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SICKLE CELL ANEMIA

Engineering a Crisis . . . . . Level I

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INSTRUCTOR'S GUIDE TO CHANGES IN THIS EDITION

CASEBOOK

Patient Presentation

- New patient case: This is a 38-year-old man with different presenting findings.
- Blood gases and chest x-ray abnormalities still exist, indicating acute chest syndrome.
- Priapism and constipation have been added as problems.

Clinical Course

- Revised to include ongoing constipation.

INSTRUCTOR'S GUIDE

Problem Identification

- Problems include acute chest syndrome, acute pain crisis, priapism, and constipation.

Desired Outcome

- Revised due to this patient's current medical problems.

Therapeutic Alternatives

- Additional information provided on the treatment of priapism and constipation.

Optimal Plan

- Broad-spectrum antibiotics that cover organisms causing community-acquired pneumonia (CAP) are needed. The patient does not have penicillin allergy, so ceftriaxone and azithromycin or levofloxacin may be used.
- Revised analgesic regimen using a morphine PCA.
- Hydration and analgesics are recommended as initial therapy for the patient's stuttering priapism.
- A bowel regimen should be initiated for constipation treatment.

Outcome Evaluation

- Adapted for this patient's optimal plan.

Clinical Course

- Bowel regimen and education are warranted.
- The patient has been taking a hydroxyurea regimen, so the focus was shifted to monitoring adherence and toxicity.

Patient Education

- Information included on bowel regimen, including adverse effects.

References

- Reviewed, no updates.

CASE SUMMARY

A 38-year-old man with a history of sickle cell anemia presents with a 2-day history of pain in his right shoulder, elbow, and lower back that is not relieved by his maximized home oxycodone 10 mg regimen. He also has shortness of breath with low blood oxygen saturation, fever, priapism, and constipation. Based on his history, physical examination, and laboratory findings, the patient is considered to be in sickle cell crisis with chest radiograph indicative of acute chest syndrome. Supportive treatment for acute chest syndrome is the most immediate goal along with relief of the patient's pain and reversal of priapism and constipation. Hydration is also indicated in this patient. The patient should continue his hydroxyurea regimen and begin a regular bowel regimen.

QUESTIONS

Problem Identification

1.a. Create a list of the patient's drug therapy problems.

- Painful sickle cell crisis unresolved by present analgesic regimen
- Acute chest syndrome.
- Stuttering priapism (recurring episodes lasting from 30 minutes to 4 hours).
- Constipation likely secondary to increased opioid usage.
- Anemia with appropriately elevated reticulocyte count secondary to chronic hemolysis.
- Alloimmunization from previous transfusions as evidenced by the (+) anti-E red cell antibody.

1.b. What signs, symptoms, and laboratory values are consistent with an acute sickle cell crisis in this patient?

Signs:

- The findings on the lung physical examination of bibasilar crackles and dullness to percussion along with the chest x-ray support the diagnosis of acute chest syndrome. This is indicative of a sickle pain crisis, although crises can and do occur without pulmonary signs or symptoms.
- The bilateral lower extremity tenderness, erythema, and inflammation may represent tissue damage secondary to vaso-occlusive crisis.
- Splenomegaly is often present in patients with sickle cell disease, although it is consistent with a chronic finding rather than an acute crisis.
- The distended abdomen with guarding and hypoactive bowel sounds supports the patient's report of constipation.

Symptoms:

- Acute onset of pain unrelieved by his maximized home oxycodone 5 mg/acetaminophen 325 mg regimen. Pain is the only presenting feature in patients experiencing vaso-occlusive crises.
- Priapism occurs in patients with sickle cell anemia due to the sickled cells getting trapped in the corpora cavernosa.

Laboratory values:

