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Diagnostic challenges from conflicting results of tests and imaging

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Abstract

Accurate diagnosis is the foundation of clinical care but accurate diagnosis is not easily reached in some cases. In rare instances, even a sophisticated multidisciplinary team at an academic medical center cannot reliably reach an accurate diagnosis after extensive testing and imaging, and has to wait until histological diagnosis or even autopsy results are available. The underlying reason of challenging diagnoses is mostly conflicting data from history, tests, and imaging that point to different diagnoses. In this issue of *World Journal of Clinical Cases*, Huffaker *et al* reported such a challenging case of a tricuspid mass in a patient with Li-Fraumeni syndrome. The case by Huffaker *et al* powerfully illustrates the occasional diagnostic challenges inherent in our current diagnostic approach and the current technology. Clinicians should realize that in rare situations, agnosticism in diagnosis is unavoidable but a treatment has to be initiated so long as the principle of *primum non nocere* is upheld.

Key Words: Li-Fraumeni syndrome; Cardiac mass; Thrombus; Challenging diagnosis; Histological diagnosis; False positive results

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Core Tip: The underlying reason of challenging diagnoses is mostly conflicting data from history, tests, and imaging that point to different diagnoses. The case by Huffaker *et al* powerfully illustrates the occasional diagnostic challenges inherent in our current diagnostic approach and technology. Clinicians should realize that in rare situations, agnosticism in diagnosis is unavoidable but a treatment has to be initiated so long as the principle of *primum non nocere* is upheld.

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INTRODUCTION

Accurate diagnosis is the foundation of clinical care but accurate diagnosis is not easily reached in some cases. In rare instances, even a sophisticated multidisciplinary team at an academic medical center cannot reliably reach an accurate diagnosis after extensive testing and imaging, and has to wait until histological diagnosis or even autopsy results are available. The underlying reasons of challenging diagnoses fall into two categories: Much more commonly, conflicting data from history, tests, and imaging that point to different diagnoses, and less commonly, failure to recognize a potential novel disease[1].

CONFLICTING DIAGNOSTIC RESULTS

Conflicting results from tests and imaging are quite common in clinical practice; most experienced clinicians are well versed in teasing out common conflicting results from tests and imaging. For example, normal hemoglobin A1c in a patient with history of poorly controlled diabetes and severe hyperglycemia who has just received blood transfusion is well recognized as a false negative result due to transfusion. As the disease becomes rarer, specialists need to be called upon to interpret conflicting results. For example, pancreastatin and chromogranin A, both markers of neuroendocrine tumor, may be much elevated and normal, respectively, but elevated pancreastatin can be false positive due to spurious test method[2]. Our experience with imaging follows the same pattern. It is well known that renal cell carcinoma can have normal fluorodeoxyglucose (FDG) uptake on positron emission tomography (PET) so that a normal FDG uptake cannot rule out the cancer. When dodecane tetraacetic acid octreotate (DOTATATE)-PET first became available, uptake at the pancreatic head/neck region without computed tomography (CT) correlates often was thought as evidence of pancreatic neuroendocrine tumor. Accumulating experience and research over the years now show that the DOTATATE uptake at the pancreatic head/neck region is most often due to pancreatic polypeptide cell pseudohyperplasia[3]. Thus at academic centers, multidisciplinary teams of experts from various specialties usually can reach a correct diagnosis based on history, laboratory tests, and imaging, before histological evidence is required. Once in a while, even a team of experts cannot reliably make an accurate diagnosis.

AN ILLUSTRATIVE CASE

In this issue of World Journal of Clinical Cases, Huffaker *et al*[4] reported such a challenging case of a tricuspid mass in a patient with Li-Fraumeni syndrome (LFS). LFS is an autosomal dominant disease of multiple malignancies due to inactivating mutations of tumor suppressor P53. Common malignancies in LFS include soft tissue sarcoma, osteosarcoma, and breast cancer. The 30-year-old female described by Huffaker *et al*[4] had clearly diagnosed LFS with history of multiple LFS-defining malignancies. She also had two atrial septal defects so underwent periodic echocardiogram for signs of right heart enlargement. The latest transthoracic echocardiogram showed a 1-cm mass on the tricuspid valve, which had not been present a year before. Clinically she was well and exhibited no cardiac signs or symptoms.

The differential diagnosis of a cardiac mass includes tumor, thrombus, and vegetation[5]. To pinpoint the diagnosis without histology is often challenging. Clinical history and imaging characteristics of the mass are helpful predictors of a diagnosis. For example, a left ventricular mass in a patient with embolic stroke and reduced left ventricular wall motion is most likely a thrombus[6]. In this young female with LFS, tumor was a concern as cardiac sarcoma has been reported in LFS[7]. The patient was also at high risk of thrombus due to hypercoagulability associated with extensive malignancy history. The case report did not specify whether the patient was taking oral contraceptives or other hormonal therapies, which has been associated with tricuspid thrombus presumably due to hormonally-related hypercoagulability[8]. As she overall felt well and presumably did not have fever or anemia, vegetation was highly unlikely and could be ruled out clinically. There are no laboratory tests to differentiate a cardiac tumor from a thrombus; detailed imaging is needed to further characterize the tricuspid mass. Transesophageal echocardiogram describes the location, shape, and motion of a cardiac mass in real time but does not particularly tell the nature of the mass. In this case, transesophageal echocardiogram showed that the mass was attached to the anterior tricuspid valve leaflet, presumably without abnormal blood flow through the right heart. Magnetic resonance imaging (MRI) is the most commonly used imaging modality to differentiate a cardiac tumor from a thrombus with the late gadolinium enhancement protocol based on the reasonable assumption that a thrombus should not have significant blood supply[9]. In this case, gadolinium enhancement was noted on the tricuspid mass, which was interpreted as imaging evidence of tumor. Could the authors use additional imaging? FDG-PET/CT has been used to differentiate a cardiac tumor from a thrombus but it has also been subject to falsely suggesting malignancy in a case of organized thrombus[10].

In a challenging case like this one, the next critical question is whether making an accurate diagnosis (*i.e.*, a tricuspid tumor *vs* thrombus) affects management? A tricuspid tumor would require surgical resection but a tricuspid thrombus could potentially be treated with anticoagulation. Anticoagulation, however, is associated with risk of embolism, and in this case, pulmonary embolism, which is a serious adverse effect[11]. The authors opted to stop at the MRI and proceeded with surgical resection, regardless whether this was a tricuspid tumor or thrombus. The histology showed that the tricuspid mass was actually an organized thrombus.

CONCLUSION

The case by Huffaker *et al*[4] powerfully illustrates the occasional diagnostic challenges inherent in our current diagnostic approach and the current technology. Clinicians should realize that in rare situations, agnosticism in diagnosis is unavoidable and an accurate diagnosis simply cannot be made, but a treatment has to be initiated so long as the principle of *primum non nocere* is upheld. Technological advances such as radiomics and artificial intelligence may aid us achieving a more accurate diagnosis[12,13].

FOOTNOTES

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