NEET PG Pathology Sample Paper-2

Duration: 20 Minutes **Maximum Marks: 100**

Instructions

- This paper contains **25** Multiple Choice Questions.
- Each correct answer carries **+4** mark. Incorrect answer: **−1** marks. Only **one** correct option.
- Unattempted questions carry **0** marks.
- Use of mobile phones, smartwatches, or any electronic gadgets is strictly prohibited.

Q1. A male presenting with chronic myeloid leukemia undergoes a bone marrow biopsy. The cytogenetic analysis reveals a $t(9;22)(q34;q11)$ translocation. Which of the following best describes the molecular consequence of this genetic alteration?

(A) Formation of a PML-RARA fusion protein that blocks myeloid differentiation

(B) Upregulation of MYC proto-oncogene leading to autonomous cell proliferation

(C) Creation of a BCR-ABL1 chimeric gene with constitutive tyrosine kinase activity

(D) Loss of function of the TP53 tumor suppressor gene via dominant negative mutation

Q2. A 62-year-old male smoker presents with hemoptysis and a central lung mass. A biopsy reveals invasive squamous cell carcinoma. Histological evaluation shows individual cell keratinization and prominent intercellular bridges. Which of the following cellular structures corresponds to these intercellular bridges?

(A) Hemidesmosomes

(B) Desmosomes

(C) Gap junctions

(D) Tight junctions

Q3. A 28-year-old female experiences sudden severe lower abdominal pain. Laparoscopy reveals an ectopic pregnancy in the fallopian tube. Histopathological examination of the excised tissue shows extensive areas of cell death where cellular outlines are preserved, but cytoplasmic eosinophilia and nuclear pyknosis are prominent. This patterns of tissue necrosis is primarily driven by which mechanism?

(A) Rapid enzymatic digestion by lysosomal hydrolases

(B) Denaturation of structural proteins and cellular enzymes

(C) Saponification of membrane lipids by activated lipases

(D) Liquefaction induced by heterolytic neutrophilic infiltration

Q4. A 54-year-old male with long-standing poorly controlled hypertension presents for a routine check-up. An echocardiogram reveals concentric left ventricular hypertrophy. At the sub-cellular level, this adaptation is primarily characterized by which of the following alterations?

(A) Increased recruitment of quiescent stem cells into the myocardial lineage

(B) Increased synthesis of contractile proteins and structural myofilaments

(C) Epigenetic activation of hyperplastic cellular division protocols

(D) Accumulation of lipofuscin granules within vacuolated sarcoplasm

Q5. A 35-year-old male undergoes an appendectomy for acute appendicitis. Microscopic examination reveals dense neutrophilic infiltration within the muscularis propria. The rolling phase of these leukocytes along the activated endothelial surface is primarily mediated by the interaction of which pair of molecules?

(A) LFA-1 (CD11a/CD18) and ICAM-1

(B) VLA-4 and VCAM-1

(C) Sialyl Lewis X and P-selectin

(D) PECAM-1 (CD31) and PECAM-1

Q6. A 19-year-old female presents with a distinct butterfly rash across her malar eminences, arthralgia, and mild proteinuria. Serological testing is strongly positive for anti-double-stranded DNA (anti-dsDNA) antibodies. The tissue injury seen in this patient's kidneys is predominantly classified under which hypersensitivity mechanism?

(A) Type I (IgE-mediated mast cell degranulation)

(B) Type II (Antibody-dependent cellular cytotoxicity)

(C) Type III (Immune complex-mediated complement activation)

(D) Type IV (T-cell mediated delayed-type hypersensitivity)

Q7. During an autopsy of an 82-year-old female who died of progressive senile dementia, the brain demonstrates significant atrophy of the frontal and parietal lobes with widening of the sulci. Microscopic examination reveals intracellular neurofibrillary tangles and extracellular plaques. Which of the following processes is the primary driver of this cellular atrophy?

(A) Ubiquitin-proteasome mediated degradation of cytoskeleton and autophagic clearance

(B) Ischemic coagulative necrosis secondary to microvascular amyloid angiopathy

(C) Hyperplastic replacement of functional neurons by reactive astrocytic scar tissue

(D) Microglial phagocytosis induced by acute suppurative inflammatory signaling

Q8. A 9-month-old male infant is brought to the clinic due to recurrent pyogenic respiratory infections since 6 months of age. Laboratory evaluation reveals a profound reduction in all serum immunoglobulin classes, while the absolute number of circulating T lymphocytes is completely normal. Flow cytometry

shows an absence of CD19+ and CD20+ B cells. Which developmental defect explains this condition?

(A) Defective expression of Class II MHC molecules on antigen-presenting cells

(B) Mutation in the Bruton tyrosine kinase (BTK) gene halting B-cell maturation

(C) Deletion of chromosome 22q11 leading to third and fourth pharyngeal pouch thymic hypoplasia

(D) Missense mutation in the adenosine deaminase (ADA) gene causing lymphocyte toxicity

Q9. A 65-year-old male is evaluated for generalized fatigue and weight loss. Physical examination reveals marked splenomegaly extending into the left iliac fossa. A peripheral blood smear shows leukocytosis ($120,000/\mu$L) with the presence of granulocytes at all stages of differentiation, including a prominent peak in myelocytes and segmented neutrophils. The blast count is 3%. Which of the following findings would most definitively rule out a leukemoid reaction in favor of Chronic Myeloid Leukemia?

(A) Elevated leukocyte alkaline phosphatase (LAP) score

(B) Presence of toxic granulations and Döhle bodies in mature neutrophils

(C) Low leukocyte alkaline phosphatase (LAP) score accompanied by $t(9;22)$

(D) Prominent absolute eosinophilia and monocytosis without basophilia

Q10. A 4-year-old boy presents with progressive pallor, lethargy, and multiple bruises on his shins. Physical examination reveals generalized lymphadenopathy and hepatosplenomegaly. A complete blood count reveals a hemoglobin level of 6.5 g/dL, a platelet count of $22,000/\mu$L, and a total leukocyte count of $85,000/\mu$L. The peripheral smear is dominated by large cells with a high nucleo-cytoplasmic ratio, fine chromatin, and indistinct nucleoli. These cells are strongly positive for terminal deoxynucleotidyl transferase (TdT) and CD10. What is the most likely diagnosis?

(A) Acute Myeloid Leukemia (AML-M3)

(B) B-cell Acute Lymphoblastic Leukemia (B-ALL)

(C) Chronic Lymphocytic Leukemia (CLL)

(D) Juvenile Myelomonocytic Leukemia (JMML)

Q11. A 30-year-old pregnant female at 28 weeks of gestation presents with severe dyspnea and fatigue. Her laboratory workup shows: Hb 7.2 g/dL, MCV 115 fL, MCH 34 pg, and normal platelet and WBC counts. A peripheral blood smear shows macro-ovalocytes and hypersegmented neutrophils (6 lobes). Which of the following cellular features or biochemical changes would be expected in her bone marrow aspiration?