- There is no laboratory value directly indicative of an acute pain crisis, nor is any abnormality predictive of the severity, duration, or frequency of an acute crisis. The laboratory abnormalities discussed below are chronic changes seen in patients with sickle cell anemia.
- The hematocrit falls acutely only during splenic sequestration crises and hemolytic crises.
- The moderately elevated lactate dehydrogenase (LDH) in this patient reflects chronic hemolysis seen in sickle cell disease.
- The elevated reticulocyte count reflects an appropriate response to anemia. A reticulocyte count in patients with a normal hematocrit is 0.5–1.5%. The bone marrow is capable of increasing red cell production by at least 10-fold if there is a physiologic demand (i.e., anemia) and all elements required to make new cells are present. It is not unusual for patients with sickle cell disease to have chronic reticulocyte counts of 10–20%. Erythropoietin is required to stimulate reticulocytosis, and patients with sickle cell disease typically have elevated, but blunted, endogenous erythropoietin concentrations in response to anemia.
- Hemoglobin (Hgb) S is responsible for the primary molecular pathogenesis of the disease due to polymerization on deoxygenation and subsequent change of the red blood cell (RBC) into a sickle shape. The Hgb S percentage in this patient (92%) is representative of a homozygous sickle cell trait (presence of two sickling genes). The usual Hgb S range in these patients is 85–95%.
- Low (5–15%) fetal Hgb (Hgb F) is seen in homozygous patients with an increased number of pain crises. Hgb F has been shown to inhibit the polymerization of Hgb S and consequently decrease RBC sickling. In heterozygous patients (one sickling gene paired with one unaffected gene), Hgb F accounts for 38–42% of total Hgb. These patients rarely experience sickling crises and have normal to low-normal Hgb values. The low Hgb F (6%) in this patient is characteristic of a patient with sickle cell trait.
- Hgb A_2 makes up 98% of Hgb in patients without sickle cell anemia but is extremely low (2–3%) in sickle cell patients.

1.c. What signs, symptoms, and laboratory values support a diagnosis of acute chest syndrome in this patient?

Signs:

- Crackles on auscultation and dullness to percussion are the most common physical examination findings.
- The vital signs, more likely to be abnormal in children, indicate tachypnea and hypoxia (respiratory rate [RR] 20), with corresponding tachycardia (pulse [P] 110). Due to decreased O_2-carrying capacity of the sickled Hgb and decreased air exchange in the lungs, the body is attempting an appropriate cardiovascular response.
- The patient's chest radiograph also supports acute chest syndrome. Upper and middle lobe disease is predominantly seen in young children, whereas adults more often have lower and multilobe involvement.[1,2] Infection, especially CAP, is one etiology for acute chest syndrome. The most common causative organisms include *Chlamydia*, *Mycoplasma*, and respiratory syncytial virus. Bacteremia is uncommon in adults, occurring in <2% of patients.[1] Other etiologies include bone marrow fat embolism and, less commonly, pulmonary infarction.

Symptoms:

- Productive cough, shortness of breath, fever, and chills.
- The most common symptoms in acute chest syndrome are fever, cough, and chest pain.
- Patients present less frequently with shortness of breath, wheezing, hemoptysis, chills, and productive cough.
- Fever is more common in young children, whereas chest pain, productive cough, and shortness of breath are more common in adults.[2]

Laboratory values:

- There are no specific laboratory abnormalities in acute chest syndrome.
- The increased bicarbonate indicates a compensatory response to respiratory acidosis from decreased O_2 exchange and increased carbon dioxide (CO_2) retention.
- An increased white blood cell (WBC) count is seen in approximately 70% of acute chest syndrome patients but is not diagnostic and may be indicative of pneumonia or other infection in this patient.[2] An increase in segmented neutrophils (left shift) may or may not be present, as the etiology of acute chest syndrome may be infectious (precipitated by pneumonia) or noninfectious (fat embolism or atelectasis). The elevated WBC count plus complete blood count (CBC) differential with 81.5% neutrophils plus bands in this patient is highly suspicious for infection.

1.d. What additional information is needed to satisfactorily assess this patient?

- Medical record and clinic notes for history and assessment of baseline Hgb and hematocrit to determine the severity and time course of prior crises.
- Vaccination status, including pneumococcal, meningococcal, and *Haemophilus B* vaccines.
- Although not absolutely necessary, past pain medication requirements, specifically starting dosages for opioids, can be helpful in pain control for patients with sickle cell anemia. Patients often require higher doses of opioids than commonly used for other diseases, and more rapid pain control can be attained using IV PCA and knowing what has worked for the patient during past crises.

Desired Outcome

2. What are the goals of pharmacotherapy in this case?

- Relief of pain secondary to sickle cell crisis.
- Supportive treatment until resolution of acute chest syndrome.
- Supportive treatment until resolution of acute chest syndrome and priapism.
- Correction and prevention of constipation.

Therapeutic Alternatives

3.a. What nondrug therapies might be useful for this patient?

