

Question 1. A 33-year-old white male with past medical history of depression and prior suicide attempts was found in the basement with a 6-foot long orange electrical cord wrapped around his neck. A suicide note was present at the scene. The external examination of the body revealed the ligature mark above the level of the Adam's apple and fine petechial hemorrhages on the face. The internal organs were largely unremarkable except for a 3 cm in diameter, subcapsular mass in the liver (see gross and microscopic images). Which of the following **IS NOT** a feature of this lesion?

- A. It can occur at any age, but mostly in third to fifth decade of life
- B. It's more common in males
- C. It's asymptomatic in 80% of the cases
- D. Hemoperitoneum is extremely rare
- E. Multicentricity is seen in 20% of adults and a higher percentage of pediatric cases

The correct answer is B. *Focal nodular hyperplasia* (FNH) is a localized, well-demarcated lesion, consisting of hyperplastic hepatocyte nodules with a central fibrous scar. The nodules appear in non-cirrhotic livers and may reach up to many centimeters in diameter. Focal nodular hyperplasia is not a neoplasm but a nodular regeneration. It occurs in response to local vascular injury. It is usually an incidental finding, most commonly seen in women of reproductive age (female to male ratio 2:1 to 8:11). FNH can occur in any age group including childhood; however, most cases are seen during the third to fifth decade of life. In contrast with liver cell adenoma, hemoperitoneum is extremely rare. The lesion is usually solitary; multicentricity has been described in 20% of adults and a higher percentage of pediatric cases. Multicentric cases may be associated with vascular malformations of various organs and neoplasms of the brain.

References:

1. Robbins Basic Pathology, edition 8, chapter 16.
2. Rosai and Ackerman, Surgical pathology, edition 9, volume 1, p. 992.

Question 2. A 19-year-old female was found dead at home by her aunt. According to the relatives, the deceased delivered a term baby boy 4 days ago in the hospital. She did not have any prenatal care. The deceased had no significant past medical history. However, she was complaining of shortness of breath, dry cough and headaches for several days prior to her death. She did not seek medical advice and was taking Tylenol and Robitussin cough syrup for symptoms relief. Due to circumstances, the body was sent to the Medical Examiner's office for an autopsy. At the postmortem examination, the uterus measured 22x12x8.5 cm and weighed 560 grams. The cut surfaces revealed focal hemorrhages. The right and left lungs weighed 410 grams and 390 grams respectively. The lung parenchyma was congested and moderately edematous. The rest of the organs were grossly unremarkable. A surgical pathology report on the placenta obtained from the local hospital, described no pathologic changes. Since the cause of death was not clear at the time of autopsy, the brain was fixed in formalin pending examination by a neuropathologist. Two weeks later, the microscopic examination of the lungs and the brain revealed the following changes (see images). The pathologist who signed the report on the placenta was contacted and notified of the findings. Repeated examination of the placenta revealed no gross abnormalities. Multiple additional sections of the placenta were submitted for microscopic examination, and a small lesion identical to the findings in the lungs and the brain was identified. The histological findings in the lungs and the brain are consistent with the diagnosis of:

- A. Metastatic malignant melanoma
- B. Chorangiomas
- C. Metastatic choriocarcinoma
- D. Primary CNS lymphoma metastatic to the lungs
- E. Disseminated fungal infection

The correct answer is C. *Choriocarcinoma* is the most aggressive form of the gestational trophoblastic disease, which mostly occurs following a complete hydatidiform mole. It can also be preceded by a partial mole, ectopic pregnancy, non-molar intrauterine abortion or term pregnancy. In the latter instance, the tumor may appear as one or more masses in an otherwise normal placenta or develop following the delivery. The natural history of untreated choriocarcinoma is characterized by the development of early hematogenous metastases, the most common sites being the lung, brain, liver, kidney and bowel. The fetus is rarely involved, even in case of widespread metastatic disease. Residual tumor in the uterus in patients dying of disseminated choriocarcinoma may be inconspicuous or absent. Women with metastases to the lungs may have a dry cough, hemoptysis, chest pain or shortness of breath. Brain metastases are often associated with symptoms that suggest a brain tumor or stroke.

