D.[1], Patricia Thomas, M.D.[2], Danielle Staecker, M.D.[3]
University of Kansas Medical Center, Kansas City, KS
[1]Department of Radiation Oncology
[2]Department of Pathology
[3]Department of Obstetrics and Gynecology

Introduction

Ectopic deciduosis is a common finding in pregnant patients and is rarely symptomatic.[1] Decidua is the name that is applied to the mucous membrane of the uterus in preparation of the ovum during the cytotrophic phase of gestation.[2] Although it is a common phenomenon, there are only nine reported cases of life-threatening intraperitoneal hemorrhage and one incidence of massive gastrointestinal hemorrhage during pregnancy in the English language since 1900.[3] We present a unique case of life-threatening hemorrhagic deciduosis at the time of caesarean section.

Case Report

A 26-year-old primigravida, on an out-of-state business trip and at 35 weeks gestational age with an obstetric history remarkable only for gestational diabetes mellitus, type A_1 (GDMA1), was admitted to labor and delivery for painful contractions and vaginal bleeding. The patient underwent a primary, low flap caesarean section for failure of fetal descent and persistent deep variable decelerations of fetal heart rate. Significant post-partum bleeding was noted and the patient was treated for uterine atony with oxytocin and methylergonovine maleate.

The pelvis was explored and a massive amount of blood was found along the posterior aspect of the uterus with abundant hemorrhagic lesions covering the uterus and adnexae. Other findings included a left hemicolon densely adherent to the left fallopian tube and ovary, an inflammatory process obliterating the posterior cul-de-sac, and a fungating hemorrhagic vascular mass of tissue on the antimesenteric portion of proximal sigmoid colon.

A 9.3 cm segment of colon was resected containing florid nodules of deciduosis. Surgical pathology (see Figures 1 and 2) revealed multiple extensive areas of ectopic decidual tissue and acute hemorrhage in the colonic serosa, polypoid submucosal nodules, pericolonic fat, left fallopian tube and left ovary; the largest nodule measured 5.0 x 0.4 x 0.4 cm. The right fallopian tube and ovary were left intact and the uterus was returned to the abdominal cavity.

During her operative course, there was an estimated blood loss of 1.5 liters and six units of packed red blood cells were transfused along with six liters of crystalloid. She was transferred to the surgical ICU on a ventilator, because of the significant fluid changes and a prolonged surgery. The patient was stabilized without complications and discharged from the hospital the following week. She has since been lost to follow-up.

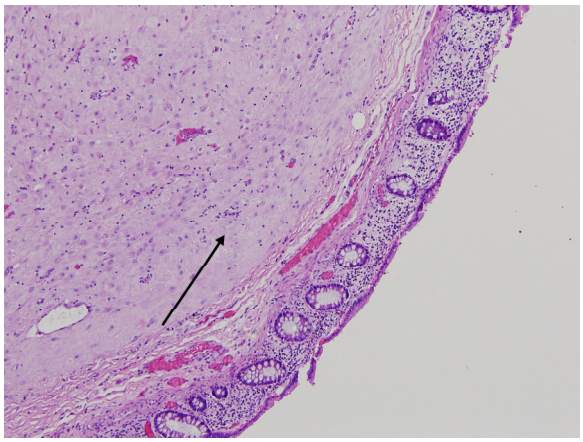


Figure 1. Deciduosis within submucosa of the colon (hematoxylin and eosin stain, x 100).

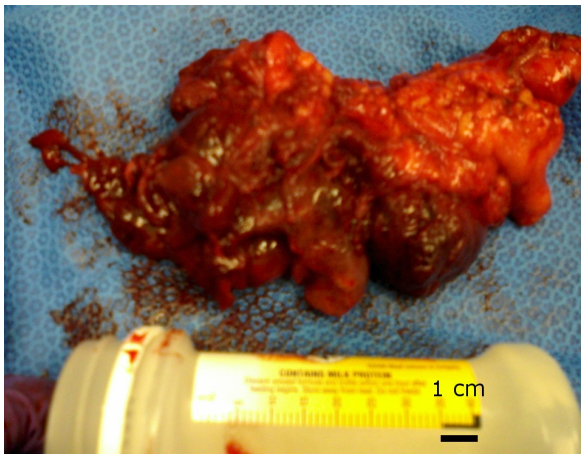


Figure 2. Deciduosis along the margin of resected colon.

Discussion

The etiology of deciduosis is unclear. It may be related to increased levels of progesterone and its effects on sub-coelomic stromal cells during pregnancy,[4] however, ectopic deciduosis has been noted in nulliparous patients.[5,6] Malpica and colleagues[1] noted that gross massive lesions are rare and seldom evident. In most instances, lesions are only 0.2 to 2.0 cm in their maximum dimension. In contrast, our case revealed copious gross decidual lesions that surpassed these measurements.

Nine cases of life-threatening intraperitoneal decidual hemorrhaging were reported from 1900-2006.[3] Eight of the nine previous encounters of this disease presented with lower abdominal pain. Other associated symptoms included gross deciduosis peritonei obstructing labor,[1] vaginal bleeding,[7] hydronephrosis,[8] hematuria,[8] appendicitis,[9] and pneumothorax.[10]

Our patient had no previous medical history other than GDMA1 and exercise-induced asthma. Diabetes in conjunction with hypertension was tied to decidual arteriopathy,[11] but not ectopic decidualization. There were no associations with asthma.