(A) Asynchrony between nuclear and cytoplasmic maturation where nuclear development lags

(B) Microcytic erythroid precursors with ringed sideroblasts arranged around nuclei

(C) Marked megakaryocytic hypoplasia with absence of nuclear lobulation

(D) Uniform normoblastic hyperplasia with condensed, small, eccentrically placed nuclei

Q12. A 23-year-old African-American male presents to the emergency department with severe, deep bony pain in his lower extremities and abdomen, precipitated by an upper respiratory infection. His peripheral blood smear reveals crescent-shaped erythrocytes and target cells. What is the fundamental molecular abnormality responsible for this condition?

(A) Substitution of valine for glutamic acid at the 6th position of the beta-globin chain

(B) Deletion of two alpha-globin genes on chromosome 16 causing chain imbalance

(C) Defect in the anchoring proteins ankyrin and spectrin within the RBC membrane

(D) Substitution of lysine for glutamic acid at the 6th position of the beta-globin chain

Q13. A 58-year-old female presents with severe fatigue and mucosal bleeding. A peripheral blood smear demonstrates an abundance of large, atypical promyelocytes containing numerous Auer rods clustered in groups (faggot cells). Genetic testing confirms a $t(15;17)$ translocation. Which therapeutic agent acts directly by binding the altered receptor generated by this translocation to induce differentiation of these malignant cells?

(A) Imatinib mesylate

(B) All-trans retinoic acid (ATRA)

(C) Rituximab

(D) Fludarabine phosphate

Q14. A 34-year-old male presenting with asymptomatic cervical lymphadenopathy undergoes an excisional lymph node biopsy. Microscopic evaluation demonstrates a nodular architectural pattern composed of small lymphocytes mixed with large, atypical cells that display a polylobated, delicate nucleus resembling popcorn (LH cells). Immunophenotyping reveals these cells are CD20+ and CD45+, but negative for CD15 and CD30. Which variant of Hodgkin lymphoma is most consistent with these findings?

(A) Nodular Sclerosis Hodgkin Lymphoma

(B) Mixed Cellularity Hodgkin Lymphoma

(C) Nodular Lymphocyte Predominant Hodgkin Lymphoma

(D) Lymphocyte Depleted Hodgkin Lymphoma

Q15. A 62-year-old female presents with persistent epigastric pain. Upper gastrointestinal endoscopy reveals a well-defined, ulcerated submucosal mass measuring 4.5 cm in the gastric body. Histopathological assessment displays interlacing bundles of spindle cells. Immunohistochemical staining reveals strong, diffuse positivity for KIT (CD117) and DOG1. Which of the following is the most likely diagnosis?

(A) Gastric Adenocarcinoma

(B) Leiomyosarcoma

(C) Gastrointestinal Stromal Tumor (GIST)

(D) Gastric Schwannoma

Q16. A 54-year-old male presentation with progressive dyspnea and a dry cough. A high-resolution CT scan of the chest reveals a subpleural, basal-predominant reticular pattern with honeycombing. A surgical lung biopsy shows a patchy interstitial inflammatory infiltrate along with dense collagenous fibrosis alternating with normal lung, architectural distortion, and fibroblastic foci. What is the correct histopathological diagnosis?

(A) Desquamative Interstitial Pneumonia (DIP)

(B) Non-Specific Interstitial Pneumonia (NSIP)

(C) Cryptogenic Organizing Pneumonia (COP)

(D) Usual Interstitial Pneumonia (UIP)

Q17. A 48-year-old chronic alcoholic is brought to the hospital with sudden-onset hematemesis and signs of hemorrhagic shock. Endoscopy reveals ruptured varices in the lower third of the esophagus. This anatomical pathology develops directly due to collateral shunting between which pair of venous systems?

(A) Left gastric vein and the azygos vein

(B) Right gastric vein and the inferior vena cava

(C) Superior mesenteric vein and the splenic vein

(D) Short gastric veins and the hemiazygos vein

Q18. A 42-year-old female presents with jaundice, pruritus, and xanthomas. Laboratory tests show markedly elevated serum alkaline phosphatase (ALP) and gamma-glutamyltransferase (GGT) levels. Serological testing reveals high titers of anti-mitochondrial antibodies (AMA). A liver biopsy demonstrates a chronic nonsuppurative destructive cholangitis affecting the small intrahepatic interlobular bile ducts. What is the diagnosis?

(A) Primary Sclerosing Cholangitis

(B) Primary Biliary Cholangitis

(C) Autoimmune Hepatitis Type 1

(D) Secondary Biliary Cirrhosis

Q19. A 50-year-old male presents with gross hematuria. Cystoscopy reveals a papillary mass on the lateral wall of the urinary bladder. The biopsy shows a neoplasm composed of thickened transitional epithelium with nuclear pleomorphism, loss of polarity, and atypical mitotic figures extending deep into the detrusor muscle layer. How should this tumor be pathologically classified?

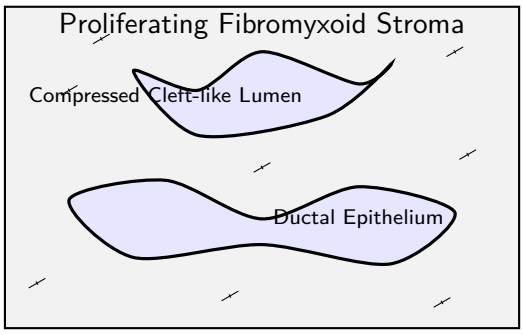
(A) Low-grade non-invasive papillary urothelial carcinoma

(B) High-grade muscle-invasive urothelial carcinoma

(C) Carcinoma in situ (CIS) of the bladder

(D) Squamous cell carcinoma of the bladder

Q20. A 28-year-old female presents with a painless, firm, well-circumscribed, highly mobile mass measuring 3 cm in the upper outer quadrant of her left breast. A core needle biopsy is performed, and the structural morphology is mapped schematically below:



Based on the clinical history and the histopathological pattern shown above, what is the correct diagnosis?

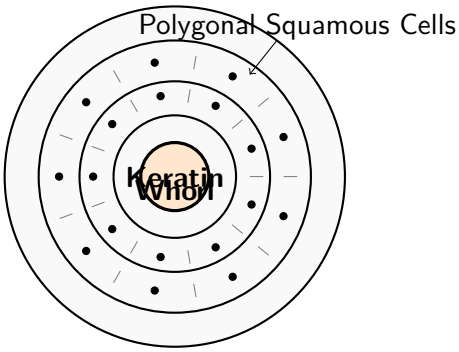
(A) Intraductal Papilloma

(B) Invasive Ductal Carcinoma

(C) Fibroadenoma

(D) Phyllodes Tumor

Q21. A 62-year-old male with a history of chronic smoking presents with a growth on his lower lip. An incisional biopsy reveals a malignant epithelial tumor characterized by sheets and nests of atypical squamous cells that breach the basement membrane and invade the underlying dermis. The tumor nests exhibit a specific concentric structural layout illustrated below:



What is the most accurate architectural feature depicted above?