References:

1. Rosai and Ackerman, Surgical pathology, edition 9, volume 2, p. 1744-76.
2. Redline R, Abdul-Karim FW. Pathology of gestational trophoblastic disease. *Semin Oncol* 1955; 22: 96 – 108.

Question 3. A 23-year-old black male was seen driving at a high rate of speed in the wrong direction on a highway US 666 before he collided head-on with an SUV. He was unrestrained but had only a few, minor external injuries. He was pronounced dead upon arrival by EMS. The autopsy revealed an intact spleen with an unusual appearance (see gross photograph). The family later confirmed a history for the decedent. The peripheral smear obtained from the local hematologist showed the following (see the picture). What is the etiology of the disease involving the spleen?

- A. Single base mutation $\beta 6\text{glu}\rightarrow\text{val}$
- B. Single base mutation $\beta 6\text{glu}\rightarrow\text{lys}$
- C. Single base mutation $\beta 26\text{glu}\rightarrow\text{lys}$
- D. Fusion between δ and β genes

The correct answer is A. The peripheral smear/ electrophoresis, gross and microscopic appearance of the spleen are consistent with sickle cell anemia. The etiology of sickle cell anemia is a single base mutation in the sixth amino acid on the 6-beta globin chain leading to a substitution of glutamic acid for valine. Substitution of the lysine by glutamic acid 6-beta globin chain accounts for hemoglobin C variant (answer B). Hemoglobin E is a result of $\beta 26\text{glu}\rightarrow\text{lys}$ mutation (answer C). $\text{Hb}_{\text{Le pore}}$ is the result of a fusion between δ and β genes (answer D). Hemoglobin Constant Spring (HbCS) results from a mutation in the α gene stop codon, producing an abnormally long transcript that is unstable (answer E).

References:

1. Quick Compendium of Clinical Pathology: 2nd Edition, Daniel D. Mais, Chapter 4: "Diseases of red blood cells".

Question 4. A 65-year-old black male was found unresponsive by his neighbor on the back yard. He was pronounced dead upon arrival by EMS. The neighbor stated that the deceased was a known drinker and smoker but could not provide any information about his past medical history. The deceased house was found unkept with multiple liquor bottles, litter and dog feces on the floor. The external examination of the body revealed a thin male, status post right below the knee amputation. The skin of the left lower extremity displayed multiple light brown, scaly patches and superficial ulcers. At autopsy, moderate atherosclerotic cardiovascular disease, hepatosplenomegaly and steatosis of the liver were identified. The kidneys weighed 120 and 110 grams and had granular surfaces with multiple irregular depressions. Upon bisection, marked thinning of the cortical tissue was seen bilaterally. Microscopically, both kidneys displayed the following (see pictures). What is the underlying medical condition involving the kidneys?

- A. Hypertension
- B. Amyloidosis
- C. Systemic lupus erythematosus
- D. Alcoholic nephropathy
- E. Diabetes mellitus

The correct answer is E. The kidneys are a prime target of diabetes mellitus. The progression of the disease leads to the increase of mesangial cellularity with formation of nodules in the glomerular tuft. Known as Kimmelstiel-Wilson nodules, they are spherical, eosinophilic and positive with PAS and methenamine-silver stains. In hypertension (answer A), arterionephrosclerosis is the primary finding. In amyloidosis (answer B), the kidneys may appear unchanged, or may be abnormally large, pale, gray, and firm; in long-standing cases,

the kidney may be reduced in size. Microscopically, the amyloid deposits are found principally in the glomeruli, but they are also present in the interstitial peritubular tissue and in the walls of the blood vessels. The glomerulus first develops focal deposits within the mesangial matrix and diffuse or nodular thickenings of the basement membranes of the capillary loops. With progression, the deposition encroaches on the capillary lumina and eventually leads to total obliteration of the vascular tuft. Amyloidosis can be confused with diabetic nephropathy. Congo red, PAS and silver stains in conjunction with clinical information and/or autopsy findings are helpful in differential diagnosis. Glomerulonephritis in SLE (answer C) involves deposition of DNA/anti-DNA complexes within the glomeruli. According to revised classification, there are 6 classes of lupus nephritis. None of them presents as a nodular lesion. There is no such an entity as alcoholic nephropathy (answer D).

