In this Journal feature, information about a real patient is presented in stages (boldface type) to an expert clinician, who responds to the information, sharing his or her reasoning with the reader (regular type). The authors’ commentary follows.

A Growing Problem

Wendy W. Yeh, M.D., Sanjay Saint, M.D., M.P.H., and Steven E. Weinberger, M.D.

A 36-year-old pregnant woman at 21 weeks of gestation presented with a 4-week history of a dry, nonproductive cough. Acute onset of cough in the patient’s age group is most commonly due to a respiratory tract infection, typically viral. However, in the absence of other clinical findings suggesting an infectious cause, the most common causes of cough are postnasal drip (also called the upper airway cough syndrome), asthma, and gastroesophageal reflux. Because gastroesophageal reflux commonly develops or worsens during pregnancy, it should be considered in a pregnant woman with new-onset cough. Other, less common airway or parenchymal lung diseases are also potential causes of new cough but would not be the initial diagnostic considerations.

The patient said she had no fever, chills, dyspnea, chest pain, or weight loss. She had no new pets, environmental exposures, or sick contacts. It was her first pregnancy, and there were no complications. She had no medical conditions and did not smoke or drink alcohol. She was a financial consultant and enjoyed running and hiking. She had traveled to Australia, Central Asia, and sub-Saharan Africa in the past.

Given the absence of symptoms to suggest either a current or recent respiratory tract infection, an infectious cause of the patient’s cough becomes much less likely. However, pertussis can manifest primarily with persistent cough, and both the upper airway cough syndrome and gastroesophageal reflux can result in cough even when no other symptoms are apparent. Similarly, in so-called cough-variant asthma, patients may have cough without overt dyspnea or wheezing, so this diagnosis remains possible. The most important of the parenchymal lung disorders that might cause cough in an otherwise asymptomatic person in the age group of our patient is sarcoidosis, since granulomatous involvement of the airways or parenchyma is not infrequently associated with cough, even in the absence of dyspnea.

The patient appeared well, with appropriate weight gain for the second trimester of her pregnancy. The temperature was 37.2°C, the heart rate 95 beats per minute, the respiratory rate 12 breaths per minute, and the oxygen saturation 99% while she was breathing ambient air. She had no cervical lymphadenopathy, and her lungs were clear on auscultation. The remainder of the physical examination was normal.

Although the patient’s healthy appearance and her normal physical examination are reassuring, they do not really help distinguish among the diagnostic possibilities already mentioned. The heart rate of 95 beats per minute is most likely related to her pregnancy and does not at this point arouse concern about an underlying cardiac or pulmonary process. Her relatively low respiratory rate, combined with normal
oxygen saturation, suggests that she does not have significant underlying pulmonary dysfunction. Asthma or sarcoidosis remains a possible cause of her presentation.

Her cough was initially attributed to asthma and improved, but did not resolve, with the use of an inhaled bronchodilator. Her symptom persisted for another month, and she was started on an H$_2$-blocker for empirical treatment of gastroesophageal reflux disease. She reported no heartburn or regurgitation but continued to use an H$_2$-blocker for the remainder of her pregnancy, since she believed that its use improved her cough. Imaging was not performed at this point, because of the patient's pregnancy. She had an uncomplicated vaginal delivery 4 months later. She continued to have intermittent dry cough after childbirth but otherwise felt well. She presented again to her primary care physician 2 months after delivery for a reevaluation of her cough.

Once a cough has lasted more than 8 weeks, it is considered chronic. Given the patient's ongoing symptoms, chest radiography is warranted. Although her apparent improvement earlier, when taking H$_2$-blockers, made it reasonable to defer imaging, chest radiography during pregnancy exposes the fetus to minimal amounts of radiation and is acceptable if medically indicated. It is prudent to use abdominal shielding and, when reasonable, to perform the radiography after the first trimester to avoid even this small amount of radiation during the critical early period of fetal development. If chest radiography were negative, I would empirically treat this patient for postnasal drip, given that it is a common cause of chronic cough. If this treatment were not effective, I would also consider empirical treatment with inhaled corticosteroids for nonasthmatic eosinophilic bronchiitis, another more recently recognized cause of chronic cough characterized by eosinophilic inflammation of the airway without airway hyperresponsiveness.

A chest radiograph revealed a soft-tissue mass, 7 cm in diameter, adjacent to the right heart border (Fig. 1).

This unexpected abnormality on chest radiography is probably related to the patient's cough, rather than being a coincidental finding. Since the mass is adjacent to (and appears to obscure) the right border of the heart, the first question is whether it is within the lung or within the mediastinum. Given the smooth, well-defined border of the lesion, the second question is whether it is cystic or solid. This information can best be obtained with the use of computed tomography (CT) of the chest, which would be my next diagnostic step. I would also want to know whether the patient has undergone chest radiography previously, since it would be useful to compare the current film with previous ones. Pending results of further imaging, my leading diagnosis would be a pericardial or bronchogenic cyst. Although rare, an abnormality in the right cardiophrenic region can also represent the herniation of abdominal contents through a diaphragmatic foramen (Morgagni’s foramen).