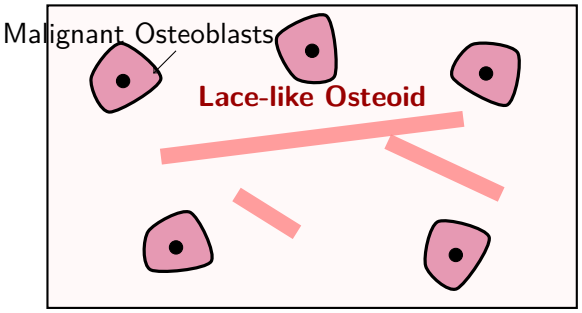
(A) Psammoma bodies in papillary thyroid carcinoma

(B) Keratin pearls in well-differentiated squamous cell carcinoma

(C) Call-Exner bodies in granulosa cell tumor

(D) Schiller-Duval bodies in yolk sac tumor

Q22. A 14-year-old boy presents with progressive swelling and deep localized pain in the distal metaphysis of his right femur over the past three months. Radiographic imaging reveals a destructive osteolytic lesion with a sunburst periosteal reaction and lifting of the periosteum creating a Codman triangle. A biopsy shows malignant mesenchymal cells producing unmineralized bone matrix, schematically depicted below:



Which of the following represents the correct diagnosis?

(A) Osteoclastoma (Giant Cell Tumor)

(B) Ewing Sarcoma

(C) Osteosarcoma

(D) Chondrosarcoma

Q23. A 68-year-old male presents with urinary frequency, urgency, and nocturia. Digital rectal examination reveals a symmetrically enlarged, nodular, elastic prostate gland. Transrectal ultrasound-guided needle biopsies show hyperplastic nodules composed of varying proportions of proliferating glandular acini and fibromuscular stroma. What is the key hormonal driver of this hyperplastic transformation?

(A) Active aromatization of testosterone into estradiol within stromal cells

(B) Intracellular conversion of testosterone to Dihydrotestosterone (DHT) by 5-alpha-reductase type 2

(C) Downregulation of androgen receptors leading to compensatory growth factor release

(D) Direct systemic hypersecretion of Luteinizing Hormone (LH) by the anterior pituitary

Q24. A 38-year-old female presents with an enlarged thyroid gland. Biopsy findings reveal a malignant follicular epithelial tumor characterized by ground-glass or empty-appearing nuclei (Orphan Annie eye nuclei), prominent nuclear grooves, and intra-nuclear inclusions. Psammoma bodies are also noted. Which molecular oncogenic rearrangement is most commonly linked with this specific carcinoma?

(A) RET/PTC rearrangement

(B) PAX8/PPARG fusion gene

(C) BRAF V600E point mutation alone without rearrangements

(D) RAS point mutation

Q25. A 58-year-old male presents with persistent hematuria, flank pain, and a palpable abdominal mass. A CT scan confirms a large, well-demarcated exophytic solid mass on the upper pole of the right kidney. Gross examination reveals a golden-yellow cut surface with areas of focal hemorrhage and necrosis. Microscopic analysis highlights nests of polygonal cells with abundant clear cytoplasm surrounded by a delicate network of branching sinusoidal vessels. What is the typical genetic mutation associated with the hereditary form of this disease?

(A) Mutation of the MET proto-oncogene on chromosome 7

(B) Loss of the VHL tumor suppressor gene on chromosome 3p

(C) Deletion of the WT1 gene on chromosome 11p

(D) BAP1 gene inactivation on chromosome 3p21

Detailed Solutions

Q1.

Solution

Concept:

Chronic Myeloid Leukemia (CML) is a myeloproliferative neoplasm characterized by a defining reciprocal chromosomal translocation that alters cellular signaling pathways. This genetic rearrangement produces a unique fusion gene, creating a mutant protein that drives unregulated hematopoiesis. Understanding this molecular mechanism is key to target-specific therapies in clinical oncology.

Solution:

(a) The reciprocal translocation $t(9;22)(q34;q11)$ is known as the Philadelphia chromosome, a hallmark finding present in more than 95% of cases presenting with Chronic Myeloid Leukemia.

(b) This structural rearrangement relocates the ABL1 proto-oncogene from chromosome 9 to the Breakpoint Cluster Region (BCR) gene on chromosome 22.

(c) The fusion creates a chimeric $BCR-ABL1$ gene that translates into an abnormal $p210$ fusion protein.

(d) This fusion protein functions as a constitutively active tyrosine kinase, bypassing normal cellular regulatory checkpoints.

(e) The continuous kinase activity triggers downstream signaling pathways like JAK/STAT, RAS/MAPK, and PI3K/AKT, driving autonomous granulocytic proliferation and suppressing normal apoptosis.

(f) Alternative options describe other hematological malignancies: option A defines acute promyelocytic leukemia ($t(15;17)$), option B describes Burkitt lymphoma ($t(8;14)$), and option D indicates general tumor suppressor loss seen in advanced disease progression.

Final Answer: The molecular consequence is the creation of a BCR-ABL1 chimeric gene with constitutive tyrosine kinase activity.

Answer: (C)

Go Back to Question 1

Q2.

Solution

Concept:

Squamous cell carcinoma presents distinct histopathological hallmarks linked to its epithelial tissue of origin. Malignant epithelial cells retain structural components responsible for cell-to-cell attachment. Recognizing these altered structural features under light microscopy is critical for distinguishing squamous tumors from poorly differentiated adenocarcinomas or undifferentiated carcinomas.

Solution:

(a) Under high-power microscopic examination, well-differentiated to moderately differentiated squamous cell carcinomas display distinct intercellular bridges or spine-like projections connecting adjacent epithelial cells.

(b) These bridges represent desmosomes, which are specialized anchoring cell junctions that link the intermediate filament cytoskeletons of adjacent cells via cadherin proteins.

(c) When tissues undergo routine formal fixation, the artifactual shrinkage of cells pulls the plasma membranes apart everywhere except at these rigid desmosomal attachment points, creating a bridge-like appearance.

(d) The individual cell keratinization observed alongside these bridges reflects the production of cytokeratin intermediate filaments, which anchor into these very same desmosomal complexes.

(e) Other cell junctions do not form these visible structures: hemidesmosomes link cells to the extracellular matrix basement membrane, tight junctions seal intercellular spaces apically, and gap junctions function as metabolic communication channels.

Final Answer: The cellular structures corresponding to intercellular bridges are desmosomes.

Answer: (B)

Go Back to Question 2

Q3.

Solution

Concept:

Tissue necrosis represents irreversible cellular injury that manifests in distinct morphological patterns depending on the nature of the insult, tissue architecture, and balance between protein denaturation and enzymatic digestion. The microscopic preservation of underlying tissue architecture is a key diagnostic feature of specific ischemic injuries.

Solution:

(a) The clinical description outlines an acute ischemic event within the fallopian tube due to an ectopic pregnancy, resulting in a classical pattern of coagulative necrosis.