- *Hydration.* Patients in crises may have diminished urine concentrating ability due to renal infarcts and/or hemodynamic changes associated with chronic anemia. Hydration using IV fluids to provide 3–5 L per day during crises aids in rehydration and mobilizing sickled cells. Fluid therapy should include 5% D_5W because it allows free water to enter red cells, decreasing the relative intracellular Hgb concentration. This reduces the tendency of Hgb to polymerize and sickle. The addition of 0.45% or 0.9% sodium chloride to fluid therapy increases intravascular volume to a greater extent than D_5W or water alone, thereby aiding in the mobilization of sickled cells in capillaries. Caution should be used in patients with underlying renal or cardiac dysfunction to avoid fluid overload and effusions. Hydration is also helpful for the treatment of priapism along with encouragement to urinate.

- *PRBC transfusions and transfusion exchange therapy.* Patients with Hgb values <7.5 g/dL typically are symptomatic at rest (e.g., fatigue, palpitations) and compensate for hypoxemia through cardiac mechanisms such as tachycardia and increased stroke volume. However, patients with sickle cell anemia typically have significant reductions in baseline Hgb. These patients would not have signs or symptoms of low Hgb unless they have a decrease from this already lowered baseline level. In acute sickle cell crises, the hematocrit does not usually fall below precrisis values, except during splenic sequestration and hemolytic or aplastic crises. Transfusions are not routinely administered during sickle cell crises.[3] However, in cases of symptomatic acute and chronic anemia (e.g., associated with renal failure), priapism, surgery with general anesthesia, and acute chest syndrome with hypoxia, administering normal red cells to aid in O_2 delivery is indicated. The risk of recurrent stroke in children with sickle cell anemia has also been shown to decrease with repeated transfusions.[1] The purpose of transfusion is to decrease the relative Hgb S concentration, with the greatest benefits being seen when Hgb is <30%.
- Unlike simple transfusion, which involves only the addition of donor blood, exchange transfusion combines the removal of the patient's blood with addition of equal amounts of warmed, fresh donor blood. Exchange transfusion decreases the Hgb S concentration most rapidly because addition of nonsickled cells is combined with their removal from circulation. Either exchange transfusion or simple transfusion can be used for acute chest syndrome. Exchange transfusion is preferred if Hgb values are 9–10 g/dL, whereas simple transfusion is more beneficial if Hgb is 6 g/dL or less. Sickle cell patients are predisposed to developing anti-E, anti-C, Kell, and Duffy red cell antibodies. Blood banks have the capability to screen red cells for these antibodies to avoid immune-mediated hemolysis. Additionally, iron accumulation is a concern in patients with sickle cell disease who receive chronic transfusions. This excess iron is able to penetrate numerous organs, including the liver, heart, and endocrine organs, leading to tissue damage. An oral iron chelator, deferasirox (Exjade), can now be used as an alternative to the older parenteral deferoxamine mesylate (Desferal).[4] Simple transfusion is likely indicated (rather than exchange transfusion) in this case due to the patient's low Hgb (7.7 g/dL) and presence of acute chest syndrome. Since he likely receives blood products on an infrequent basis because his sickle crises are usually uncomplicated, he is unlikely to have iron overload; however, iron and ferritin levels could be assessed if this were a concern.
- *Oxygen.* The use of O_2 during crises improves patient comfort but has no demonstrable effect on O_2 saturation or on the course of sickle cell crises. However, patients often perceive it to be useful, and therefore it may relieve anxiety. Oxygen is typically provided at lower rates (e.g., 2 L/min) via nasal cannula. In one study, O_2 was only required for patients with acute chest syndrome if O_2 saturation was <90% and/or partial pressure of arterial O_2 was <60 mm Hg.[1] Oxygen is used in patients with acute chest syndrome to overcome the decrease in diffusion capacity experienced due to the ongoing pulmonary process (e.g., pneumonia).
- *Incentive spirometry.* An incentive spirometer measures lung inspiratory capacity and is used to encourage deeper lung effort. In sickle cell anemia patients hospitalized with pain crisis and/or acute chest syndrome, it has been shown to significantly decrease the occurrence of atelectasis and pulmonary infiltrates, which can be related to the development and severity of acute chest syndrome. Patients should be encouraged to use the incentive spirometer often. One regimen studied was 10 maximal inspirations every 2 hours between 8 am and 10 pm and while awake during the night while hospitalized.[5]

3.b. What feasible pharmacotherapeutic alternatives are available for treatment of the patient's pain?