The white-cell count was 7700 per cubic millimeter, with 72% neutrophils, 21% lymphocytes, 3% monocytes, and 3% eosinophils. The hematocrit was 37%, and the platelet count was 244,000 per cubic millimeter. The results of a chemistry panel and liver-function tests were normal. High-resolution CT scans of the chest confirmed the presence of a homogeneous and fluid-filled structure without septa, thought to be in the mediastinum (Fig. 2A and 2B). Subsequent echocardiography also confirmed a simple cystic structure with thin walls surrounding echo-free fluid that was indenting the right atrium.

The CT scan has provided valuable information re-
Lating to both of the above questions. The lesion is cystic. In my opinion, it appears to be within the lung rather than within the mediastinum. Given the thin wall of the cyst and the homogeneous appearance of the fluid within it, it is most likely a bronchogenic cyst or, given the patient’s travel history, an echinococcal (hydatid) cyst. Although one might contemplate aspirating fluid from the cyst to make the diagnosis, the leakage of fluid during aspiration of a hydatid cyst can result in spread of the infection or in an anaphylactic reaction to antigenic material within the cyst. Therefore, I would further evaluate this possibility by performing serologic testing for echinococcus and by reviewing any available cross-sectional images through the liver obtained on CT that might show coexisting hepatic echinococcal cysts.

On the basis of the findings on radiology and echocardiography, the clinicians caring for the patient thought that the thoracic mass was most likely a benign pericardial cyst. Because she was not experiencing dyspnea, the patient decided not to undergo surgical resection. However, her cough worsened over the next few months, and she consulted a thoracic surgeon for elective resection. It is appropriate to consider complete surgical resection, which is the traditional management for either a bronchogenic or an echinococcal cyst. However, I would still conduct preoperative serologic studies for echinococcus, since a positive result helps the surgeon plan preoperatively to avoid intraoperative spillage of the cyst contents. The absence of dyspnea perhaps suggests that the need for surgical resection is not urgent, but it does not dissuade me from believing that surgery is indicated. Although it remains possible that the cyst is bronchogenic, I am worried that it is an echinococcal cyst, given the patient’s travel history and the fact that her symptoms appear to be progressive, perhaps reflecting a slow increase in the size of the cyst.

Intraoperative findings revealed an intraparenchymal pulmonary cyst in the right lung that was not attached to the pericardium or bronchus. The cyst was removed completely without gross spillage of the contents. Staining of the cyst wall with hematoxylin and eosin after cross sectioning showed an acellular laminated layer. Microscopical examination of the cyst contents showed protoscolices with hooklets and suckers (Fig. 3A and 3B) in a background of histiocytes and eosinophilic debris consistent with Echinococcus granulosus.

The patient probably acquired the parasite during one of her previous travels, although it is unclear precisely where, since E. granulosus is present in all the regions where she traveled. Patients with hydatid cysts are often asymptomatic, particularly if involvement is confined to the liver. With pulmonary cysts, patients may have cough, and symptoms may become more dramatic, eventually including fever, if the cyst ruptures. The time course of the patient’s disease was typical, since cysts are often present for years before clinical detection (if detection ever occurs). The cysts typically grow slow-
ly. In this case, the size of the cyst had probably increased sufficiently over the recent past to cause cough through compression or irritation of the adjacent pulmonary parenchyma or airways.

CT of the abdomen after removal of the thoracic cyst revealed no evidence of hepatobiliary disease. Postoperative screening for serum antibody against echinococcus was positive. Praziquantel was administered for 10 days after surgery and albendazole for 1 month after surgery, with no complications. After this course of therapy, the patient had resolution of her cough and returned to her normal level of activity, without evidence of recurrent disease on follow-up CT 6 months after surgery.

**Commentary**

Our patient had an uncommon cause of a common symptom. She initially presented with a nonproductive cough, a symptom seen often by primary care physicians. Postnasal drip, asthma, gastro-esophageal reflux disease, sequelae of upper respiratory infections, and eosinophilic bronchitis are responsible for at least 90% of cases of chronic cough. In the current case, symptoms were initially attributed to gastroesophageal reflux disease, presumably because pregnancy is known to be associated with this condition and because the patient initially reported improvement in cough with empirical H$_2$ blockade. However, the persistence of symptoms after delivery, and despite treatment for gastroesophageal reflux disease, appropriately resulted in further evaluation. As the discussant points out, pregnancy is not an absolute contraindication to chest radiography, and this procedure would have been appropriate earlier, had the persistent nature of the patient’s symptoms been clear to her physicians.