(b) Coagulative necrosis is characterized by the preservation of basic structural outlines of the dead cells and tissue architecture for several days following cell death.

(c) The primary molecular driver of this pattern is the rapid denaturation of structural proteins as well as cellular enzymes, including lysosomal hydrolases.

(d) This widespread denaturation blocks the enzymatic proteolysis of the dead cell contents, leaving tombstone-like cellular remnants that exhibit intense cytoplasmic eosinophilia and nuclear changes like pyknosis, karyorrhexis, and karyolysis.

(e) Eventually, these dead cellular ghosts are cleared via phagocytosis by infiltrating inflammatory cells.

(f) Liquefactive necrosis, driven by rapid lysosomal digestion or heterolytic neutrophilic infiltration, occurs in brain infarcts and bacterial abscesses where tissue architecture is completely destroyed.

Final Answer: This pattern of tissue necrosis is primarily driven by denaturation of structural proteins and cellular enzymes.

Answer: (B)

Go Back to Question 3

Q4.

Solution

Concept:

Cellular adaptations occur in response to persistent physiological or pathological stress, allowing cells to alter their size, number, or phenotype to survive. Terminally differentiated cells that have lost the capacity for mitotic division undergo specific modifications when exposed to mechanical overloads.

Solution:

(a) Chronic, poorly controlled systemic hypertension increases the hemodynamic afterload on the left ventricle, forcing cardiac myocytes to adapt to higher workloads.

(b) Because adult cardiac myocytes are permanent, terminally differentiated cells, they cannot undergo hyperplasia to distribute the structural workload.

(c) Instead, the myocytes adapt exclusively via hypertrophy, which involves a marked increase in individual cell size without any corresponding cellular division.

(d) At the sub-cellular level, mechanical stretch sensors activate transcriptional pathways that stimulate the synthesis of additional contractile proteins, structural myofilaments, and organelles like mitochondria.

(e) This coordinated protein synthesis leads to the assembly of new sarcomeres, expanding the width of individual myofibers and manifesting clinically as concentric ventricular wall thickening.

(f) Recruitment of stem cells or reactivation of cell division cycles does not occur significantly in adult myocardial tissue, and lipofuscin accumulation represents an unrelated degenerative aging change rather than an active hypertrophic response.

Final Answer: This adaptation is primarily characterized by increased synthesis of contractile proteins and structural myofilaments.

Answer: (B)

Go Back to Question 4

Q5.

Solution

Concept:

Leukocyte extravasation is a tightly regulated, multi-step cascade essential for the delivery of inflammatory cells from the vascular lumen to interstitial sites of tissue injury or infection. Each phase of this cascade is mediated by distinct, sequential interactions between specific adhesion molecules on leukocytes and the endothelial surface.

Solution:

(a) Acute appendicitis triggers the release of pro-inflammatory cytokines such as IL-1 and TNF-alpha, which rapidly activate the local vascular endothelium.

(b) The initial phase of leukocyte recruitment is rolling, where leukocytes slow down and tumble along the endothelial wall.

(c) This rolling phase is mediated by transient, low-affinity interactions between selectins and their carbohydrate ligands. Specifically, Sialyl Lewis X oligosaccharides expressed on leukocytes bind to P-selectin and E-selectin up-regulated on activated endothelial cells.

(d) The loose binding slows the leukocyte down, allowing it to sample the local chemokine microenvironment.

(e) Subsequent steps require higher affinity binding: firm adhesion and arrest are mediated by the interaction of leukocyte integrins like LFA-1 and VLA-4 with endothelial immunoglobulin superfamily molecules like ICAM-1 and VCAM-1.

(f) Transmigration or diapedesis across the endothelial basement membrane is primarily mediated by homophilic PECAM-1 (CD31) interactions.

Final Answer: The rolling phase is primarily mediated by Sialyl Lewis X and P-selectin.

Answer: (C)

Go Back to Question 5

Q6.

Solution

Concept:

Immune-mediated tissue injury is categorized into four primary hypersensitivity mechanisms based on the immunological components involved and the pathways leading to cellular damage. Autoimmune conditions often exhibit specific hypersensitivity patterns that target vascular structures and visceral organs.

Solution:

(a) The patient presents with classic features of Systemic Lupus Erythematosus (SLE), including a malar rash, joint pain, proteinuria, and highly specific anti-double-stranded DNA (anti-dsDNA) autoantibodies.

(b) The underlying pathophysiology of lupus nephritis involves Type III hypersensitivity, which is an immune complex-mediated disease process.

(c) High affinity autoantibodies bind to circulating self-antigens, forming abundant antigen-antibody (immune) complexes within the systemic circulation.

(d) These complexes escape normal reticuloendothelial clearance and deposit within vascular basement membranes, particularly inside the renal glomeruli.

(e) Once trapped, the deposited immune complexes fix and activate the classical complement cascade. This activation generates potent chemoattractants like C5a, which recruit neutrophils and macrophages to the glomerulus.

(f) The recruited inflammatory cells release lysosomal enzymes and reactive oxygen species, driving intense local tissue damage, glomerular basement membrane injury, and subsequent proteinuria.

(g) Type I is IgE-mediated, Type II involves direct antibody binding to fixed tissue antigens, and Type IV is cell-mediated.

Final Answer: The tissue injury is predominantly classified under Type III hypersensitivity mechanism.

Answer: (C)

Go Back to Question 6

Q7.

Solution

Concept:

Cellular atrophy is an adaptive response characterized by a reduction in cell size and substance, leading to a decrease in the overall mass of the affected organ. This process involves a controlled balance between metabolic shutdown, protein degradation, and structural clearance pathways.

Solution:

(a) The clinical presentation and autopsy findings describe Alzheimer's disease, showing characteristic gross cortical atrophy along with microscopic neurofibrillary tangles and senile amyloid plaques.

(b) The reduction in brain volume is driven by cellular atrophy and eventual dropout of functional cortical neurons.

(c) At the cellular level, atrophy is primarily mediated by two interrelated pathways: the ubiquitin-proteasome pathway and autophagic vacuole clearance.

(d) Nutrient deprivation, structural detachment, or metabolic stress activates cellular ubiquitin ligases, which tag structural cytoskeletal proteins with chains of ubiquitin peptides.

(e) These tagged proteins are targeted to the proteasome complex for rapid degradation into minor peptide components.

(f) Simultaneously, starving or stressed cells create autophagic vacuoles that fuse with intracellular lysosomes, allowing the cell to digest its own damaged organelles to preserve basic metabolic homoeostasis.

(g) This coordinated degradation reduces the cell's volume without immediately triggering necrotic cell death pathways or inducing an acute suppurative inflammatory response.

Final Answer: The primary driver of this cellular atrophy is ubiquitin-proteasome mediated degradation of cytoskeleton and autophagic clearance.

Answer: (A)

Go Back to Question 7

Q8.

Solution

Concept:

Primary immunodeficiency disorders arise from inherited genetic defects that halt the normal development and maturation of specific immune cell lineages. Mapping the point of developmental arrest via immunophenotyping allows for accurate differentiation among distinct B-cell and T-cell immunodeficiencies.