- *Fentanyl*, *hydromorphone*, and *morphine* are opioids that have been used safely and effectively for pain control in sickle cell crises.
- *Meperidine* should not be used because prolonged, high doses in sickle cell disease patients with renal dysfunction result in accumulation of the neurotoxic metabolite normeperidine. Accumulation of this metabolite predisposes patients to seizures that can be exacerbated, rather than reversed, with naloxone.
- Pain control is best achieved initially through the parenteral route, but the oral route may be used provided that the agents used have a rapid onset and adequate doses are given for relief.
- PCA is a beneficial option that allows patients to dictate their own regimens. Continuous infusions with patient-controlled doses as needed provide around-the-clock pain control with an "on-demand" dose for breakthrough needs. Consideration of prior opioid therapy should be used in determining a patient's tolerance to therapy and the need for dosage increases.
- Frequent pain crises and chronic pain may lead to significant opioid tolerance and therefore higher dose requirements than opioid-naïve patients.

3.c. What feasible pharmacotherapeutic alternatives are available for treating opioid-induced constipation?

- Patients on opioid therapy commonly develop opioid-induced constipation. Stool softeners in combination with stimulant laxatives have shown to be the most effective for opioid-induced constipation. Opioid receptors in the gut mediate anal sphincter tone, intestinal and colon peristalsis, absorption of water and electrolytes, and defecation response.[6] Agonist activity at these receptors results in constipation that is exacerbated in sickle cell patients by decreased mobility (especially during hospitalization) and dehydration.
- *Stool softeners (e.g., docusate sodium)* increase GI secretions and require adequate oral fluid intake to exert benefits. Use as sole therapy is frequently inadequate, and combination with a stimulant agent is recommended.
- *Stimulant laxatives (e.g., senna, bisacodyl)* increase longitudinal smooth muscle contraction. These agents should be used on a scheduled basis for maximum effects.
- *Osmotic agents (e.g., sorbitol, lactulose)* can be considered for refractory constipation. These drugs act by causing osmotic influx into the small intestine, resulting in subsequent peristalsis and stool softening. In this patient, use of one of the agents regularly may be necessary to initiate a bowel movement and correct the current constipation.
- *Bulk-forming agents (fiber, psyllium)* are not recommended due to their potential for causing obstruction (bulk mass effect with already decreased gut mobility).

Optimal Plan

4. Outline a detailed therapeutic plan to treat all facets of this patient's acute sickle cell crisis, acute chest syndrome, priapism, and constipation. For all drug therapies, include the dosage form, dose, schedule, and duration of therapy.

Antibiotics:

- Ceftriaxone 1 g IV once daily plus azithromycin 500 mg IV once daily are typically recommended to cover the most common organisms that can cause CAP, which is often the etiology of acute chest syndrome.

- Levofloxacin 500 mg po once daily may also be used, because it is indicated as single-agent therapy of CAP. Because a 14-day course is required for this patient due to the potential for atypical organisms, oral levofloxacin will likely be the preferred regimen since ceftriaxone is only available IV.
- A higher-dose regimen of levofloxacin 750 mg po daily for a duration of 5 days is also an alternative that has demonstrated similar clinical success and microbiologic eradication rates compared to levofloxacin 500 mg po daily for 10 days in patients with mild to severe CAP.
- Other fluoroquinolones with enhanced activity against *Streptococcus pneumoniae* with high-level resistance to penicillin include moxifloxacin 400 mg daily and gatifloxacin 400 mg daily.

Pain:

- A morphine PCA should be started with a 4–5 mg/h continuous basal rate with 2–2.5 mg as often as every 10 minutes. A loading dose of 8–10 mg IV may be given initially to control the patient's pain. A 3.3-mg/h basal dose is equivalent to the amount of oxycodone the patient was using in a 24-hour period (oxycodone 20 mg every 4 hours). This conversion was done using the following equations:

$$\frac{1 \text{ mg po oxycodone}}{2 \text{ mg po morphine}} = \frac{120 \text{ mg po oxycodone per day}}{X \text{ mg po morphine per day}}$$

$$X = 240 \text{ mg po morphine per day}$$

$$\frac{3 \text{ mg po morphine}}{1 \text{ mg IV morphine}} = \frac{240 \text{ mg po morphine per day}}{X \text{ mg IV morphine per day}}$$

$$X = 80 \text{ mg IV morphine per day}$$

80 mg IV morphine per 24 hours = 3.3 mg/h of IV morphine

Because the home oxycodone regimen was not relieving the patient's pain, a higher basal dose (4–5 mg/h) may be chosen, representing a 25–50% increase from the original regimen. The PCA should be adjusted and continued until his pain begins to resolve. His oral home regimen can then be used on discharge.