The finding of a mass on chest radiography surprised both our discussant and the clinicians caring for the patient. Additional imaging showed that the mass had thin walls and a lack of complex structures, features suggestive of a benign cyst. The clinicians caring for the patient interpreted the CT scan as suggesting that the lesion was in the mediastinum rather than in the lung parenchyma. Conservative care has been reported previously for asymptomatic patients whose radiologic results strongly suggest the diagnosis of pericardial cyst. Accordingly, our patient chose to delay surgery until her symptoms progressed.

Although before the surgery, our discussant correctly considered echinococcus as a cause of the cyst, the patient’s clinicians did not, for several reasons. Echinococcal disease in the liver or lung usually shows multilocular daughter cysts on radiography. Moreover, patients who present with advanced hydatid cystic disease are usually immigrants from a country where the disease is hyperendemic. Our patient was North American, and her epidemiologic exposures were brief and temporally distant from her clinical presentation, both of which presented a particular challenge in linking her travel history to her current disease. Finally, _E. granulosus_ most commonly causes hepatic cysts, rather than thoracic cysts. Although hydatid cysts can be found in any organ, tissue, or cavity (including the kidney, spleen, peritoneal cavity, skin, muscles, bone, and pericardium), they are most frequently present in the liver (in 50 to 70% of patients), followed by the lung (in 20 to 30%...
of patients). Because there are many potential sites for infection, patients in whom echinococcosis is suspected should undergo thoracic or abdominal imaging, since the presence of multifocal disease may affect therapy.

Echinococcosis is a zoonosis caused by the long-term growth of hydatid cysts in intermediate hosts, such as sheep or humans, that have ingested eggs shed in the feces of definitive hosts, such as dogs and wolves. In the intermediate hosts, the larvae are transported through blood or lymph vessels to the liver, lung, and other organs, where they develop into hydatid cysts. These cysts consist of two parasite-derived layers: an inner nucleated germinatal layer and an outer acellular, laminated layer. Brood capsules and protoscolices bud from the germinatal membrane. Although E. granulosus has a worldwide geographic distribution, it is most prevalent in northwestern Kenya, southern Sudan, Central Asia, and South America.

The incubation period of cystic echinococcosis is many months to years. Asymptomatic disease is common in regions where the parasite is endemic, and up to 75% of infected people may remain free of symptoms for more than 10 years. The growth rates of the cysts are usually related to the compliance of surrounding tissues. In the liver, cysts grow approximately 1 cm in diameter per year. Persons are often asymptomatic until the cyst compresses adjacent structures or ruptures into them. Less commonly, complications such as bacterial superinfection or anaphylaxis due to the release of cyst fluid can cause symptoms.

In patients with echinococcal cysts, diagnostic aspiration is not usually recommended because of the risk of fluid leakage, which could result in the dissemination of infection or in anaphylaxis. Antibody detection is the primary diagnostic test most commonly used. Though useful for follow-up of patients after surgical or pharmacologic treatment, the detection of circulating E. granulosus antigens in serum is less sensitive than is antibody detection.

The management of echinococcal cysts usually involves a combination of surgical resection and anthelmintic therapy. In uncomplicated cases of hepatic hydatid cysts, percutaneous aspiration and instillation of a scolicidal agent is an option. Percutaneous aspiration and instillation of anthelmintic chemotherapeutic agents has also been shown to be as effective as cystectomy in cases of hepatic echinococcosis, with a lower rate of complications and a shorter hospital stay. However, data regarding the use of this treatment method in children and pregnant women are lacking. In our patient, surgery was the treatment of choice, since percutaneous aspiration and instillation has a higher rate of complications in patients with pulmonary cysts than in those with hepatic cysts.

Albendazole kills protoscolices and is given a few days before surgical intervention to reduce the risks associated with spillage of cyst contents, followed by at least 4 weeks of therapy, depending on the site and extent of disease. If patients are not eligible for surgery or percutaneous aspiration and instillation, treatment with albendazole alone results in the disappearance of up to 48% of cysts and in a substantial reduction in size of a further 24%. Praziquantel, which is active against protoscolices in vitro and increases serum concentrations of albendazole fourfold, has been used in combination with albendazole, with improved efficacy over albendazole alone. Data for guiding the timing of the use of praziquantel in the perioperative setting are limited. Praziquantel has been shown to be effective in preventing encystment of protoscolices after perioperative spillage.

This case illustrates the importance of not ignoring a growing problem, even if the presentation seems benign. The diagnosis may end up being an unusually large surprise.

Supporting information can be found in the online version of this article.

No potential conflict of interest relevant to this article was reported.

We thank Dr. Edward T. Ryan for his clinical insights and help in caring for the patient.
15. Taylor DH, Morris DL. Combination chemotherapy is more effective in post-spillage prophylaxis for hydatid disease than either albendazole or praziquantel alone. Br J Surg 1989;76:954.

Copyright © 2007 Massachusetts Medical Society.