Solution:

(a) The clinical scenario describes an infant male presenting with recurrent pyogenic infections following the loss of protective maternal IgG antibodies around six months of age.

(b) Laboratory findings highlight pan-hypogammaglobulinemia combined with an absence of mature circulating B lymphocytes (CD19+ and CD20+ cells), alongside entirely normal T lymphocyte levels.

(c) This clinical pattern is diagnostic for X-linked Agammaglobulinemia (XLA), or Bruton's agammaglobulinemia.

(d) XLA is caused by an inactivating mutation in the Bruton tyrosine kinase (BTK) gene located on the X chromosome.

(e) The BTK enzyme is critical for transducing survival and maturation signals from the pre-B cell receptor during early bone marrow lymphopoiesis.

(f) Without functional BTK, B-cell development is completely halted at the pre-B cell stage, preventing the generation of mature B cells and plasma cells, which leaves the patient unable to produce immunoglobulins.

(g) DiGeorge syndrome (22q11 deletion) causes T-cell defects, MHC deficiencies alter antigen presentation, and ADA deficiency causes severe combined immunodeficiency affecting both lineages.

Final Answer: The condition is explained by a mutation in the Bruton tyrosine kinase (BTK) gene halting B-cell maturation.

Answer: (B)

Go Back to Question 8

Q9.

Solution

Concept:

Differentiating an aggressive leukemoid reaction from Chronic Myeloid Leukemia (CML) is a classic clinical dilemma, as both present with extreme leukocytosis and a left-shifted myeloid spectrum in peripheral blood. Relying on objective cytogenetic biomarkers and enzymatic activity scoring is essential for accurate diagnosis.

Solution:

(a) A leukemoid reaction represents an exaggerated, benign reactive granulocytic proliferation seen during severe infections or toxic states, mimicking the peripheral blood picture of leukemia.

(b) To reliably differentiate CML from a leukemoid reaction, clinicians assess the alkaline phosphatase enzyme activity within the granules of mature circulating neutrophils using the Leukocyte Alkaline Phosphatase (LAP) score.

(c) In a leukemoid reaction, the mature neutrophils are functionally intact and reactive, leading to an elevated or normal LAP score.

(d) Conversely, in Chronic Myeloid Leukemia, the proliferating granulocytes are neoplastic and functionally defective, resulting in a characteristically low or completely absent LAP score.

(e) Definitive confirmation of CML requires demonstrating the presence of the unique $t(9;22)(q34;q11)$ Philadelphia chromosome or its corresponding $BCR-ABL1$ fusion transcript.

(f) Toxic granulations and Döhle bodies are classic features of reactive leukemoid states, whereas absolute basophilia is a major diagnostic clue favoring a primary myeloproliferative disorder like CML.

Final Answer: The finding that rules out a leukemoid reaction is a low leukocyte alkaline phosphatase (LAP) score accompanied by t(9;22).

Answer: (C)

Go Back to Question 9

Q10.

Solution

Concept:

Acute lymphoblastic leukemia is the most common childhood malignancy, characterized by the uncontrolled clonal proliferation and accumulation of immature lymphoid progenitors (blasts) within the bone marrow and peripheral circulation. Identifying lineage-specific surface markers and nuclear enzymes is crucial for classification.

Solution:

(a) The patient presents with clinical signs of acute bone marrow failure, including anemia (pallor), thrombocytopenia (bruising), and a markedly elevated total leukocyte count driven by circulating blasts.

(b) The physical findings of generalized lymphadenopathy and hepatosplenomegaly indicate significant extramedullary tissue infiltration, which is common in acute leukemia.

(c) Microscopic analysis reveals classic lymphoblasts characterized by a high nucleo-cytoplasmic ratio, fine open chromatin, and inconspicuous nucleoli.

(d) The key diagnostic confirmation comes from immunophenotyping: the blasts are strongly positive for terminal deoxynucleotidyl transferase (TdT), a unique DNA polymerase expressed exclusively in immature pre-B and pre-T lymphoblasts.

(e) Positive expression of CD10 (Common Acute Lymphoblastic Leukemia Antigen, or CALLA) along with TdT confirms a lineage diagnosis of B-cell Acute Lymphoblastic Leukemia (B-ALL).

(f) AML-M3 blasts are TdT negative and display Auer rods, CLL is a disease of elderly adults with mature-appearing lymphocytes, and JMML has a distinct myelomonocytic profile without TdT positivity.

Final Answer: The most likely diagnosis is B-cell Acute Lymphoblastic Leukemia (B-ALL).

Answer: (B)

Go Back to Question 10

Q11.

Solution

Concept:

Megaloblastic anemia is a macrocytic anemia that stems from impaired deoxyribonucleic acid synthesis within rapidly dividing hematopoietic lineages. When replication slows down while cytoplasmic expansion proceeds uninhibited, precursors display a unique morphology during maturation. This biochemical imbalance characteristically affects both the erythroid line and myeloid elements within the marrow cavity.

Solution:

(a) The patient is a pregnant female presenting with severe macrocytic anemia accompanied by prominent macro-ovalocytes and hypersegmented neutrophils on her peripheral blood smear, confirming a clinical diagnosis of megaloblastic anemia.

(b) Megaloblastic conditions are primarily triggered by deficiency states involving vitamin B12 or folate, both of which serve as essential coenzymes in the thymidylate synthesis pathway necessary for DNA replication.

(c) At the subcellular level, inadequate DNA synthesis causes a notable delay in nuclear replication cycles and condensation profiles within developing hematopoietic blasts.

(d) Meanwhile, ribonucleic acid synthesis and cytoplasmic building blocks progress at a normal pace, as structural protein assembly does not depend on thymidine availability.

(e) This mismatch generates a classic architectural hallmark known as nuclear-cytoplasmic asynchrony, where the immature, fine chromatin pattern of the nucleus lags behind a well-developed cytoplasm.

(f) Other options present distinct anomalies: ringed sideroblasts reveal defective mitochondrial iron utilization, megakaryocytic hypoplasia points toward aplastic processes, and uniform normoblastic patterns signify normal homeostatic regeneration.

Final Answer: The expected finding is asynchrony between nuclear and cytoplasmic maturation where nuclear development lags.

Answer: (A)

Go Back to Question 11

Q12.

Solution

Concept:

Hemoglobinopathies involve qualitative structural mutations within the globin protein chains, leading to altered physical properties under hypoxic or stressful conditions. A single nucleotide substitution can dramatically change the spatial configuration and stability of the entire hemoglobin tetramer, precipitating microvascular complications.

Solution:

(a) The presentation describes a young African-American male presenting with an acute painful vaso-occlusive crisis, classical crescent-shaped sickled erythrocytes, and target cells, confirming a diagnosis of Sickle Cell Anemia.

(b) The underlying molecular defect is an autosomal recessive missense mutation located in the sixth codon of the beta-globin gene on chromosome 11.