Of the nine reported cases of intraperitoneal hemorrhage, there were two maternal and five neonatal deaths, whereas our patient and her neonate survived with little morbidity. In a similar scenario, Bashir and colleagues[12] found massive gastrointestinal hemorrhage during pregnancy caused by deciduosis of the terminal ileum and colon. Their patient, however, presented with acute, new onset, massive hematochezia at 20-weeks gestational age. The patient also had a previous history of multiple medical and gynecological complications including, renal cell carcinoma, endometriosis, and four miscarriages.

Of the nine cases reported by O'Leary[3], four had preterm births, as did our patient. There are currently no studies in the literature that included ectopic deciduosis as a cause of preterm labor, but decidua is known to produce prostaglandins.[13] The irreversible, committed step of the prostaglandin biosynthetic pathway is catalyzed by the prostaglandin endoperoxide H synthase isoenzymes (PGHS-1 and 2).

Mijovid and colleagues[13] found that PGHS-1 and 2 mRNA levels were increased in idiopathic preterm labor. The presence of ectopic decidua may have increased the level of prostaglandins and induced labor. In fact, in cases of cervical deciduosis, patients were at increased risk for miscarriage and preterm delivery.[14]

In summary, ectopic deciduosis should be considered in cases of severe hemorrhage during labor in patients with a benign obstetric history. There should be heightened concern in preterm labor patients as ectopic decidua may increase prostaglandin levels. Though all conjectures about preterm labor and ectopic deciduosis are speculative, further investigation may be warranted.

References

[1] Malpica A, Deavers MT, Shahab I. Gross deciduosis peritonei obstructing labor: A case report and review of the literature. Int J Gynecol Pathol 2002; 21:273-275.

[2] Melody GF. Deciduation and massive hemorrhage of the omentum in the final month of pregnancy. West J Surg Obstet Gynecol 1950; 58:460-462.

[3] O'Leary SM. Ectopic decidualization causing massive postpartum intraperitoneal hemorrhage. Obstet Gynecol 2006; 108(3 Pt 2):776-779.

[4] Zaytsev P, Taxy JB. Pregnancy-associated ectopic decidua. Am J Surg Pathol 1987; 11:526-530.

[5] Elemenoglou J, Trihia H, Zizi-Serbetzoglou A, Bournia H, Vasilakaki T. Deciduoma of the sigmoid colon in a nulliparous woman. A case report. Eur J Gynaecol Oncol 1996; 17; 140-143.

[6] Rodriguez FJ, Abraham SC, Sendelbach KM, Nascimento AG. Florid decidual reaction mimicking gastrointestinal malignancy in a primipara woman. Histopathology 2006; 49:82-85.

[7] Orr CJ, Pedlow PR. Deciduosis of the cervix manifesting as antepartum hemorrhage and simulating carcinoma. Am J Obstet Gynecol 1961; 82:884-886.

[8] Bettinger HF. Ectopic decidua in the renal pelvis. J Pathol Bacteriol 1947; 59:686.

[9] Löfwander M, Haugen G, Hammarström C, Røkke O, Mathisen Ø. [A pregnant woman with abdominal pain and fever]. (Norwegian.) Tidsskr Nor Laegeforen 2007; 127:2528-2529.

[10] Flieder DB, Moran CA, Travis WD, Koss MN, Mark EJ. Pleuro-pulmonary endometriosis and pulmonary ectopic deciduosis: A clinicopathologic and immunohistochemical study of 10 cases with emphasis on diagnostic pitfalls. Hum Pathol 1998; 29:1495-1503.

[11] Kitzmiller JL, Watt N, Driscoll SG. Decidual arteriopathy in hypertension and diabetes in pregnancy: Immunofluorescent studies. Am J Obstet Gynecol 1981; 141:773-779.

[12] Bashir RM, Montgomery EA, Gupta PK, et al. Massive gastrointestinal hemorrhage during pregnancy caused by ectopic decidua of the terminal ileum and colon. Am J Gastroenterol 1995; 90:1325-1327.

[13] Mijovic JE, Zakar T, Angelova J, Olson DM. Prostaglandin endoperoxide H synthase mRNA expression in the human amnion and decidua during pregnancy and in the amnion at preterm labour. Mol Hum Reprod 1999; 5:182-187.

[14] Nikolov A, Negentsov N, Maĭnkhard K, Mekhandzhiev Ts. [Course of pregnancy and delivery in cases with cervical deciduosis.] (Bulgarian.) Akush Ginekol (Sofiia) 2007; 46:3-7.

Keywords: gynecologic surgical procedures, decidua, hemorrhage, pregnant women, case report

Capnocytophaga Canimorsus Septicemia Caused by a Dog Bite in an Asplenic Patient

Dalia Hammoud, M.D.[1], Rayane Nassar, M.D.[1], Martin Griffey, M.D.[1,2]
University of Kansas
School of Medicine - Wichita
[1]Department of Internal Medicine
[2]Norton County Hospital, Norton, KS

Introduction

Capnocytophaga canimorsus is a gram-negative bacillus, non-spore-forming, facultative aerobe that causes a zoonotic disease, most commonly in asplenic patients.[1] This organism has a long, fusiform appearance on gram stain. It is a member of the normal gingival flora of dogs and cats and can cause fulminant sepsis with disseminated intravascular coagulation (DIC). About 1.6 to 16% of bite wounds inflicted by dogs become infected.[2] Pasteurella multocida frequently is isolated from such wounds.[3,4] Occasionally, *Capnocytophaga canimorsus* also is isolated.[3] Splenectomy, alcoholism, and chronic lung disorder are significant risk factors.