Hydration:

- Dextrose 5% with either 0.45% or 0.9% sodium chloride at 125 mL/h. Rehydration is necessary to expand intravascular volume and mobilize sickled cells, which will also aid with decreasing priapism.
- Fluids such as lactated Ringer's and 0.9% sodium chloride alone are not optimal for rehydration because of a lack of free water.
- Continued hydration should be governed by clinical signs of fluid overload (peripheral/pulmonary edema, decreased urine output).
- IV hydration should be discontinued as soon as the patient has been rehydrated and is able to maintain adequate oral hydration.

Bowel regimen:

- Docusate sodium 100–200 mg po BID with senna one to two tablets po at bedtime should be started. Onset of effect can be expected in 6–12 hours. An osmotic agent such as polyethylene glycol 17 g po once or twice daily until he has a bowel movement may also be used to treat the current constipation. He should remain on a daily bowel regimen while on daily opioids for prevention of opioid-induced constipation after normal bowel habits have returned. His frequency of bowel movements should be assessed daily and the bowel regimen adjusted accordingly.

Oxygen:

- Oxygen at a rate of 1–2 L/min via nasal cannula may be initiated if the patient feels it to be helpful. It is not required in this case due to O_2 saturation >90% and partial pressure of arterial O_2 >60 mm Hg.
- As the acute chest syndrome resolves, the O_2 requirement will decrease as perfusion capability increases, and weaning should be attempted.

Outcome Evaluation

5.a. What clinical and laboratory parameters are necessary to evaluate therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?

Antibiotics:

- Monitor for resolution of fever and respiratory symptoms, including shortness of breath and productive cough.
- An increased O_2 saturation and a decrease in pulmonary infiltrates on lung radiograph and WBC should be seen as infection (if present) resolves. Rarely is the causative organism identified. However, if a lower respiratory sputum culture is acquired and an organism identified, antibiotic therapy may be tailored to the findings. Atypical organism coverage should be continued regardless of the organisms cultured due to the high rate of occurrence in acute chest syndrome patients.
- On daily physical examination, monitor for adverse effects, including nausea, vomiting, diarrhea, and headache, although they occur rarely.

Pain:

- Monitor for subjective relief of pain and the ability to tolerate conversion to oral therapy.
- Monitor PCA adverse effects through monitoring vital signs every 8 hours (O_2 saturation, RR).
- As pain resolves, the patient should return to his oral home regimen.

Hydration:

- Monitor for resolution of crisis through daily assessments of pain control, hematocrit, and presence of sickled cells on peripheral smear.
- Fluid accumulation could produce pulmonary edema (wheezes, crackles on lung exam) and/or peripheral edema.
- Perform daily physical examinations to assess hydration status.

Priapism:

- Monitor for resolution of symptoms and pain control.

Bowel regimen:

- Ask the patient about the number of bowel movements every day.
- Continue daily therapy even after constipation has resolved, unless diarrhea develops.

5.b. Considering this information, what changes (if any) in the pharmacotherapeutic plan are warranted while the patient is hospitalized?

- *Antibiotics:* The levofloxacin should be continued for a total of 14 days. The patient will likely continue on this medication when discharged to finish the full regimen.

- *Pain:* The continuous infusion PCA pump should be discontinued while keeping a bolus dose for breakthrough pain. His home oral regimen should be reinstituted as his opioid needs decrease and pain resolves. Even though the patient is only using two to three demands on the PCA, he is still receiving more than 120 mg of oxycodone equivalents a day, so discontinuing the basal PCA will help to assess whether the oral pain medication will still be adequate.
- *Hydration:* Fluids should be discontinued if hydration is adequate, pain is resolving, and the patient is able to maintain his fluid status orally.
- *Constipation:* A daily bowel regimen should be continued even after bowel habits have normalized. It can be stopped if diarrhea occurs.

5.c. What evidence exists to suggest that the patient is adherent with hydroxyurea therapy, and how should this therapy continue to be monitored?