(c) This specific genetic alteration substitutes a hydrophilic glutamic acid residue with a hydrophobic valine residue, giving rise to abnormal Hemoglobin S.

(d) Under conditions of low oxygen tension, dehydration, or acidic shift, the hydrophobic valine residues on adjacent beta-chains interact, causing the molecules to polymerize into long, rigid crystalline polymers.

(e) These fibrous aggregates distort the red blood cell membrane into the classic sickle shape, leading to microvascular occlusion, tissue infarction, and chronic hemolytic anemia.

(f) Alternative choices represent separate pathologies: alpha-gene deletions cause alpha-thalassemia syndromes, ankyrin or spectrin defects disrupt vertical structural membrane interactions to cause hereditary spherocytosis, and lysine substitutions produce Hemoglobin C.

Final Answer: The fundamental molecular abnormality is the substitution of valine for glutamic acid at the 6th position of the beta-globin chain.

Answer: (A)

Go Back to Question 12

Q13.

Solution

Concept:

Acute Promyelocytic Leukemia (APL), classified as AML-M3, is uniquely defined by a reciprocal cytogenetic translocation that disrupts standard nuclear receptor signaling. Targeted molecular therapies leverage this specific disruption, forcing neoplastic progenitors to bypass their maturation arrest and transition into functional, mature cells.

Solution:

(a) The patient presents with clinical signs of bleeding and fatigue, paired with a bone marrow smear displaying numerous promyelocytic blasts crowded with bundled Auer rods, which points to Acute Promyelocytic Leukemia.

(b) The diagnostic hallmark of APL is the $t(15;17)(q24;q21)$ translocation, which fuses the Promyelocytic Leukemia (PML) gene on chromosome 15 to the Retinoic Acid Receptor Alpha (RARA) gene on chromosome 17.

(c) The resulting PML-RARA chimeric protein binds with high affinity to nuclear co-repressor complexes, firmly blocking the transcription of genes needed for myeloid differentiation.

(d) All-trans retinoic acid (ATRA) acts as a highly specialized targeted agent by binding directly to the modified RARA domain of this chimeric protein.

(e) This pharmacological binding breaks down the co-repressor complex and activates transcription, driving the malignant promyelocytes to mature into fully developed neutrophils and clearing the clonal population.

(f) Other listed drugs target alternative pathways: imatinib inhibits BCR-ABL1 kinase, rituximab binds CD20 on mature B-cells, and fludarabine serves as a purine analogue for chronic lymphocytic processes.

Final Answer: The therapeutic agent is All-trans retinoic acid (ATRA).

Answer: (B)

Go Back to Question 13

Q14.

Solution

Concept:

Hodgkin Lymphoma encompasses distinct clinicopathological entities divided into classic forms and non-classic variants based on cellular background, neoplastic cell morphology, and immunophenotypic markers. Identifying unique neoplastic configurations and marker profiles prevents misclassification and guides appropriate therapeutic regimens.

Solution:

(a) The histological description details an asymptomatic lymphadenopathy displaying a nodular architecture rich in small, mature lymphocytes mixed with distinctive large neoplastic cells featuring delicate, polylobated nuclei termed popcorn cells.

(b) These characteristic structures are Lymphocyte and Histiocyte (LH) variants, which set this entity apart from classic Reed-Sternberg cells.

(c) Immunophenotypic analysis reveals that these popcorn cells retain active B-cell lineage markers, testing strongly positive for CD20 and CD45, while remaining completely negative for classic Hodgkin markers CD15 and CD30.

(d) This specific morphological configuration and antigen expression profile are pathognomonic for Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL).

(e) In contrast, classic variants like Nodular Sclerosis or Mixed Cellularity feature Reed-Sternberg cells that show the exact inverse profile, expressing CD15 and CD30 while missing CD20 and CD45.

(f) Lymphocyte depleted variants present a sparse background with bizzare, pleomorphic malignant cells, unlike the well-organized lymphocytic background seen here.

Final Answer: The variant is Nodular Lymphocyte Predominant Hodgkin Lymphoma.

Answer: (C)

Go Back to Question 14

Q15.

Solution

Concept:

Mesenchymal tumors of the gastrointestinal tract must be distinguished from epithelial neoplasms using immunohistochemical profiling. These stromal proliferations often rely on specific tyrosine kinase mutations that alter baseline growth signaling pathways, providing excellent targets for structural diagnostics.

Solution:

(a) The patient presents with a large, ulcerated intramural gastric mass composed histologically of sweeping bundles of uniform spindle cells, raising suspicion for a mesenchymal neoplasm.

(b) Differential diagnosis includes leiomyosarcoma, schwannoma, and gastrointestinal stromal tumor (GIST).

(c) The definitive distinction is established via immunohistochemistry, which shows diffuse, intense expression of the KIT (CD117) protein alongside Discovered on GIST 1 (DOG1).

(d) CD117 is an epitope on the extracellular domain of the c-KIT transmembrane receptor tyrosine kinase, which is mutated and constitutively activated in over 85% of GIST cases.

(e) This persistent activation drives downstream proliferative signaling pathways independent of external ligands, confirming a diagnosis of Gastrointestinal Stromal Tumor.

(f) Adenocarcinoma displays an epithelial glandular architecture testing positive for cytokeratins, leiomyosarcoma reveals smooth muscle differentiation with desmin or actin positivity, and schwannomas express S100 protein while remaining completely negative for CD117.

Final Answer: The most likely diagnosis is Gastrointestinal Stromal Tumor (GIST).

Answer: (C)

Go Back to Question 15

Q16.

Solution

Concept:

Idiopathic interstitial pneumonias form a complex group of diffuse lung diseases differentiated by their architectural patterns on high-resolution imaging and surgical tissue biopsy. Recognizing spatial and temporal heterogeneity within the pulmonary parenchyma is crucial for identifying restrictive lung disease processes.

Solution:

(a) The clinical description highlights a progressive restrictive lung disease manifesting with basal-predominant honeycombing on high-resolution chest tomography.

(b) The surgical lung biopsy confirms diagnostic hallmarks, showing patchy interstitial fibrosis that demonstrates both spatial and temporal heterogeneity.

(c) Spatial heterogeneity is evidenced by dense collagen scars alternating directly with patches of completely preserved, normal alveoli within the same tissue section.

(d) Temporal heterogeneity is confirmed by the coexistence of old dense collagen deposition alongside active, early-stage collections of proliferating myofibroblasts known as fibroblastic foci.

(e) This specific combination of architectural distortion, subpleural accentuation, and active fibroblastic foci defines the Usual Interstitial Pneumonia (UIP) pattern.

(f) UIP is the histological correlate of Idiopathic Pulmonary Fibrosis.

(g) Other patterns differ: Non-Specific Interstitial Pneumonia exhibits uniform, temporally homogenous inflammation; Desquamative Interstitial Pneumonia features diffuse intra-alveolar macrophage accumulation; and Cryptogenic Organizing Pneumonia presents with intra-alveolar loose connective tissue plugs (Masson bodies).

Final Answer: The correct histopathological diagnosis is Usual Interstitial Pneumonia (UIP).