Case Report

A 45 year-old Caucasian man presented to an outside facility with two days of abdominal pain, nausea, vomiting, shortness of air, and fever. He was anxious and in moderate distress. He required intubation secondary to tachypnea and hypoxia, then was transferred to our hospital.

The patient had been in Montana with his girlfriend for the prior three weeks. He had two abscessed teeth extracted while in Montana. He also had a tick bite and a dog bite on the right arm while in Montana (the dog was current on his immunizations).

The patient had a history of hepatitis C with a splenectomy four years prior secondary to idiopathic thrombocytopenic purpura (ITP). He was a heavy smoker and drinker with history of drug use, but no IV drugs. He enjoyed hunting and fishing, and had been fishing frequently.

On admission to our hospital, the patient was intubated. His temperature was 99.4^{o} F, pulse 130 bpm, respiratory rate 15 per minute, and blood pressure 65/40 mmHg. His oxygen saturation was 95% on the ventilator with assisted-controlled mode and the fraction of inspired oxygen was 100%.

The patient was confused and mildly agitated. He had a flushed face, poor oral hygiene, black eschar around his lips, and some icteric sclera. His heart sounds were regular and lungs were coarse to auscultation bilaterally. His abdomen was nontender. There were multiple tattoos on the extremities, trace edema, purplish discoloration above the umbilicus, arms, legs, feet, palms, and soles, with superimposed maculopapular rash. There was also an eschar on the right arm with mild ecchymosis located at the site of the previous dog bite.

His laboratory studies showed a white blood cell (WBC) count of 14900 with 26% bands, 63% segmented, 11% lymphocytes, hemoglobin 16.3mg/dl, and platelets 21000. His sodium level was 135 mEq/L, potassium 3.4 mEq, bicarbonate 21.1 mmol/L, glucose 110 mg/dl, blood urea nitrogen 21 mg/dL,

and creatinine 1.8 mg/dl. His transaminases were normal.

The patient was admitted to the intensive care unit, maintained on the ventilator, and started on piperacillin/tazobactam and pressors including norepinephrine and dopamine. On hospital day 2, he remained intubated, but was more alert and awake. He was febrile with a temperature of 101° F and had left-sided weakness. His WBC increased to 41000 with 53% bands. His total bilirubin was 2.0 mg/dL, AST 2515 U/L, ALT 946 U/L, alkaline phosphatase 75 U/L, and INR 1.7. A CT scan of the head showed no acute abnormalities. Antibiotics were changed to ampicillin/sulbactam, ceftriaxone, and doxycycline to cover skin infection and dog bite.

On hospital day 3, the pressors were titrated off. The patient had hemorrhagic and purpuric blisters on the hands and feet. A peripheral blood smear showed fusiform extracellular rods. Blood cultures were still negative.

Blisters and bruising worsened on hospital day 5 and extended to the arms and legs. Tick-borne serology was negative. The patient remained intubated on hospital day 6. His hands and feet became necrotic and required amputation. He underwent a bilateral below knee amputation. No overall change in patient's outlook occurred and the family agreed to comfort care. The patient died few days later. A polymerase chain reaction test was back weeks later and was positive for *Capnocytophaga canimorsus*.

Discussion

Capnocytophaga canimorsus, formerly called dysgenic fermenter 2 (DF-2), was first described in 1976.[5,6] The current name was given in 1989 and is based on the carbon dioxide requirement (capnocyto-phaga means "eater of carbon dioxide") and usual vector of transmission (canimorsus means "dog bite").

Capnocytophaga canimorsus, an anaerobic non-spore forming gram-negative rod, rarely but regularly, has been isolated from dog or cat bite infections (Figure 1). This organism has a long, fusiform appearance on gram stain (Figure 2). It can cause fulminant sepsis with disseminated intravascular coagulation (DIC), meningitis, endocarditis, acral gangrene, disseminated purpura, and rare ocular infections.[6,7] Persons at increased risk of developing *C. canimorsus* infections include patients who have undergone a splenectomy, are immunosuppressed, and those who abuse alcohol.[6] More than 40% of the patients have no obvious risk factors.

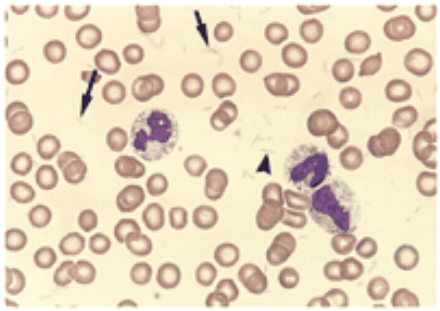


Figure 1. Peripheral blood smear showing fusiform rods 2-4 um in length (arrows) and in pairs (arrow head) mostly extracellular. (Used with permission.[8])

