Received: 2 May 2019 | Accepted: 9 May 2019

DOI: 10.1002/jgf2.264

CLINICAL PROBLEM-SOLVING

Journal of General and Family Medicine Open Access WILEY

# All that glitters is not gold

Junki Mizumoto MD[1] | Taro Shimizu MD, MPH, MBA, PhD[2]

[1]Department of Family Practice, Ehime Seikyou Hospital, Ehime, Japan

[2]Department of Diagnostic and Generalist Medicine, Dokkyo Medical University, Tochigi, Japan

**Correspondence**
Taro Shimizu, Department of Diagnostic and Generalist Medicine, Dokkyo Medical University, Tochigi, Japan.
Email: shimizutaro7@gmail.com

A 79-year-old Japanese woman presented with acute and diffuse abdominal pain. Seventeen hours before being admitted, she had developed postprandial abdominal pain. The pain was dull in quality, had started gradually, and had continuously worsened over several hours without waxing or waning. Eating was the only provocative factor, while sitting and bending her body forward were alleviating factors. The pain had not radiated to any other part of the body. Five hours after she had vomited twice, she visited our facility for the evaluation of her symptoms. On questioning, she denied any history of chills, rigors, diarrhea, constipation, chest pain, melena, hematochezia, headache, or dyspnea.

Abdominal pain lasting for less than a few days, with progressive worsening, is categorized as acute onset rather than chronic, although there is no strict division between the two based on duration. An acute abdominal condition includes a number of differentials. Vascular, inflammatory (especially infectious), obstruction of luminal organs (eg, urinary, digestive system, biliary system), and metabolic and endocrine disorders are the usual speculations. The patient has acute and diffuse abdominal pain that indicates vascular ischemia, peritonitis, or endocrine and metabolic as the probable etiology. Vascular ischemia includes ischemia of heart and/or the major vessels. Cardiac ischemia is less likely without chest pain, but it should be considered because patients at this age can manifest rather vague systemic symptoms than the classic symptoms of cardiac ischemia. Major vessel ischemia from aortic dissection or mesenteric ischemia can cause diffuse and severe abdominal pain. Since the patient is old, and given other possible vascular risk factors, the likelihood of a vascular condition can be quite high. Typically, on abdominal wall palpation, these conditions usually reveal a soft and nontender abdomen besides severe pain. Peritonitis can cause diffuse abdominal pain and can exhibit peritoneal signs on physical examination. Endocrine and metabolic disorders, such as diabetic ketoacidosis, adrenal insufficiency, thyrotoxicosis, hypercalcemia, and toxic exposure including lead, can demonstrate diffuse abdominal pain.

In addition, visceral pain precedes somatic pain in the early phase of the pain in a specific organ. Visceral pain is characterized as a diffuse, dull, vague sensation, which is difficult to localize. At the time of presentation, if the patient's pain was initially visceral, the pain could be located somewhere as somatic pain. Hence, diffuse abdominal pain does not necessarily rule out pain from a specific organ that is, typically, localized later.

In this case, the continuous pain points against luminal organ pathology such as digestive system and genitourinary system. Pain in these organs wax and wane unless necrosis from ischemic change or peritonitis due to perforation occurs.

Determining the precipitating or alleviating factors of the pain can be of help in narrowing the differentials. In this case, the pain would decrease when the patient would sit and bend forward and become aggravated upon eating. In pain due to pleuritis and pericarditis, sitting up and leaning forward offers relief; however, postprandial pain is not consistent in this scenario. Another cause of pain alleviated by sitting up and leaning forward is pancreatitis. The pain ameliorates on leaning forward or lying prone but aggravates with eating suggests duodenal compression by the superior mesenteric artery. Lying still alleviates the pain in peritonitis due to less motion-related irritation to the peritoneum. Incidence of pain after eating, especially within an hour, indicates a gastric origin or mesenteric ischemia. The pain from foodborne disease (ie, gastroenteric infection) may occur after eating certain foods. The incubation period for pain usually correlates with the distance of the location of pain from the mouth. Therefore, it is essential to ascertain the contents and timing of the meal from the patient before the pain. Conversely, alleviation of pain after eating indicates the possibility of duodenal ulcers; however, the pain can recur after several hours.