Answer: (D)

Go Back to Question 16

Q17.

Solution

Concept:

Portal hypertension secondary to decompensated liver disease forces venous blood to bypass hepatic parenchymal resistance. This blood diverts into lower-pressure collateral pathways where systemic and portal venous systems naturally anastomose, inducing structural vessel dilation prone to catastrophic failure.

Solution:

(a) Severe chronic alcoholism frequently culminates in liver cirrhosis, characterized by widespread fibrous bands and regenerative nodules that compress the intrahepatic portal venules.

(b) This structural compression impedes blood flow through the liver, raising pressures within the portal vein trunk and causing backward congestion throughout its tributaries.

(c) Seeking lower pressure return pathways to the heart, the congested portal blood flows backward through collateral channels at key porto-systemic cross-connections.

(d) At the distal gastroesophageal junction, this reversing flow travels from the left gastric (coronary) vein, which belongs to the portal network, into the esophageal and azygos veins, which route into the systemic superior vena cava.

(e) The thin-walled submucosal veins of the lower esophagus cannot withstand this high-pressure, high-volume flow, causing them to dilate into fragile, tortuous structures known as esophageal varices.

(f) These engorged vessels are highly susceptible to mechanical trauma or pressure spikes, leading to rupture and life-threatening upper gastrointestinal hemorrhage.

(g) Other listed pairs govern separate venous territories, such as the umbilical or rectal porto-systemic drainage beds.

Final Answer: This anatomical pathology develops directly due to collateral shunting between the left gastric vein and the azygos vein.

Answer: (A)

Go Back to Question 17

Q18.

Solution

Concept:

Autoimmune cholestatic liver diseases target specific segments of the biliary tree through cell-mediated and humoral mechanisms. Documenting lineage-specific autoantibodies and matching them with the size and location of destroyed bile ducts allows for precise clinical differentiation.

Solution:

(a) The patient is a middle-aged female presenting with classic obstructive jaundice features, including pruritus, xanthomas, and elevated alkaline phosphatase and gamma-glutamyltransferase levels.

(b) The key serological biomarker is the presence of high titers of anti-mitochondrial antibodies (AMA), which specifically target the E2 subunit of the pyruvate dehydrogenase enzyme complex inside mitochondria.

(c) Histopathological evaluation matches these findings by demonstrating a chronic, non-suppurative destructive cholangitis that selectively damages the small intrahepatic interlobular bile ducts.

(d) This specific combination of autoimmune serology, cholestatic biochemistry, and small-duct granulomatous destruction is the classic definition of Primary Biliary Cholangitis (PBC).

(e) Over time, this chronic immune-mediated destruction leads to progressive ductopenia, portal scarring, and eventual biliary cirrhosis.

(f) Primary Sclerosing Cholangitis is distinct, presenting as an AMA-negative condition that displays concentric "onion-skin" fibrosis around larger intrahepatic and extrahepatic ducts, typically associated with ulcerative colitis.

(g) Autoimmune hepatitis presents with anti-smooth muscle antibodies and interface hepatitis rather than primary bile duct destruction.

Final Answer: The diagnosis is Primary Biliary Cholangitis.

Answer: (B)

Go Back to Question 18

Q19.

Solution

Concept:

Urothelial malignancies exhibit varied growth patterns, cellular grades, and depths of penetration within the layered architecture of the bladder wall. Accurately determining whether neoplastic cells have crossed anatomical boundaries into the muscular layers is the most critical factor for staging and determining surgical management.

Solution:

(a) The cystoscopic biopsy describes an exophytic papillary growth originating from the bladder wall lining, showing structural and cytological abnormalities under light microscopy.

(b) The epithelium displays high-grade features, including nuclear pleomorphism, disordered cell layers, loss of standard polarity, and atypical mitotic figures.

(c) The most significant staging finding is that these malignant sheets of cells have breached the basement membrane and lamina propria, extending deep into the detrusor muscle layer.

(d) The detrusor muscle functions as the muscularis propria of the urinary bladder wall.

(e) Finding neoplastic urothelium within this muscular layer classifies the tumor as a high-grade muscle-invasive urothelial carcinoma.

(f) This depth of invasion rules out non-invasive or low-grade papillary variants, which remain confined above the basement membrane or within the superficial lamina propria.

(g) Carcinoma in situ describes a flat, non-invasive high-grade lesion, whereas pure squamous cell carcinoma requires widespread keratinization and is etiologically linked to chronic irritation or Schistosoma infection rather than papillary transitional architecture.

Final Answer: This tumor should be pathologically classified as High-grade muscle-invasive urothelial carcinoma.

Answer: (B)

Go Back to Question 19

Q20.

Solution

Concept:

Fibroepithelial breast tumors are characterized by a dual proliferation of both stromal connective tissue components and epithelial glandular structures. Evaluating how the expanding stroma alters the architecture of adjacent ducts allows for clear identification of specific benign lesions.

Solution:

(a) The clinical history describes a young, 28-year-old female presenting with a firm, well-circumscribed, highly mobile breast mass, commonly referred to clinically as a breast mouse.

(b) The provided histopathological schematic illustrates a classic fibroepithelial tumor layout, displaying a prominent proliferation of cellular, loose fibromyxoid connective tissue stroma.

(c) As this stromal component expands, it compresses and distorts the adjacent benign double-layered ductal epithelial structures.

(d) This compression forces the ductal lumens into elongated, narrow, branching cleft-like spaces, creating the classic intracanalicular growth pattern characteristic of a fibroadenoma.

(e) The absence of significant cytological atypia, mitotic figures, stromal overgrowth, or leaf-like architectural projections rules out borderline or malignant mimics like a phyllodes tumor.

(f) Intraductal papillomas display a branching fibrovascular core growing within a dilated duct without mass stroma expansion, and invasive ductal carcinoma exhibits malignant nests infiltrating the stroma with dense, desmoplastic tissue reactions rather than benign, compressed clefts.

Final Answer: The correct diagnosis is Fibroadenoma.

Answer: (C)

Go Back to Question 20

Q21.

Solution

Concept:

Squamous cell carcinoma exhibits distinct structural patterns visible under light microscopy depending on its degree of histopathological differentiation. Highly differentiated epithelial tumors retain their physiological capacity to synthesize complex structural cytoskeletal filaments, packing them into concentric architectures that breach tissue boundaries and serve as key diagnostic features.

Solution:

(a) The incisional biopsy clinical vignette identifies a highly invasive squamous cell carcinoma, with the provided histopathological TikZ schematic highlighting concentric lamellar structures.

(b) These structural formations are keratin pearls, which are composed of layers of eosinophilic, acellular keratin scale arranged in whorled configurations.

(c) Keratinization is an inherent physiological process of normal squamous epithelium; its presence within nests invading deep into the dermis signifies that the malignancy is well-differentiated.

(d) Surrounding these central keratin whorls are large, polygonal neoplastic squamous cells that display intercellular bridges, hyperchromatic nuclei, and variable cytological atypia.