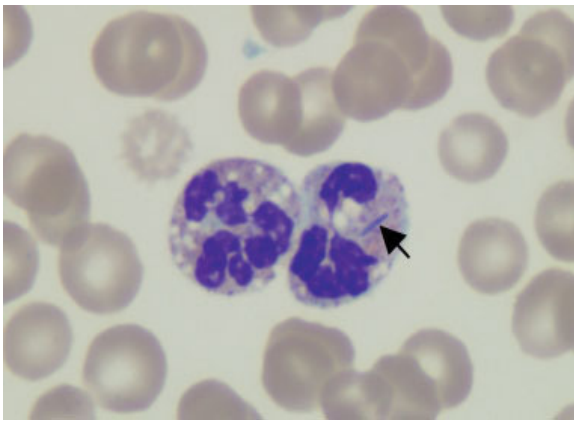


Figure 2. Wright-Giemsa stain, x100 oil immersion, showing intracellular elongated rod (arrow). (Used with permission.[9])

The clinical presentation of *C. canimorsus* infection usually involves sepsis. However, there are other clinical findings frequently present.[7,10] A maculo-papular rash is present in 13% of cases and is often purpuric (in 37%), with erythema multiforme also being described in several cases. Disseminated intravascular coagulation commonly has been associated with *C. canimorsus* septicemia (34 to 36% of cases).[7,10] Gangrenous involvement of the bite site and other areas are encountered in 15% of cases. It can involve digits, as well as entire limbs. As in our patient, gastrointestinal complaints including abdominal pain (26%), vomiting (31%), and diarrhea (26%) are commonly associated with C. canimorsus infection.[10]

Although *C. canimorsus* frequently is present in dog bite wounds, it rarely results in clinical infections.[11] This is most likely due to its slow growth, low virulence, and susceptibility to antibiotics frequently used for post-dog bite prophylaxis. Therefore, most cases of systemic infection appear in immunocompromised patients.

In one comprehensive review, 33% of systemic infections occurred in asplenic patients, 24% in alcoholics, and 5% in other immunocompromised patients.[7] Almost 41% of infections occurred in patients without any known risk factor.[7] While *C. canimorsus* has low virulence, it has a high mortality rate once systemic infection has developed. Persons with risk factors such as a history of asplenia, alcoholism, or hematologic malignancy receive antibiotic prophylaxis following animal bites.[12]

C. canimorsus infection classically is treated with penicillin G.[13] However, the increasing prevalence of beta-lactamase-producing strains of *Capnocytophaga* warrant broader first-line coverage with antibiotics such as beta-lactam/beta-lactamase inhibitors. *Capnocytophaga* is typically resistant to aminoglycosides and narrow-spectrum cephalosporins. Other active antibiotics for *C. canimorsus* include imipenem, doxycycline, rifamycin, ofloxacin, ciprofloxacin, erythromycin, and clindamycin.[13]

In conclusion, this case of fatal *C. canimorsus* emphasized that the features of a dog bite coupled with a preexisting condition of splenectomy should alert physicians to suspect this unusual organism. Furthermore, all asplenic patients after a dog bite should undergo antibiotic prophylaxis with amoxicillin/clavulanate. Since these bacteria grow slowly, laboratories also should be alerted to its potential presence, since it otherwise would be discarded as a contaminant or misidentified. Finally, physicians should inform patients with splenectomy or other immunocompromising conditions that dog ownership or bite are important risk factors for *C. canimorsus* infection.

References

1 Findling JW, Pohlmann GP, Rose HD. Fulminant gram-negative bacillemia (DF-2) following a dog bite in an asplenic woman. Am J Med 1980; 68:154-156.

2 Winkler WG. Human deaths induced by dog bites, United States, 1974-75. Public Health Rep 1977; 92:425-429.

3 Dees SB, Powell J, Moss CW, Hollis DG, Weaver RE. Cellular fatty acid composition of organisms frequently associated with human infections resulting from dog bites: Pasteurella multocida and groups EF-4, IIj, M-5, and DF-2. J Clin Microbiol 1981; 14:612-616.

4 Francis DP, Holmes MA, and Brandon G. Pasteurella multocida. Infections after domestic animal bites and scratches. JAMA 1975; 233:42-45.

5 Bobo RA, Newton EJ. A previously undescribed gram-negative bacillus

causing septicemia and meningitis. Am J Clin Pathol 1976; 65:564-569.

[6] Brenner DJ, Hollis DG, Fanning GR, Weaver RE. Capnocytophaga canimorsus sp. nov. (formerly CDC group DF-2), a cause of septicemia following dog bite, and C. cynodegmi sp. nov., a cause of localized wound infection following dog bite. J Clin Microbiol 1989; 27:231-235.

[7] Lion C, Escande F, Burdin JC. Capnocytophaga canimorsus infections in human: Review of the literature and cases report. Eur J Epidemiol 1996; 12:521-533.

[8] Alberio L, Lämmle B. Images in clinical medicine. Capnocytophaga canimorsus sepsis. N Engl J Med 1998 17; 339:1827.

[9] Wald K, Martinez A, Moll S. Capnocytophaga canimorsus infection with fulminant sepsis in an asplenic patient: Diagnosis by review of peripheral blood smear. Am J Hematol 2008; 83:879.

[10] Pers C, Gahrn-Hansen B, Frederiksen W. Capnocytophaga canimorsus septicemia in Denmark, 1982-1995: Review of 39 cases. Clin Infect Dis 1996; 23:71-75.

[11] Fischer LJ, Weyant RS, White EH, Quinn FD. Intracellular multiplication and toxic destruction of cultured macrophages by Capnocytophaga canimorsus. Infect Immun 1995; 63:3484-3490.