Ischemic pain of the heart and the major vessels has no direct or immediate association with eating, position, and motion, except for strenuous motion, which can drastically increase the systemic blood flow or vigorous strain that can raise the intrathoracic

pressure, thereby increasing shear stress in the heart and the major arteries. Additionally, the associated symptoms include vomiting, which is nonspecific but might indicate gastric irritation or dysmotility of several etiologies. Currently, no constitutional symptoms indicative of shock were present, but given the unexplained abdominal pain, I would be cautious of any potentially fatal conditions.

Thus far, I had inquired the patient regarding vascular risks and past medical history, especially regarding endocrine and metabolic diseases.

Her past medical history included well-managed type 2 diabetes mellitus and hypertension, right visual impairment due to central retinal vein occlusion, obesity, gastroesophageal reflux disease (GERD), chronic cutaneous pruritus, and bilateral knee osteoarthropathy. Seven months before, she had acalculous cholecystitis that required a 10-day admission without any administration of antibiotics. No surgery had been performed. Her prescription medications included metformin 1000 mg/d, fexofenadine 120 mg/d, amlodipine 5 mg/d, telmisartan 40 mg/d, and lansoprazole 15 mg/d. She had no known drug or food allergy. She had no allergy, but in the past, she had a history of dry cough induced by an angiotensin-converting-enzyme inhibitor.

Her past medical history suggests that she has had multiple vascular risks, including diabetes, hypertension, vascular disease history, and obesity. GERD can cause upper abdominal pain but does not cause diffuse abdominal pain. There are many causes of chronic cutaneous pruritus, such as encompassing autoimmune condition, systemic disorders, and neuropathy. She is aged and diabetic, that can contribute to chronic itch, but there can be other reasons for the symptom.

On examination, the patient was lying down on a stretcher with her hands on the abdomen because of the pain. Her mental status was intact. Her body temperature was 36.9°C blood pressure, 172/82 mm Hg; pulse, 82 beats/min and regular; respiratory rate, 30/min; and oxygen saturation, 97% while breathing ambient air. She complained of unlocalized moderate tenderness over her entire abdomen. Costovertebral angle tenderness, liver tenderness, Murphy's sign, and Carnett's sign were absent. Lungs were clear to auscultation bilaterally, without percussion dullness, and no other abnormal findings were noted. Cardiovascular examinations revealed normal heart sounds and palpable dorsal pedal pulses. There was no bruit over the neck, abdomen, and bilateral inguinal areas. Head-eyes-ears-nose-throat, back, rectal, and skin examinations were normal. Joint examination revealed no abnormal findings. She was administered acetaminophen 400 mg, orally, which transiently resolved her abdominal pain. Her respiratory rate decreased to 20 per minute.

Examination of her vital signs revealed hypertension and tachypnea, and the most prominent sign in this patient was tachypnea. Major causes of extreme tachypnea, more than 30 per minute, are not many: severe metabolic acidosis, high fever with or without distributive state, severe hypoxia, respiratory system compromise (upper airway and thoracic cage or neuromuscular problem), or severe pain especially of pleural origin. She had no tachycardia, which suggested absence of hemodynamic compromise or cardiovascular disorder, other than those because of her medical conditions that lower heart rate, such as sinus bradycardia, hypothyroidism, or use of medications that decrease heart rate.

Given the paucity of the clinical signs reflective of fever, hypoxia, or respiratory compromise, in addition to the history of metabolic or endocrine disorder and neuromuscular diseases, most of the etiologies causing elevated respiratory rate would become less likely. Moreover, the fact that her respiratory rate decreased after the administration of acetaminophen, which has both antipyretic and analgesic effects, indicates that her tachypnea could stem from pain. In this case, the patient had abdominal pain without any abnormal findings as observed from abdominal examination. Therefore, two etiologies can be considered: vascular ischemia, especially of the branches of the abdominal arteries, and generalized pain from the supra- or infradiaphragm, such as from pleuritis, empyema, or infradiaphragmatic abscess or inflammation. Gastric ulcer, duodenal ulcer, gastroenteritis, or pancreatitis usually involve abdominal tenderness but sometimes show no tenderness. Furthermore, endocrine or metabolic causes, such as diabetic ketoacidosis, hyperthyroidism, and hypercalcemia, can cause abdominal pain. However, acetaminophen does not alleviate the pain in these conditions, and in the current case, there have been no clinical signs suggesting these diagnoses thus far.