References:

1. Robbins Basic Pathology, edition 8, chapters 5, 14, 20.
2. Weening JJ, D'Agati VD, Schwartz MM, et al. The Classification of Glomerulonephritis in Systemic Lupus Erythematosus Revisited. *J Am Soc Nephrol.* 2004;15(2):241-250.

Question 5. A 22-year old white male collapsed in the middle of the college class. En route to the hospital, ventricular tachycardia followed by ventricular fibrillation was registered by EMTs. He died in the ER shortly after arrival in spite of aggressive resuscitation. Considering young age and unclear cause of lethal arrhythmia, the body was sent to Medical Examiner's office. Postmortem examination revealed cardiomegaly (600 grams) and left ventricular dilatation (4.3 cm at the level of the papillary muscles). Microscopic findings are provided below (see images). According to the relatives, approximately 10 months ago the deceased experienced flu like illness followed by gradual decrease of exercise tolerance, lack of energy and malaise. He did not seek medical help attributing his symptoms to "college fatigue". Shortly before death, he complained of dry cough and occasional chest pain. He scheduled an appointment with his family physician but skipped it due to important seminar. Prior to these events, the deceased was in excellent health. He was a captain of a water polo team, rarely consumed alcohol and never traveled outside of the US East Coast. Based on the history and the autopsy findings, forensic pathologist suspected a particular etiologic agent and sent a sample of the myocardium for cDNA hybridization study. The probe came positive. What is the most likely causative agent of this cardiac pathology?

- A. Trypanosoma cruzi
- B. Alcohol
- C. Streptobacillus moniliformis
- D. Coxsackie B virus
- E. Pseudomonas mallei

The correct answer is D. In North America, Coxsackie B virus is the most common cause of viral myocarditis and viral cardiomyopathy. In this case, history of flue like illness, symptoms of congestive heart failure and detection of the viral RNA by cDNA hybridization study points to specific viral etiology. Trypanosoma cruzi (answer A) is the cause of Chagas disease, which presents as dilated cardiomyopathy as well. However, Trypanosoma cruzi is a parasite and cannot be detected by cDNA. It usually is diagnosed by serological assays. Chagas disease is endemic in Mexico, Central and South America. Rare cases of Chagas disease attributed to local vector-borne transmission have been reported in the United States. Alcoholic cardiomyopathy (answer B) requires years of alcohol exposure and usually is accompanied by damage of other organs. Streptobacillus moniliformis (answer C) is a fastidious gram-negative bacillus transmitted to

humans by rats. Rat bite fever is occasionally complicated by acute endocarditis. *Pseudomonas mallei* (answer E) causes glanders, an infectious disease occurring primarily in horses, mules, and donkeys. Humans contract the disease through direct contacts with infected animals. Symptoms include the formation of nodular lesions in the lungs and ulceration of the mucous membranes in the upper respiratory tract.

References:

1. Quick Compendium of Clinical Pathology: 2nd Edition, Daniel D. Mais, Chapter 3: Microbiology
2. Center for disease control and prevention - <http://www.cdc.gov/>
3. Robbins Basic Pathology, edition 8, chapter 11

Question 6. A 36-year-old previously healthy Caucasian female complained of severe substernal chest pain associated with left arm radiation shortly after a 10-mile training run. She collapsed in front of her family in cardiac arrest before the ambulance arrived. Aggressive resuscitation continued for 50 minutes but was futile. The relatives reported that the deceased was in excellent health and had been actively training for Pittsburgh Marathon. She had never been pregnant and never used tobacco, alcohol or illicit drugs. Due to circumstances, the autopsy was performed at the Medical Examiner's office. The postmortem examination revealed a pathologic finding in the left anterior descending artery (see microscopic pictures). The rest of the heart and other organs were grossly unremarkable. This condition is most common in:

- A. Young women during peripartum period
- B. Young healthy non-pregnant females
- C. Young males with Marfan syndrome
- D. Elderly males with atherosclerotic cardiovascular disease
- E. Children of both sexes with Kawasaki disease

The correct answer is A. This is an example of spontaneous coronary artery dissection. True spontaneous coronary artery dissection (SCAD) is an extremely rare event with only about 150 cases reported in the literature. The majority (80%) occurs in young women during the peripartum period or in association with oral contraceptive use. Several cases of SCAD have been described in non-pregnant healthy young females (answer B). Marfan syndrome (answer C) is associated with aortic aneurysm or dissection of the ascending aorta. Atherosclerosis is a major cause of abdominal aortic aneurysm, which occurs more frequently in elderly males (answer D). Kawasaki disease is associated with coronary artery aneurysms, which can rupture. But since we are talking about true dissection of intact arteries, **A** is the correct choice.

References:

1. Robbins Basic Pathology, edition 8, chapters 7 and 10
2. Almeda FQ, Barkatullah S, Kavinsky CJ. Spontaneous Coronary Artery Dissection, Clin Cardiol 2004; 27: 377-80.

Question 7. This was an incidental finding in the parenchyma of the right upper lobe of the lung just beneath the pleura in 28-year old Hispanic male who died of combined drug overdose (see microscopic picture). Grossly, the mass was sharply delineated and lobulated. All statements about this lesion are true EXCEPT:

- A. Characteristic popcorn pattern of calcification is seen on roentgenogram in 33% of cases
- B. Chromosome 6p21 breakpoint within *HMG-I (Y)* gene or immediate surroundings is the most common genetic abnormality
- C. Some spindle cells in this lesion are positive for actin and S-100
- D. It is usually solitary and more common in males
- E. It is associated with Carney triad

The correct answer is E. This is an example of pulmonary hamartoma, which IS NOT a part of Carney triad. Carney triad consists of pulmonary chondroma (different from hamartoma!), functioning extra-adrenal paragangliomas and gastrointestinal stromal tumors (GIST). The rest of the statements are true.

References:

1. Rosai and Ackerman, Surgical pathology, edition 9, volume 1, pp. 406-407
2. Pulmonary chondroma: a tumor associated with Carney triad and different from pulmonary hamartoma, FJ Rodriguez et al, Am J Surg Pathol. 2007 Dec;31(12):1844-53

Question 8. A 65 year-old Caucasian female with a past medical history of hypertension, hyperlipidemia and insulin dependent diabetes mellitus for more than 10 years duration was found dead at home by her daughter. The daughter stated that the deceased complained of back pain and mild shortness of breath for several days prior to her death but otherwise was in her usual state of health. Due to unclear circumstances, the body was brought to Medical Examiner's office for postmortem examination. An autopsy revealed 200 cc of blood with clots within the pericardial cavity. The anterior wall of the left ventricle displayed the following findings (see gross pictures). What IS NOT true about this condition?

- A. It is seen mostly in patients older than 60 years
- B. It is reported more commonly in women than in men
- C. Pre-existing hypertension is risk factor
- D. Left ventricular hypertrophy is a risk factor
- E. It is universally fatal if complicated by cardiac tamponade

The correct answer is E. This is an example of a rupture of the ventricular free wall with hemopericardium and cardiac tamponade, which is usually fatal. Myocardial rupture complicates between 1% and 5% (up to 10% in some case series) of myocardial infarctions (MI). Rupture can occur at almost any time after MI but is most common 3 to 7 days after infarction. Risk factors for free-wall rupture include age older than 60 years, female gender, pre-existing hypertension, **lack of left ventricular hypertrophy**, and no previous MI (pre-existing scarring tends to prevent myocardial tearing).