[12] Goldstein EJ. Bite wounds and infection. Clin Infect Dis 1992; 14:633-638.

[13] Jolivet-Gougeon A, Buffet A, Dupuy C, et al. In vitro susceptibilities of Capnocytophaga isolates to beta-lactam antibiotics and beta-lactamase inhibitors. Antimicrob Agents Chemother 2000; 44**:**3186-3188.

Keywords: capnocytophaga, hemorrhagic septicemia, splenectomy, bites, case report

Dynamic Interventricular Septal Hematoma Following Blunt Chest Trauma Presents as ST Elevation Myocardial Infarction

Priyantha Ranaweera, M.D., F.R.A.C.P., F.A.C.S.A.N.Z., F.A.C.C.,
Vikram Panwar, M.D., M.P.H.
Mercy Regional Hospital, Manhattan, KS

Introduction

Motor vehicle accidents are the most common cause of blunt chest trauma leading to cardiac complications.[1] These complications can result in arrhythmias to sudden death.[2] The left anterior descending (LAD) artery is the most common vessel involved because of its relation to the anterior chest wall.[2] Blunt trauma to the chest can cause acute myocardial infarction (AMI) from dissection of the vessel, intimal tear, or epicardial hematoma.[3]

Intramyocardial hematoma has been described after septal artery perforation during percutaneous coronary intervention, but it is less common with blunt chest trauma.[4] Diagnosis of LAD artery involvement is suggested by precordial ST changes. It usually is confirmed by invasive coronary angiography.[5] Echocardiography is helpful in diagnosing pericardial fluid collections and in delineating regional wall motion abnormalities. Its role in delineating intramyocardial hematomas is less defined.

We present a case of a 33-year-old man with blunt chest trauma, anterior ST segment elevation, and a dynamic intramyocardial hematoma.

Case Report

A 33-year-old male presented with chest pain following a motor vehicle accident. A chest CT scan was unremarkable. An electrocardiogram showed anterior ST segment elevation (Figure 1). Troponin was elevated. The echocardiogram showed anterior akinesia and a dynamic intramyocardial hematoma in the mid interventricular septum (Figure 2). The hematoma had a diameter of 11mm during systole and 20mm during diastole. It was largest beyond the end of the T wave (see Figure 2). Ejection fraction was 45%. He was transferred to a cardiac surgical facility where the coronary angiogram showed a dissection of LAD. He was managed with thrombectomy. He made an unremarkable recovery.

Discussion

This case highlighted the dynamism of an intramyocardial hematoma due to coronary flow dynamics. Coronary blood flow is maximal in diastole.[6] During systole the hematoma compressed and probably dissipated to the surrounding tissues to some extent. During diastole, the muscles relaxed and the pressure fell accommodating more blood from the surrounding tissues and also likely from the LAD through a perforation. The mechanism could have been similar to a pseudo-aneurism. However, several hours after the echocardiogram was done, the angiogram showed only a dissection and thrombus in the LAD with no perforation. It is likely that a small perforation may have sealed itself.

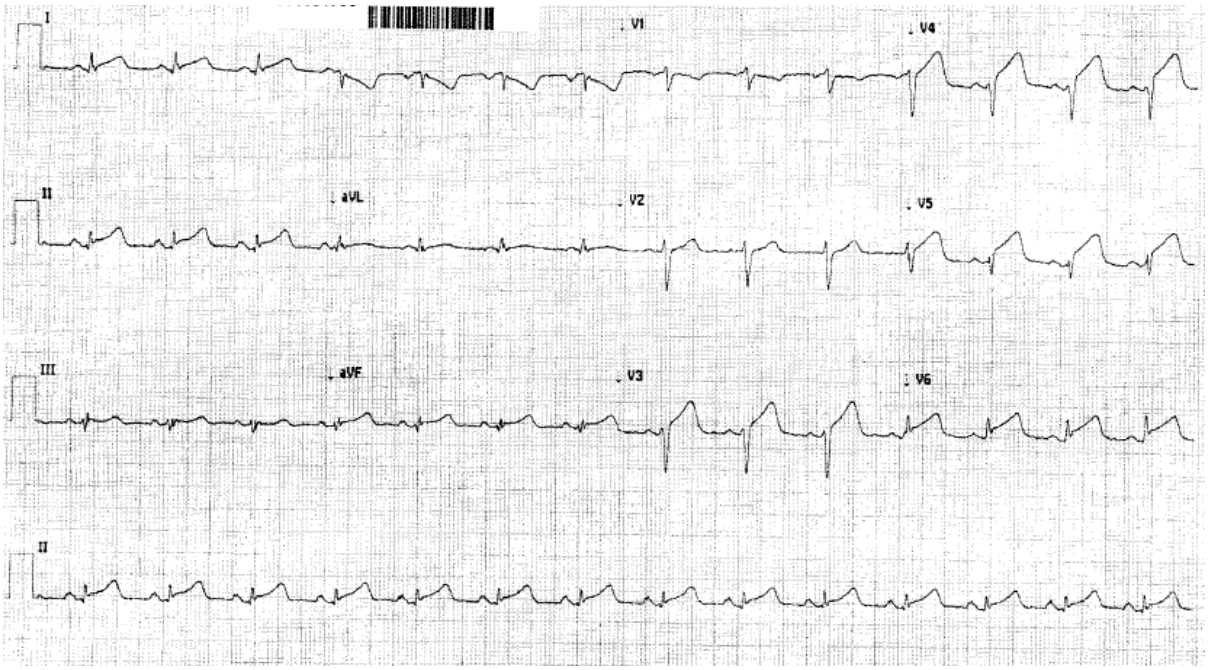


Figure 1. The electrocardiogram shows the ST segment elevation.