- This patient is currently receiving a hydroxyurea regimen and appears to be adherent as evidenced by an increased MCV. The goal of hydroxyurea therapy is to balance the beneficial effects of increasing Hgb F percent with the potentially toxic myelosuppressive effects. Though Hgb F percent can be measured using electrophoresis, the MCV is used as a surrogate marker and can be obtained with a regular CBC. An increase in MCV corresponds to an increase in Hgb F percent. The greatest benefits have been found when the Hgb F is >0.5 g/dL (Hgb [g/dL] = Hgb F [%] × total Hgb concentration [g/dL]).[7] This patient's Hgb F is 0.616 g/dL. An exact correlation between Hgb F percentages and MCV values has not been established and varies among individuals. However, a general MCV goal is 110–120 μm^3.
- Reinforce the importance of medication adherence because long-term follow-up of sickle cell patients at 9 years has shown that hydroxyurea decreases frequency and duration of hospitalizations for acute pain crisis and number of acute chest syndrome episodes. Hydroxyurea inhibits DNA synthesis and has been shown to increase Hgb F percentages through an unknown mechanism. All-cause mortality was 23.7% in patients receiving hydroxyurea and 26.5% in patients not receiving the drug. The most common cause of death in both groups was pulmonary disease followed by infection and renal and cardiovascular diseases. Overall survival was related to frequency of vaso-occlusive events and Hgb F concentration. Of the patients receiving hydroxyurea, 38% achieved an Hgb F concentration of >0.5 g/dL compared with 8% of those not treated with hydroxyurea.[7] The greatest benefits were seen in patients with six or more crises in the previous 12 months.
- Hydroxyurea has carcinogenic and teratogenic potential. Patients should be informed of these risks prior to therapy initiation and instructed to use effective birth control measures during treatment. Evaluation of long-term risks for malignancy in patients on hydroxyurea is limited, but available data suggest minimal risk. In the study described above, of the 299 patients followed, 3 cases of carcinoma (2 breast, 1 uterine) were reported.[7] Additionally, rare reports of leukemia developing in patients after hydroxyurea exist in case studies.
- Therapy should be withheld if myelosuppression occurs (defined as an absolute neutrophil count $<2.0 \times 10^3/mm^3$, a platelet count $<80 \times 10^3/mm^3$, or Hgb <4.5 g/dL).
- Once optimal dosing with minimal myelosuppression has been determined, regular CBC monitoring intervals may be extended from 2 to 4–6 weeks.

Patient Education

6. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?

Hydroxyurea:

- Hydroxyurea, when taken daily, may decrease the number of painful crises and need for hospitalization.
- Your blood counts will be monitored every 2 weeks while your optimal dose is being determined. The drug may reduce the number of WBCs, RBCs, and platelets. WBCs help fight infection, and lowering these cells may put you more at risk for infection. RBCs carry oxygen to the cells in body. If these cells get too low, you may feel more tired. Platelets help your blood to clot, so you may be at risk for increased bleeding if they get too low. Frequent monitoring can help prevent these complications.
- Other rare side effects include nausea, mouth sores, hair thinning, and fever. Be sure to let your health care professional know if you experience any of these adverse effects.
- It is very important to take this drug every day as prescribed to get the maximum benefits.
- This medication can be harmful to an unborn child, so you must use appropriate methods of birth control to prevent pregnancy. If you suspect that you are pregnant, stop taking the drug immediately and consult your health care professional as soon as possible.

Folic acid:

- This vitamin is needed for the production of RBCs.
- It is important that you keep taking this medication as prescribed.

Levofloxacin:

- This antibiotic is being used to treat your lung infection.
- Adverse effects are rare but may include headache, nausea, and vomiting. Contact your physician if you experience muscle pain (especially in the legs), chest pain, or discomfort.
- Avoid taking this drug within 2 hours of any products containing calcium, magnesium, or iron, including dairy products.
- It is important to finish the entire quantity of this antibiotic even if you feel that all of your symptoms have resolved. It is possible that you may still have some infection even if you no longer have a fever or cough. Stopping the antibiotic early may make the infection harder to treat the next time.

Bowel regimen (e.g., docusate and senna):

- Opioid medications commonly cause constipation, so it is important to begin taking these medications whenever you start taking oxycodone to prevent constipation from developing.
- Continue taking your bowel regimen every day unless loose stools develop.
- Drink plenty of fluids each day (six to eight large glasses) to optimize the therapy.
- Side effects are generally mild but may include abdominal cramping or bloating. Additionally, senna may cause your urine to become red or yellowish brown. This side effect is harmless and will go away when the drug is stopped.

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