References:

1. Robbins Basic Pathology, edition 8, chapter 11.

Question 9. A 24-year-old black male was found dead the morning after a party at his friend's house. His friends stated that the deceased had "some breathing problem" since he was a kid. They also reported that the deceased "never drank too much". At autopsy the only significant finding was in the respiratory system. The lungs were distended and hyper-inflated. The microscopic picture revealed the following (see images). The toxicology results were positive for blood alcohol of 0.02%. All the statements about this condition are true EXCEPT:

- A. This is a restrictive pulmonary disease
- B. Basement membrane thickening and hypertrophy of bronchial smooth muscle are key features of this condition
- C. T_H2 cytokines IL-4, IL-5, and IL-13 are important mediators
- D. Eosinophils and mast cells predominate in inflammatory infiltrate
- E. Significant increase in the incidence of this disease has been observed over the past 3 decades

The correct answer is A. This is an example of status asthmaticus with over-distended lungs, mucus plugs and airway remodeling. Asthma is a prototype of an obstructive (not restrictive) pulmonary disease. The rest of the statements are true.

References:

1. Robbins Basic Pathology, edition 8, chapter 13.

Question 10. A 25-year-old, 34 week pregnant female was found obtunded by her husband in bed surrounded by empty medicine bottles and pills of various colors and shapes. The husband reported that they had a violent quarrel three days ago, after which he left the house. He stayed at his parents' house and did not have any contact with his wife since his departure. According to him, she was having a difficult time coping with college and part-time work. She did not have prior suicide attempts or ideations. Upon admission to the hospital, she was noted to have severely altered mental status, mild icteric sclera and blood pressure of 90/60 mmHg. The blood chemistry panel showed thrombocytopenia, prolonged PT, PTT, AST of 8460 IU/L, ALT of 4640 IU/L, and alkaline phosphatase of 338 IU/L. Due to absence of fetal movements, an emergency C-section was attempted. An appropriate for gestational age stillborn boy was delivered. In spite of aggressive treatment including massive doses of fresh frozen plasma and NovoSeven, the mother developed multi-organ failure and expired next day. Both bodies were sent to Medical Examiner's office. An autopsy of the mother revealed a moderately jaundiced Caucasian female. All internal organs displayed scattered petechial hemorrhage. Severe pulmonary congestion, bilateral pleural effusion, ascites and hepatomegaly with steatosis were observed. Microscopic findings in the liver are shown in the picture (see image). All of the following about the main culprit of this female's demise is true EXCEPT:

- A. In healthy individuals, the potentially toxic dose is over approximately 150 mg/kg
- B. Rumack-Matthew nomogram is used to predict which patients are at risk for hepatic necrosis
- C. False positive levels of this agent have been reported in hyperbilirubinemic patients
- D. Conjugation of this substance with glucuronide forms the toxic metabolite responsible for hepatic failure
- E. Mucomyst is used for treatment

The correct answer is D. This is an example of acetaminophen toxicity with fulminate hepatic failure. Confluent centrilobular necrosis extending sometimes to the entire lobules and minimal inflammation is a characteristic microscopic picture. There are two main pathways of acetaminophen metabolism. Most of it is

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conjugated with glucuronide or sulfate in the liver to form ***NONTOXIC*** metabolites. A small amount is metabolized by the P₄₅₀ system into the ***TOXIC*** metabolite N-acetyl-p-benzoquinoneimine (NAPQI). NAPQI is normally detoxified by glutathione, but glutathione reserves are quickly overwhelmed in toxic ingestions. Any agent that induces the P₄₅₀ system increases the proportion of acetaminophen processed to NAPQI, enhancing toxicity. *N*-acetylcysteine (Mucomyst) is the antidote for acute acetaminophen poisoning. It promotes metabolism of acetaminophen via the conjugation pathways decreasing the formation of NAPQI. The rest of the statements are true.

References:

1. Quick Compendium of Clinical Pathology: 2nd Edition, Daniel D. Mais, Chapter 1: Toxicology.
2. Robbins Basic Pathology, edition 8, chapter 16.

Notes for question set:¹

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