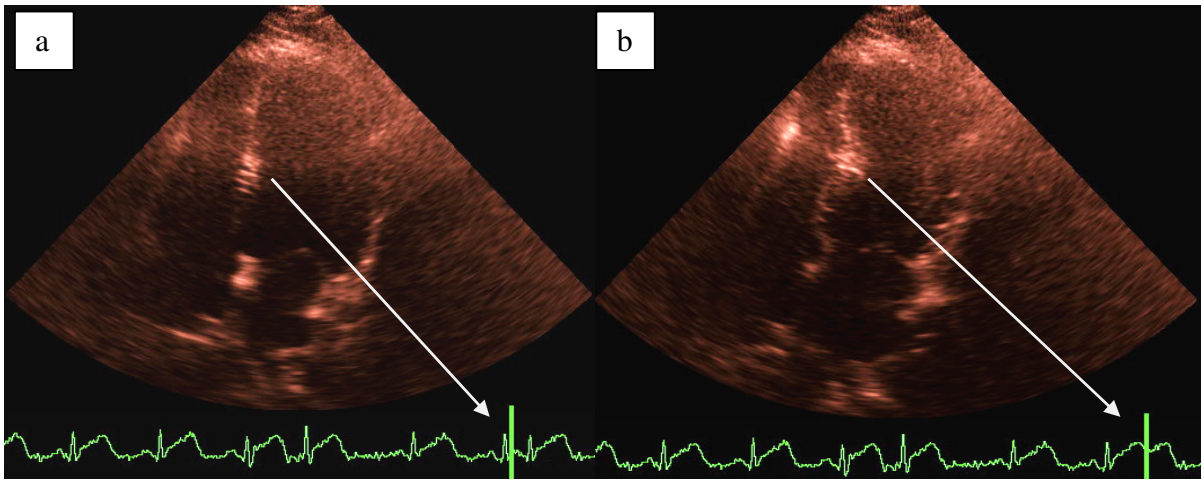


Figure 2. (a) During systole, the midseptum is unremarkable. (b) During diastole, the septum is thickest, suggesting an abnormal diastolic expansion of the region coinciding with increase in coronary blood flow during this phase of the cardiac cycle. (Arrows point toward septum size.)

References

[1] Oghlakian G, Maldjian P, Kaluski E, Saric M. Acute myocardial infarction due to left anterior descending coronary artery dissection after blunt chest trauma. Emerg Radiol 2010; 17(2):149-151.

[2] Bjørnstad JL, Pillgram-Larsen J, Tønnessen T. Coronary artery dissection and acute myocardial infarction following blunt chest trauma. World J Emerg Surg 2009; 4:14.

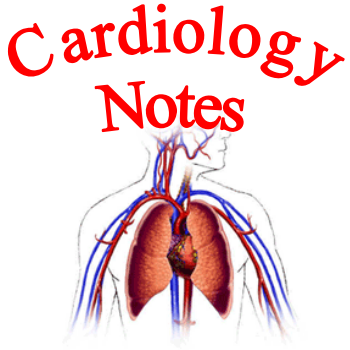
[3] Baccouche H, Beck T, Maunz M, Fogarassy P, Beyer M. Cardiovascular magnetic resonance of myocardial infarction after blunt chest trauma: A heartbreaking soccer-shot. J Cardiovasc Magn Reson 2009; 11:39.

[4] Biria M, Raxwal V, Wilson D. Dissection of left anterior descending artery following a motor vehicle accident. Clin Cardiol 2009; 32(7):10.

[5] Lobay KW, MacGougan CK. Traumatic coronary artery dissection: A case report and literature review**.** J Emerg Med 2010; Jun 3 [Epub ahead of print].

[6] Ganong WF. Review of Medical Physiology. 17th ed. Stamford, CT: Appleton and Lange, 1995, p. 566.

Keywords: intraventricular septal defects, hematoma, chest injuries, myocardial infarctions, case report



An Unusual Cardiac Manifestation of Multiple Myeloma

Bassem Chehab, M.D., Mark Wiley, M.D., Peter Tadros, M.D.
University of Kansas Medical Center
Cardiovascular Research Institute;
Cardiovascular Division
Kansas City, KS

Introduction

Amyloidosis is a systemic or organ-limited disease in which there is extracellular deposition of amyloid fibrils that gradually replace normal tissue in various organs in different pathological states, leading to loss of normal tissue architecture.[1] The extent and location of amyloid deposition is directly responsible for the degree of cardiac failure.[1,2]

Usually 25% of the myocardium is replaced by amyloid deposition for symptoms to appear with congestive heart failure being the most common presentation of cardiac amyloidosis. In the clinical workup of patients with diastolic heart failure and myocardial hypertrophy, cardiac amyloidosis is an important differential diagnosis. Once congestive heart failure occurs, the median survival is less than six months in untreated patients, and is the most common cause of death.[2]

Case Report

A 57-year-old female with a history of hypertension, diabetes mellitus, paroxysmal atrial fibrillation, morbid obesity, and multiple myeloma presented for recurrent episodes of shortness of air for the past six months. The initial echocardiogram revealed normal left ventricular systolic function, moderate tricuspid and mitral valve regurgitation, severe diastolic dysfunction, and a “speckled-like" pattern suggestive of possible amyloid disease. She underwent multiple fat biopsies without any conclusive evidence of amyloidosis. Cardiac MRI also was performed and was non-conclusive for the diagnosis of cardiac amyloid. Meanwhile, she had worsening dyspnea and interval increase in her pericardial effusion size along with worsening tricuspid and mitral valve regurgitation.

