Pathology

Summary

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"اللهم لا سهل الا ماجعلته سهلا و انت تجعل الحزن إذا شئت سهلا"

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Good luck

Functional classification

	Hyperfunction (hyperthyroidism)	Hypofunction (hypothyroidism)
Overview	Hypermetabolic state induced by excessive amounts of thyroid hormone and over activity of the sympathetic nervous system	thyroid gland can't make enough thyroid hormone to keep the body running normally
Cause	-Graves disease	Primary : -Postablative: Surgery, radioiodine therapy -Autoimmune: Hashimoto thyroiditis - iodine deficiency -Drugs : lithium Secondary : -pituitary insufficiency
Symptoms	-CVS : Palpitations -CNS : Nervousness, tremor, irritability -GIT : hyper mortality , weight loss despite increased appetite , diarrhea -ocular : Wide, staring gaze and lid lag Skin : Soft, warm, and flushed skin	-in early fetal life : Cretinism 1)severe mental retardation 2)Short stature 3)protruding tongue In adult : Myxedema 1)mental sluggishness 2)Shortness of breath 3)Broadening and coarsening of facial features 4)Enlargement of the tongue , deepening of the voice 5)Cold and pale skin 6)Constipation , obesity 7)In later stages : heart is enlarged, and heart failure may supervene
Diagnosis	-low TSH -high T3 and T4	-high TSH -low T3, T4

Etiological classification

Gravis disease	Overview	The most common cause of endogenous hyperthyroidism
	Pathogenesis	-Thyroid-stimulating immunoglobulin: lgG antibody that binds to the TSH receptor and mimics the action of TSH -Thyroid growth-stimulating immunoglobulins : directed against the TSH receptor -TSH-binding inhibitory immunoglobulins : prevent TSH from binding to its receptor
	Clinical feature	Thyrotoxicosis : Diffusely enlarged, hyperfunctional thyroid Ophthalmopathy : Exophthalmos caused by Accumulation of glycosaminoglycan
	Morphology	Macroscopic : Enlarged gland usually symmetrically Microscopic: columnar cell , colloid is pale (clear vasculated) , Lymphoid infiltrates
	Diagnosis	-decrease TSH -increase T3, T4 -increase radioactive iodine uptake
Thyroiditis — Hashimoto Thyroiditis Chronic Lymphocytic Thyroiditis	Overview	Chronic inflammation of thyroid gland , most common cause of hypothyroidism in areas of the world where iodine levels are sufficient
	Characteristic	gradual thyroid failure secondary to **autoimmune destruction**
	Clinical features	-Painless enlargement of the thyroid -Hashitoxicosis:cycle through an initial period where there is too much thyroid hormone in the body and demonstrate symptoms of hyperthyroidism.
	Pathogenesis	Circulating autoantibodies against thyroid antigens leads to progressive depletion of thyroid epithelial cells associated with lymphocytic infiltrates and fibrosis.
	Risk factor	Mutation of CTLA4 gene
	Morphology	-Mononuclear inflammatory infiltrate (lymphocytes, plasma cells) with germinal centre formation -Hürthle cells : atrophic follicles of thyroid Cytoplasm : eosinophilic, granular
	de Quervain Thyroiditis Subacute Granulomatous Thyroiditis — Cause	-caused by a viral infection
	Characteristic	-Pain in the neck , Fever and malaise -Variable enlargement of the thyroid.
	Clinical features	-Transient hyperthyroidism -Transient hypothyroidism -with most patients returning to a euthyroid (self limited)
	Morphology	-Disruption of thyroid follicles extravasation of colloid polymorphonuclear infiltrate -granulomatous reaction with giant cells -Healing occurs by resolution of inflammation and fibrosis
	Subacute Lymphocytic Thyroiditis — Definition	postpartum thyroiditis : onset of disease follows pregnancy , most likely autoimmune in etiology
	Clinical features	Painless neck mass or features of thyroid hormone excess
	Morphology	lymphocytic infiltration and hyperplastic germinal centers.
	Riedel thyroiditis — Definition	Rare disorder of unknown etiology
	Clinical features	hard and fixed thyroid mass
	Morphology	extensive (sever) fibrosis