Therefore, laboratory tests, including blood count and tests for measuring glucose and hemoglobin A1c, were performed. In addition, the patient's abdominal examinations were performed again, especially detailed examination of the diaphragm. In case of no remarkable findings, an imaging study can help reveal any ambiguities. Because the patient is obese, the detection of abnormalities of the chest and abdomen from physical examination is difficult. Therefore, in this case, computed tomography (CT) is the next test of choice.

Laboratory data (Table 1) revealed the following: white blood cell count, 13.4 × $10^3$/μL (normal range, 3.0-8.5 × $10^3$/μL); lactate dehydrogenase, 245 IU/L (normal range, 106-211 IU/L); alkaline phosphatase, 402 IU/L (normal range, 104-338 IU/L); serum blood glucose, 201 mg/dL (normal range, 74-106 mg/dL); and C-reactive protein, 0.39 mg/dL (normal range, −0.3 mg/dL). Aspartate aminotransferase level, alanine aminotransferase level, ɤ-glutamyl transpeptidase level, total bilirubin level, and amylase level were within normal ranges as shown in Table 1. Routine testing two weeks before revealed the following: lactate dehydrogenase, 214 IU/L; alkaline phosphatase, 380 IU/L; and hemoglobin A1c (National GIycohemoglobin Standardization Program), 7.3% (normal range, 4.5%-6.2%). Serum calcium was not required to be measured. Repeat lung and abdominal examination did not show any remarkable results. The chest radiograph revealed no infiltration. The electrocardiogram was within the normal limits. An abdominal CT scan without contrast enhancement revealed slight enlargement of the gallbladder with biliary sludge in the neck. There was no lung infiltration or pleural effusion. The wall of the abdominal aorta and its branches were partially calcified. There was no aneurysm or vascular dissection.

**TABLE 1** Laboratory data on admission

| | | Normal range |
|---|---|---|
| WBC | $13.4 \times 10^3/\mu L$ | $3.0\text{-}8.5 \times 10^3$ |
| Hb | 12.1 g/dL | 10.8-14.9 |
| PLT | $19.0 \times 10^4/\mu L$ | $15.0\text{-}36.1 \times 10^4$ |
| AST | 23 IU/L | 8-38 |
| ALT | 24 IU/L | 4-44 |
| LDH | 245 IU/L | 106-211 |
| ALP | 203 IU/L | 104-338 |
| γ-GTP | 24 IU/L | 4.7-52 |
| T-Bil | 0.9 mg/dL | 0.2-1.2 |
| Cre | 0.31 mg/dL | 0.4-0.8 |
| BUN | 9.3mg/dL | 7.0-18.0 |
| Amylase | 41 IU/L | 33-150 |
| CPK | 88 IU/L | 29-192 |
| Na | 139 mEq/L | 136-145 |
| K | 3.7 mEq/L | 3.5-5.1 |
| Cl | 98 mEq/L | 98-107 |
| Glucose | 201 mg/dL | 74-106 |
| CRP | 0.39 mg/dL | 0-0.30 |

The patient was admitted because of loss of appetite and hesitation to eating foods that required continuous fluid repletion. Under the tentative diagnosis of gallbladder infection, given her abdominal pain and the CT scan result, intravenous administration of cefmetazole 1 g every 8 hours was initiated for antibiotic coverage against intestinal bacteria such as *Escherichia coli* and *Klebsiella* spp.

As she was started on treatment for the gallbladder or biliary infection, I was skeptical of this working diagnosis. Only biliary sludge can be observed in normal individuals, and the sludge itself is not pathognomonic. Nevertheless, the diagnosis of gallbladder and biliary infection still can be possible. This patient presented after a very short period following the onset of the pain; therefore, the lesion might take a longer time to become apparent even on an imaging study. Moreover, sites other than the gallbladder or biliary system could become apparent as locations of the true lesion as time passes and manifest as localized pain or imaging findings. As this time, the patient underwent an abdominal CT scan without contrast and it provided limited information about the evaluation of disorders in the abdomen. Therefore, I would suggest extending the scanning to the chest for the detection of possible lesions above the diaphragm and to add abdominal CT scan with contrast to reveal any hidden inflammation or vascular condition.