Her physical exam was positive for a 3/6 systolic murmur at the level of the mitral valve radiating to the axillary region and bilateral lower extremities edema. Chest x-ray revealed only mild cardiomegaly. Her electrocardiogram obtained at rest is shown below in Figure 1. She underwent elective pericardiocentesis and pericardial fluid analysis revealed only chronic inflammatory pattern with modest improvement in her symptoms. She was started on diuretic therapy with good response and significant improvement in her symptoms. She underwent a right heart catheterization and a right ventricular biopsy revealing a positive Congo red staining consistent with cardiac amyloidosis.

Discussion

Cardiac amyloidosis is an invariably progressive infiltrative cardiomyopathy that carries a grave prognosis. Cardiac involvement may be present in up to one-third of patients with primary amyloidosis (designated AL) resulting from plasma cell dyscrasias.[1,2] Although only 10% of the

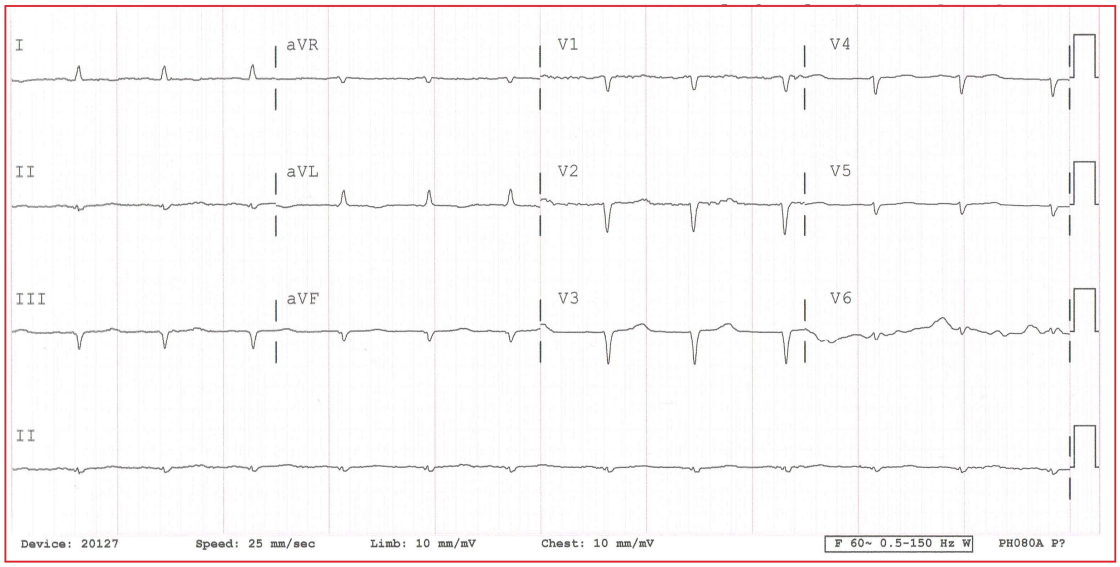


Figure 1. ECG revealing normal sinus rhythm with left axis deviation. Note the low voltage findings, anterior wall infarct (pseudo-infarct pattern), absent R wave in precordial leads, and possible inferior wall infarct. Artifacts noted in lead V6.

patients with multiple myeloma develop systemic light-chain amyloid disease, their prognosis is very poor, especially in the presence of cardiac amyloidosis.[3] Myocardial infiltration tends to be less with secondary amyloidosis (designated AA), in which the AA protein deposits tend to be smaller and more perivascular in location, thus less likely to produce myocardial dysfunction.[2,4] Other forms include familial and senile amyloidosis.[2]

The term amyloidosis means "starch-like." The heart infiltrated with amyloid appears tan and waxy and is rubbery in consistency. The atria also are enlarged significantly. Histologically, amyloid deposits can be detected with Congo red or Sirius red staining and are present between cardiac myocytes.[2,5]

There are four overlapping syndromes that may occur with cardiovascular involvement of amyloidosis, including restrictive cardiomyopathy, systolic heart failure, orthostatic hypotension, and presentation with conduction system disease. Most commonly, patients with cardiac amyloidosis present with signs of congestive heart failure with preserved systolic and abnormal diastolic function.[2,4]

Cardiomegaly may be present on chest roentgenography. The electrocardiogram most often reveals low QRS voltage, and bundle branch block and abnormal axis are also common. A pattern of old anterior myocardial infarction may be simulated by diminutive or absent R waves in the right precordial leads, or by an old inferior infarction by inferior Q-waves (pseudo-infarct pattern).[2,6] Amyloid infiltration of the atrium predisposes to atrial fibrillation, and ventricular arrhythmias are also common. Atrioventricular conduction defects are common and electro-physiological testing is usually necessary to detect significant intrahisian block. Sinus node dysfunction is also common and the ECG may show sick sinus syndrome.[6]