	Follicular adenoma	Papillary carcinoma	Follicular carcinoma	Medullary carcinoma	Anaplastic carcinoma
Neoplastic nodule	Benign	Malignant			
Overview		-the most common form of thyroid cancer -well-differentiated thyroid cancer		neuroendocrine neoplasms derived from the parafollicular cells	undifferentiated thyroid carcinoma, is a rare, highly aggressive malignant tumor
Risk factor		previous exposure to ionizing radiation	More frequent in areas with dietary iodine deficiency		
Spread		metastasis in a cervical lymph node	bloodstream		
Pathogenesis		rearrangements of the tyrosine kinase receptors RET or NTRK1 or activating point mutations in BRAF	Mutations in the RAS family of oncogenes	Medullary Thyroid Carcinomas: Familial medullary thyroid carcinomas occur in multiple endocrine neoplasia type 2 (MEN-2) RET in proto oncogene mutation	Inactivating point mutations in the p53 tumor suppressor gene
Morphological changes	Grossly : solitary, , encapsulated (covered by capsule)		solitary	solitary nodule or may manifest as multiple lesions	
	Microscopically : -well-defined, intact capsule -eosinophilic granular cytoplasm -Hürthle cell changes	-nuclear changes : Orphan Annie eye" nuclei = optically clear (grooved clear nucleus) , nuclear enlargement, and elongated , Very finely dispersed chromatin -intranuclear inclusions (pseudoinclusions) -calcified (body) structures =psammoma bodies	uniform cells forming small follicles,,it can be widely invasive that infiltrate the thyroid parenchyma or minimally invasive which are sharply demarcated lesions. -capsular and/or vascular invasion	-polygonal to spindle-shaped cells, that form nests -Amyloid deposits -C cell hyperplasia characteristic features of familial medullary carcinomas	-large pleomorphic giant cell occasional osteoclast-like multinucleated giant cells -spindle shaped cell with sarcomatous appearance -mixture spindle and gait cell -small cells
Diagnosis	-radionuclide scanning : cold nodule -ultrasonography -fine needle aspiration biopsy	-nonfunctional tumors (cold nodule) -fine needle aspiration biopsy (based on nuclear features)	-cold thyroid nodules	-congo and red stain -secrete calcitonin measured in diagnosis and postoperative follow-up of patients	
Prognosis	excellent prognosis and do not recur or metastasize	indolent lesions, with 10-year survival rates in excess of 95%	Minimally invasive (well encapsulated) will have 10 year survival rate 90%. If Widely invasive,10 year survival rate less than 50%.		-the prognosis is very bad Lethal (100%)

Cushing syndrome

	Exogenous	Endogenous			
	glucocorticoids (iatrogenic) Most common cause of Cushing syndrome	ACTH- dependent		ACTH- independent	
		Cushing disease 70%	Ectopic ACTH 10%	Adrenal adenoma 10%	Adrenal carcinoma 5%
Morphology	Cortical atrophy	Bilateral nodular cortical hyperplasia	Bilateral cortical hyperplasia	-Yellow tumors -Thin, well developed capsule -cell look normal -vacuolated neoplastic cell -no mitotic or necrotic activity	-non-capsulated -have anaplastic feature
Clinical feature	COH : anti insulin effect = hyperglycemia , redistribution of the fat : Truncal obesity, moon face , buffalo hump Catabolic effect of protein : Proximal limb weakness ,striae , easily bruised skin , Osteoporosis Increase androgen : Hirsutism , menstrual abnormalities Aldosterone like effect : hypertension				
		skin pigmentation			
Diagnosis		High level of ACTH in urine		Low level of ACTH in urine	
Note		ACTH-producing microadenoma	Usually caused by Small-Cell Carcinoma of the lung	Functional and nonfunctional tumors are not morphologically distinct	

Hyperaldosteronism

	Primary Hyperaldosteronism (excessive aldosterone secretion)			Secondary Hyperaldosteronism
	idiopathic (Most common)	Adrenocortical neoplasm		-Decreased renal perfusion -Arterial hypovolemia -Pregnancy
		adenoma secreting aldosterone (conn syndrome)	carcinoma Rare	
Morphology	Bilateral nodular hyperplasia	-Solitary, well-circumscribed , Bright yellow on cut surface -nuclear and cellular pleomorphism -Spironolactone bodies (after treatment with spironolactone)		
	suppression of the renin-angiotensin system as negative feedback			activation of the RAAS system as causes
Clinical feature	- increase Na , H2O reabsorption Secondary hypertension -decrease K level neuromuscular manifestations -metabolic alkalosis			

Hypersecretion of androgens

	Adrenocortical neoplasms carcinoma	Congenital Adrenal Hyperplasia
		-deficiency in 21-Hydroxylase -increases ACTH secretion
Clinical feature	-In males: precocious puberty -In female: masculinization: ambiguous genitalia, oligomenorrhea, hirsutism	