On her 2nd day at the hospital, her abdominal pain did not abate. The body temperature increased to 38.1°C, blood pressure was 116/62 mm Hg, pulse was 98 beats/min, respiratory rate was 20/min, and oxygen saturation was 94% when breathing ambient air. Additionally, she complained of mild diffuse abdominal pain. On examination, tenderness was more severe in the right upper quadrant of the abdomen (RUQ) compared to other abdominal areas. The point of maximum pain was 2 cm below the costal arch on the right mid-clavicular line. Liver tenderness was positive, and Murphy's sign was negative. Pulmonary examination revealed no crackles or any other abnormal sounds. Abdominal ultrasonography revealed a normal gallbladder with sludge and normal liver parenchyma. Sonographic Murphy sign was negative. Biliary dilatation, hydronephroses, liver or kidney abscesses, and intestinal wall edema were not observed. Intravenous administration of cefmetazole and oral administration of acetaminophen were continued.

At this point, the patient had fever, and the diffuse abdominal pain became localized at the RUQ. As the fever coincided with the development of the RUQ pain, it is reasonable to have assumed that the origin of fever was located at the RUQ area. RUQ pain illustrates many causes involving the lower chest and upper abdomen. The results of repeated physical examination and imaging studies decreased the possibility of fever originating from the liver, biliary, intestinal, and genitourinary systems. The patient had been receiving cefmetazole, which effectively covers gram-negative bacteria and anaerobes such as *Escherichia coli*, *Klebsiella spp.*, and *Bacteroides spp.* that frequently affect the gastrointestinal and genitourinary systems. However, despite the administration of the antibiotic, fever developed. This meant that several hypotheses could be speculated on inappropriate use (duration or spectrum) of antibiotic, concurrent diseases, wrong diagnosis, or drug fever due to the antibiotic. Another diagnostic clue at this stage was hypoxia. Hypoxia cannot be explained by the intra-abdominal or retroperitoneal lesion but can be explained by an intrathoracic lesion. While she had no abnormal lung sounds, crackles are often absent in the early phase of pneumonia with or without pleuritis.

On the 3rd day, the patient remained febrile with a body temperature of 38.2°C. Her abdominal pain was even more localized at the RUQ. She reported that on deep inspiration the pain worsened, which had begun the night before. Moreover, she had developed a mild dry cough morning. Pulmonary auscultation revealed slight pleural friction rubs over the right lower lateral thoracic region. There was no percussion dullness. Lung ultrasonography showed a small area of consolidated parenchyma below the right lower lateral area. Cefmetazole was replaced with ampicillin/sulbactam 3 g every 8 hours for anaerobes that were not covered by cefmetazole, such as *Fusobacterium* spp.

As mentioned before, the localization of the origin of fever had now become apparent. Given the presence of dry cough, pain on inspiration, and image findings suggesting lung parenchymal inflammation, the diagnosis of pneumonia with pleuritis was made.

On the 4th day, laboratory data (Table 2) showed a white blood cell count of $14.7 \times 10^3/\mu L$ (leukocytosis) and high level of C-reactive protein of 34.16 mg/dL. The aminotransferases, creatine kinase, and electrolyte levels remained normal. A chest CT scan without contrast enhancement showed infiltrations in the middle and lower lobes of the right lung, with thickening of the adjacent lung pleura and a small amount of right pleural effusion (Figure 1).

The administration of ampicillin/sulbactam was continued. Subsequently, on day 5, her temperature returned to the normal range. Her abdominal pain gradually diminished and was completely resolved by day eight. Thereafter, she was discharged on day 13, and her symptoms had not recurred on her follow-up visits.