Echocardiography is quite valuable and reveals increased ventricular wall thickness with small intracavitary chambers, enlarged atria, and a thickened interatrial septum. The walls of the ventricles often reveal a distinctive appearance with a sparkling and granular texture, most likely resulting from the amyloid deposition itself. Pericardial effusions may be present, but usually do not

advance to tamponade. Doppler echocardiography is valuable to evaluate diastolic dysfunction, the degree of which offers prognostic information.[3,6,7] Cardiac MRI has a very high sensitivity for the detection of cardiac amyloid, and also may be valuable in measuring the extent of amyloid deposition in the heart, a significant prognostic factor.[8,9]

The diagnosis of cardiac amyloidosis can be ascertained by either: (1) a positive biopsy from a noncardiac tissue in addition to sonographic evidence of amyloidosis, which includes a mean left ventricular wall thickness of greater than 12 mm in the absence of other causes of LV hypertrophy, or (2) an endomyocardial biopsy illustrating amyloid deposition in addition to laboratory and clinical evidence of organ involvement. In patients with cardiac involvement, endomyocardial biopsy is a relatively safe procedure in experienced hands with 100% sensitivity in diagnosis of cardiac amyloidosis. Biopsy specimen from the involved organ, such as the heart or from the abdominal fat pad, exhibits a red or pink color under light microscopy after chemical staining with Congo red and a dramatic apple-green birefringence under polarized light.[2,5,6]

Patients with cardiac amyloidosis have few treatment options, although there are ongoing attempts to modify the severe natural history of this disorder.[10] Approaches for patients with AL amyloidosis involve chemotherapy with alkylating agents alone or in combination with autologous bone marrow stem cell transplantation and heart transplantation.[2,11] In terms of conventional cardiac medications, the use of digitalis glycosides requires additional vigilance because patients with cardiac amyloidosis have increased sensitivity to digitalis preparations. Calcium-channel antagonists also require caution because their negative inotropic effect has the potential to exacerbate heart failure. Pacemakers are frequently indicated for conduction system disturbances, and implantable cardioverter-defibrillators may be considered. The mainstay of symptom relief in volume overloaded patients is the judicious use of diuretics, which requires very careful titration, in combination with rigorous fluid restriction.[10]

Conclusion

In summary, cardiac amyloidosis is a progressively infiltrative cardiomyopathy that should be suspected in patients with multiple myeloma and worsening dyspnea. It carries a poor prognosis even with aggressive therapy. A cardiac screening in all patients with multiple myeloma should include at least an electrocardiogram and complete cardiac sonography.

References

1 Gertz MA, Comenzo R, Falk RH, et al. Definition of organ involvement and treatment response in immunoglobulin light chain amyloidosis (AL): A consensus opinion from the 10th International Symposium on Amyloid and Amyloidosis, Tours, France, 18-22 April 2004. Am J Hematol 2005; 79(4):319-328.

2 Falk RH. Diagnosis and management of the cardiac amyloidoses. Circulation 2005; 112(13):2047-2060.

3 Dubrey SW, Cha K, Skinner M, LaValley M, Falk RH. Familial and primary (AL) cardiac amyloidosis: Echocardiographically similar diseases with distinctly different clinical outcomes. Heart 1997; 78(1):74-82.

[4] Kyle RA, Gertz MA. Primary systemic amyloidosis: Clinical and laboratory features in 474 cases. Semin Hematol 1995; 32(1):45-59.

[5] Pellikka PA, Holmes DR Jr, Edwards WD, Nishimura RA, Tajik AJ, Kyle RA. Endomyocardial biopsy in 30 patients with primary amyloidosis and suspected cardiac involvement. Arch Intern Med 1988; 148(3):662-666.

[6] Rahman JE, Helou EF, Gelzer-Bell R, et al. Noninvasive diagnosis of biopsy-proven cardiac amyloidosis. J Am Coll Cardiol 2004; 43(3):410-415.

[7] Devereux RB, Alonso DR, Lutas EM, et al. Echocardiographic assessment of left ventricular hypertrophy: Comparison to necropsy findings. Am J Cardiol 1986; 57(6):450-458.

[8] Vogelsberg H, Mahrholdt H, Deluigi CC, et al. Cardiovascular magnetic resonance in clinically suspected cardiac amyloidosis: Noninvasive imaging compared to endomyocardial biopsy. J Am Coll Cardiol 2008; 51(10): p. 1022-1030.

[9] Kusunose K, Yamada H, Iwase T, et al. Images in cardiovascular medicine. Cardiac magnetic resonance imaging and 2-dimensional speckle tracking echocardiography in secondary cardiac amyloidosis. Circ J 2010; 74(7):1494-1496.

[10] Parikh S, de Lemos JA. Current therapeutic strategies in cardiac amyloidosis. Curr Treat Options Cardiovasc Med 2005; 7(6):443-448.

[11] Seldin DC, Anderson JJ, Sanchorawala V, et al. Improvement in quality of life of patients with AL amyloidosis treated with high-dose melphalan and autologous stem cell transplantation. Blood 2004; 104(6):1888-1893.

Keywords: electrocardiography, multiple myeloma, amyloidosis, cardiomyopathies