(e) Alternative choices indicate diagnostic structures belonging to entirely separate systemic neoplasms: psammoma bodies represent concentric calcifications in papillary thyroid carcinoma, Call-Exner bodies describe rosette-like configurations enclosing eosinophilic fluid in granulosa cell tumors, and Schiller-Duval bodies mimic primitive glomeruli within yolk sac tumors.

Final Answer: The architectural feature depicted is keratin pearls in well-differentiated squamous cell carcinoma.

Answer: (B)

Go Back to Question 21

Q22.

Solution

Concept:

Primary malignant bone tumors are categorized based on the specific matrix produced by the neoplastic mesenchymal cells. Identifying the exact nature of this extracellular matrix under microscopic assessment is critical for differentiating primary osteosarcomas from other small round blue cell tumors or cartilaginous lesions.

Solution:

(a) The patient is a teenage male presenting with localized knee pain, a sunburst periosteal reaction, and a Codman triangle configuration on radiography, strongly suggesting an aggressive mesenchymal bone malignancy.

(b) The definitive diagnostic hallmark shown in the histopathological schematic is the direct production of lace-like, unmineralized bone matrix, known as osteoid, by highly pleomorphic, anaplastic stromal cells.

(c) These malignant osteoblasts possess hyperchromatic, atypical nuclei and bizarre mitotic figures, and they lay down this irregular woven osteoid matrix in a streaming or lace-like pattern between cells.

(d) This histopathological presentation establishes a definitive diagnosis of osteosarcoma.

(e) Other listed bone lesions lack this specific matrix feature: giant cell tumors are characterized by uniform osteoclast-like multinucleated giant cells within a mononuclear stroma, Ewing sarcoma presents as sheets of uniform small round blue cells without osteoid matrix production, and chondrosarcoma produces a malignant cartilaginous matrix.

Final Answer: The diagnosis is Osteosarcoma.

Answer: (C)

Go Back to Question 22

Q23.

Solution

Concept:

Benign Prostatic Hyperplasia (BPH) is a common nodular age-related proliferation affecting the glandular and stromal elements of the transition zone of the prostate. This hyperplastic growth is driven by local hormonal shifts that alter cell proliferation and survival pathways within the prostatic parenchymal microenvironment.

Solution:

(a) The patient presents with classic lower urinary tract symptoms secondary to mechanical urethral obstruction caused by an enlarged, nodular prostate gland, confirming Benign Prostatic Hyperplasia.

(b) While systemic circulating levels of testosterone decrease with advancing age, prostatic stromal and epithelial cells maintain high intracellular androgen activity through localized enzymatic conversion.

(c) The primary hormonal driver of this process is Dihydrotestosterone (DHT), an androgen with significantly higher affinity for the androgen receptor than testosterone.

(d) Circulating testosterone diffuses into prostatic stromal cells, where it is metabolized into DHT by the enzyme 5-alpha-reductase type 2, the predominant isoform expressed in prostatic tissue.

(e) Once formed, DHT acts locally in an autocrine and paracrine manner, binding to nuclear androgen receptors to stimulate the transcription of growth factors like FGF and TGF-beta, which drive the hyperplasia of stromal and epithelial cells.

(f) Systemic gonadotropin hypersecretion, aromatization to estradiol, or primary androgen receptor downregulation are not the principal drivers of this nodular hyperplastic adaptation.

Final Answer: The key hormonal driver is intracellular conversion of testosterone to Dihydrotestosterone (DHT) by 5-alpha-reductase type 2.

Answer: (B)

Go Back to Question 23

Q24.

Solution

Concept:

Thyroid malignancies comprise distinct histological classes that are highly correlated with specific, mutually exclusive somatic molecular driver mutations. Identifying these characteristic cytological nuclear alterations and matching them with underlying genetic mutations is vital for thyroid tumor classification and prognosis.

Solution:

(a) The biopsy specimen displays classic diagnostic nuclear features, including ground-glass Orphan Annie eye nuclei, prominent longitudinal nuclear grooves, and pseudoinclusions, which are pathognomonic for Papillary Thyroid Carcinoma (PTC).

(b) PTC is the most common primary thyroid malignancy and can be driven by several genetic alterations that activate the MAP kinase signaling pathway.

(c) Among the structural chromosomal rearrangements, the RET/PTC rearrangement is the most characteristically linked with classic papillary carcinoma, particularly in tumors associated with prior radiation exposure.

(d) This balanced translocation fuses the tyrosine kinase domain of the RET proto-oncogene on chromosome 10 with promoter regions of constitutively expressed genes, creating a chimeric oncogene.

(e) While the BRAF V600E point mutation is also highly prevalent in classic PTC, the query specifically asks for the molecular oncogenic rearrangement linked to this entity.

(f) Other mutations signify alternative pathways: PAX8/PPARG fusions and RAS mutations are characteristic of follicular thyroid carcinomas or the follicular variant of PTC.

Final Answer: The molecular oncogenic rearrangement is the RET/PTC rearrangement.

Answer: (A)

Go Back to Question 24

Q25.

Solution

Concept:

Renal cell carcinomas are classified into distinct subtypes based on their morphological, histopathological, and cytogenetic profiles. Identifying the underlying genetic mutations in hereditary syndromes has advanced our understanding of the metabolic pathways that drive tumor angiogenesis and cell survival.

Solution:

(a) The patient presents with the classic triad of hematuria, flank pain, and a palpable abdominal mass, alongside a golden-yellow renal tumor composed of clear cells rich in lipids and glycogen, diagnosing Clear Cell Renal Cell Carcinoma (ccRCC).

(b) The hereditary form of this disease occurs in Von Hippel-Lindau (VHL) syndrome, an autosomal dominant disorder caused by a germline mutation or deletion of the VHL tumor suppressor gene located on chromosome 3p25.

(c) The VHL protein normally functions as part of a ubiquitin ligase complex that targets Hypoxia-Inducible Factor alpha (HIF-alpha) for proteasomal degradation under normoxic conditions.

(d) Loss of functional VHL protein prevents the degradation of HIF-alpha, allowing it to accumulate and translocate to the nucleus.

(e) This accumulation triggers the transcription of pro-angiogenic growth factors, such as VEGF and PDGF, driving the prominent network of branching sinusoidal vessels characteristic of ccRCC.

(f) Alternative options involve other renal pathologies: MET mutations drive papillary renal cell carcinoma, WT1 deletions cause Wilms tumor, and BAP1 mutations are associated with aggressive, higher-grade renal tumors rather than the classic VHL syndrome pathway.

Final Answer: The typical genetic mutation is the loss of the VHL tumor suppressor gene on chromosome 3p.

Answer: (B)

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Answer Key

Q	Ans	Q	Ans	Q	Ans	Q	Ans	Q	Ans
1	C	2	B	3	B	4	B	5	C
6	C	7	A	8	B	9	C	10	B
11	A	12	A	13	B	14	C	15	C
16	D	17	A	18	B	19	B	20	C
21	B	22	C	23	B	24	A	25	B