## 1 | DISCUSSION

This is a case of pneumonia with pleuritis that initially presented with diffuse abdominal pain. Pneumonia is undoubtedly one of the diseases that primary care physicians treat most commonly. In Japan, pneumonia was the third leading cause of death, and 120 953 people have died of pneumonia in 2015, which accounted for 9.4% of total deaths.[1] In the past, active population-based surveillance for community-acquired pneumonia requiring hospitalization in adults reported that the causative microorganisms include viruses (23%), bacteria (11%), bacterial and viral pathogens (3%), and a fungal or mycobacterial pathogen (1%) among the cases in which the causative pathogen was detected (38%).[2] The most common pathogens were reported to be human rhinovirus, influenza virus, and *Streptococcus pneumoniae*. The patient was initially started on cefmetazole and was later switched to ampicillin/sulbactam. Despite the causative pathogens were not identified in this case, the patient had finally recovered. The hypotheses explaining the recovery of this patient are as follows: the causative microorganism was covered by both cefmetazole and ampicillin/sulbactam (eg, *S. pneumonia*); the causative microorganism was not covered by cefmetazole but was covered by ampicillin/sulbactam (eg, *Fusobacterium spp.*); and the microorganism was not covered by both cefmetazole and ampicillin/sulbactam, but had a self-limiting clinical course (ie, virus). If the first hypothesis was true, in retrospect, cefmetazole should not have been replaced with another antibiotic. However, given the causative organism was unidentified, the use of a broader-spectrum antibiotic especially for this elderly, immunocompromised patient may have been appropriate.

**TABLE 2** Laboratory data on day 4

| | | Normal range |
|---|---|---|
| WBC | $14.6 \times 10^3/\mu L$ | $3.0\text{-}8.5 \times 10^3$ |
| Hb | 11.7 g/dL | 10.8-14.9 |
| PLT | $14.8 \times 10^4/\mu L$ | $15.0\text{-}36.1 \times 10^4$ |
| AST | 17 IU/L | 8-38 |
| ALT | 17 IU/L | 4-44 |
| LDH | 185 IU/L | 106-211 |
| γ-GTP | 29 IU/L | 4.7-52 |
| T-Bil | 0.8 mg/dL | 0.2-1.2 |
| Amylase | 16 IU/L | 33-150 |
| CPK | 88 IU/L | 29-192 |
| Glucose | 148 mg/dL | 74-106 |
| CRP | 34.16 mg/dL | 0-0.30 |

A typical presentation of pneumonia includes fever, cough, sputum, shortness of breath, crackles on auscultation, and newly developed lung infiltrates on an X-ray image. Some patients, however, lack these findings, as in this case.[3] Older patients have fewer symptoms in terms of both respiratory and nonrespiratory systems even after adjusting the comorbidity and illness severity compared with younger patients;[4] that is, elderly patients with pneumonia often present with symptoms or findings seemingly unrelated to the lower respiratory tract or other vague complaints that do not indicate any specific organ dysfunction.

Pleuritic chest pain is a well-known symptom in patients with pneumonia. However, the area of the pain may be remote from the site of the actual lesion, such as the opposite side and the abdomen.[5] Abdominal pain is one of the nonrespiratory symptoms in pneumonia. It is reported that abdominal pain occurs in 8% of patients with pneumonia.[6] In fact, pneumonia is associated with various abdominal symptoms including pain, flatulence, nausea, vomiting, and constipation.[6]

In children, pneumonia is known to be the most common extra-abdominal cause of acute abdominal pain.[7] However, it has been pointed out that general practitioners often fail to associate the abdominal complaint with pneumonia, and this erroneous judgment may lead to a delay in the diagnosis and administration of appropriate treatment.[8] Pneumonia is a condition that must be taken into consideration as a differential diagnosis of acute abdominal pain even in adults.

This case underscores the importance of considering symptom chronology in patients who have pain. In this case, the patient's abdominal pain was initially diffuse and was then localized to the RUQ later. When a patient complains of a relatively recent onset of diffuse or vague pain, clinicians should consider that the pain

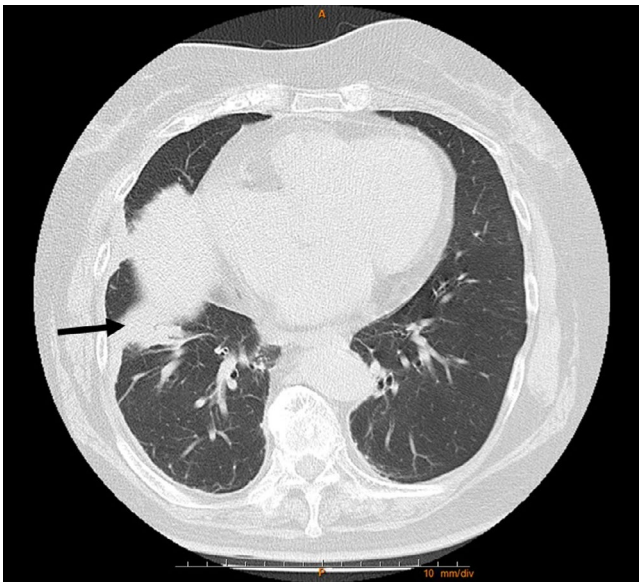

**FIGURE 1** A computed tomography image of the chest. An arrow indicates infiltration in the middle and lower lobes of the right lung with an adjacent pleural thickening and a small amount of pleural effusion