Adrenal insufficiency

	Primary hypoadrenalism (high ACTH) so associated with hyperpigmentation					Secondary hypoadrenalism
	acute (crisis)	chronic (**Addison's disease**) most common				deficiency of ACTH
	Water-Friderichsen syndrome Usually associated with Neisseria **meningitidis septicemia**	Autoimmune adrenalitis **(most common cause of Addison disease)**	Infection tuberculosis fungal	AIDS	Metastatic neoplasm	
Morphology	-Bilateral Adrenal haemorrhage and shrunken	-shrunken glands -Scattered residual cortical cells -Lymphoid infiltrate	-granulomatous -inflammatory reaction			
Clinical feature	May cause Disseminated intravascular coagulation	-decrease aldosterone : **hyperkalemia** , hyponatremia , volume depletion , hypotension , acidosis caused by high H -hyperkalemia : cause GI disturbances (anorexia, nausea, vomiting, weight loss, diarrhea) -decrease cortisol level : Hypoglycemia				
Complication		acute adrenal crisis (Coma or death can follow if corticosteroids are not replaced)				

Pheochromocytoma

Definition	Neoplasms of chromaffin cells, which release catecholamines
Etiology	-Most often sporadic but associated with genetic syndromes in approximately 25% of cases **Genetic mutation** : Multiple endocrine neoplasia type 2 (MEN2) , **Neurofibromatosis type 1 (NF1) , von Hippel-Lindau syndrome ,** Sturge-Weber syndrome -Malignant in approximately 10% of cases
Morphology	-Vascular network form small nests (Zellballen) -cell : Polygonal to spindle shape -Cytoplasm: fine granular appearance -Nuclei : pleomorphic
Clinical feature	-Hypertension -tachycardia, palpitations, headache, sweating, tremor
Diagnosis	-increased urinary catecholamines -vanillylmandelic acid test -metanephrines test -Malignancy in pheochromocytomas is diagnosed by the presence of metastases

Diabetes melitus		
4,5	DM I 10%	DM II 90%
Overview	autoimmune disease characterized by pancreatic β-cell destruction leading to an **absolute** deficiency of insulin	caused by a combination of peripheral resistance to insulin action and **relative** insulin deficiency
Etiology	-Genetic susceptibility: HLA-DR linked : (3, 4) non-HLA genes -Environmental factors : viral infection -Autoantibodies	
Risk factor	Autoimmune disease	-genetic -environmental risk factors : metabolic syndrome (obesity) , high BMI -inflammation
Pathogenesis	-immune cells reacting against beta cell antigens (failure of self-tolerance in T cells specific for Beta cell antigens) (chronic inflammation) -autoantibody	**-Insulin resistance** -Beta cell dysfunction
Clinical feature	Tired of diabetes : Polyuria , polydipsia , polyphagia	
	Diabetic Ketoacidosis	Hyperosmolar Nonketotic Coma
Diagnosis	-absent of C peptide	
Morphology	-Leukocytic infiltration of T lymphocytes (insulitis) -Reduction in the number and size of islets	-Amyloid replacement of islets (advanced stages fibrosis)
Complication	❖ Macrovascular Disease : -atherosclerosis (aorta , coronary artery (most common causes of death in diabetes) , large renal artery) , Peripheral peripheral artery disease (PAD) is a common cause of intermittent leg pain , The condition is due to atherosclerosis -Gangrene of the lower extremities ❖ Morphology : Hyaline arteriolosclerosis (thickening of the wall of the arterioles , hypertension)	
	❖ Microangiopathy : diffuse thickening of basement membranes ❖ Morphology: hyaline material composed predominantly of type IV collagen , to evaluate the basement membrane thickness we use periodic acid-Schiff stain	
	Nephropathy : ❖ **capillary basement membrane thickening** ❖ **Diffuse mesangial sclerosis** mesangial expansion : (proteinuria, hypoalbuminemia, and edema) ❖ **Nodular glomerulosclerosis :** ball-like deposits , nodules are PAS-positive , called **Kimmelstiel-Wilson lesion** ❖ **diffuse Nodular glomerulosclerosis :** ischemia causes scarring of the kidneys , granular-appearing cortical surface ❖ Pyelonephritis : more common and sever with diabetes Maltese acute : (necrotizing papillitis (or papillary necrosis)) , Chronic :	
	Ocular Complications ❖ cataract ❖ glaucoma ❖ retinopathy : **Proliferative retinopathy :** neovascularization and fibrosis **Nonproliferative retinopathy :** thickening of the retinal capillaries , Includes hemorrhages, retinal exudates (cotton wool spots) can be : Soft deposits of plasma proteins and lipids , or Hard → (deposits of plasma proteins and lipids)	
	Nephropathy : ❖ most common (Peripheral, symmetric neuropathy of lower extremity, sensory more common than motor ❖ autonomic neuropathy : disturbances in bowel and bladder function ❖ mononeuropathy : foot drop or wrist drop .	