may not have localized yet, and speculate if the pain may localize somewhere, and wait and identify the emergence of the "true" site of the pain. Fortunately, the case discussant, in this case, succeeded in avoiding anchoring to thinking of diffuse abdominal pain and waited carefully for the emergence of the localized pain. In addition, in the early phase of the case, the discussant clearly pointed out the possibility of pleuritis as a differential diagnosis judging from the patient's disproportionately prominent respiratory rate compared with other vital signs. The elevation in the respiratory rate, sometimes, gives clinicians many clues to an appropriate diagnosis, which is another learning point from this case. This patient had presented with an abdominal pain but was later diagnosed as having an intrathoracic pathology. Therefore, careful attention to the respiratory rate can help clinicians to think beyond the abdomen, and avoid fixating to an intra-abdominal pathology and premature closure of the diagnostic considerations. The other essential learning from this case is that clinicians should have a clear illness script for pneumonia and pleuritis. Illness script summarizes risk factors and epidemiology, time course, clinical presentation, and pathophysiology, constituting mental models of the disease.[9,10] When clinicians do not find any clinical clues, it is essential to repeat the history-taking process and physical examination, such that in addition to knowing a comprehensive illness script, as in this case, clinicians can ascertain important clinical clues, even the subtle ones, to make a correct diagnosis.

The adage: all that glitters is not gold—it means that not everything that looks true turns out to be so. This patient initially presented with acute abdominal pain, which seemingly suggested an intra-abdominal pathology. Abdominal pain (glitters) is not always from abdominal origin (gold). Indeed, the pain in this case turned out to be from pleurisy (other than gold). This case highlights the importance of avoiding anchoring and premature closure by establishing precise differential diagnosis with obtaining careful history and clinical signs, instead of connecting abdominal pain hastily with an intra-abdominal etiology.

## ACKNOWLEDGEMENTS

None.

## CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

## ORCID

*Junki Mizumoto* https://orcid.org/0000-0002-0783-7351

*Taro Shimizu* https://orcid.org/0000-0002-3788-487X

## REFERENCES

1. Miyashita N, Yamauchi Y. Bacterial pneumonia in elderly Japanese populations. Jpn Clin Med. 2018;9:1179670717751433.
2. Jain S, Williams DJ, Arnold SR, Ampofo K, Bramley AM, Reed C et al. Community-acquired pneumonia requiring hospitalization among U.S. adults. N Engl J Med. 2015;373(5):415–27.
3. Musher DM, Thorner AR. Community-acquired pneumonia. N Engl J Med. 2014;371(17):1619–28.
4. Metlay JP, Schulz R, Li YH, Singer DE, Marrie TJ, Coley CM, et al. Influence of age on symptoms at presentation in patients with community-acquired pneumonia. Arch Intern Med. 1997;157(13):1453–9.
5. James BH. Abdominal pain in pleurisy and pneumonia. JAMA. 1903;XL I(9):535–40.
6. Gauss H. Abdominal pain in pneumonia. Am J Dig Dis. 1946;13:73–7.
7. Tsalkidis A, Gardikis S, Cassimos D, Kambouri K, Tsalkidou E, Deftereos S, et al. Acute abdomen in children due to extra-abdominal causes. Pediatr Int. 2008;50:315–8.
8. Armeni E, Mylona V, Karlis G, Makrygiannis E. Pneumonia presenting with lower right abdominal pain and migratory polyarthritis. Respir Med Case Rep. 2012;5:29–30.
9. Bowen JL. Educational strategies to promote clinical diagnostic reasoning. N Engl J Med. 2006;355(21):2217–25.
10. Einstein DJ, Trowbridge RL, Rencic J. A problematic palsy: an exercise in clinical reasoning. J Gen Intern Med. 2015;30(7):1029–33.

**How to cite this article:** Mizumoto J, Shimizu T. All that glitters is not gold. *J Gen Fam Med*. 2019;20:180–184. https://doi.org/10.1002/jgf2.264