ZAPOROZHZHIAN STATE MEDICAL UNIVERSITY

The department of pathological anatomy

and forensic medicine

Endocrine pathology

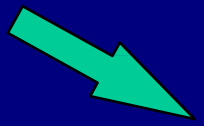
Lecture on pathomorphology
for 3-rd year students

ENDOCRINE SYSTEM

secretion of hormones (steroids, peptides)

feedback inhibition

blood

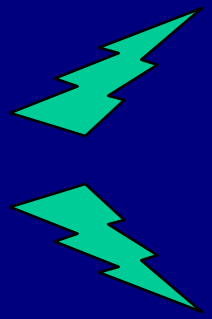


regulation of activity of various organs

Adenohypophysis

ventral lobe embryologically derived from mouth cavity

eosinophils (A cells)
basophils (B cells)
chromophobes



5 hormones:
ACTH
TSH
FSH+LH
prolactin
GH

Hyperpituitarism and adenomas of pituitary

prolactinoma	30%	from A and chromophobes
FSH + LH	15%	from B
ACTH	15%	from A and chromophobes
GH	5%	
TSH	1%	

Pituitary adenomas

majority of adenomas produce only 1 hormone

up to 30% adenomas non-functional – only local pressure effect

➡ „balloon“ expansion of sella ➡ usuration ➡ rupture of diaphragm + suprasellar growth ➡ pressure to chiasma & n. opticus, impression of brain & paranasal sinuses ➡ disturbances of vision, headache

Hormonal syndromes

prolactin	oligo-, amenorrhea, galaktorrhea, impotence
GH	gigantism up to 240 cm acromegaly, macroglossy
ACTH	Cushing's d.: obesity, moon-face, hirsutism, hypertension etc. (see adrenal)

Hypopituitarism

loss of at least 75% of parenchyma due to:

1. nonfunctional adenoma (pressure atrophy)
2. ischemic necrosis (Sheehan's sy = post-partum necrosis of enlarged hypophysis by bleeding or haemorr. shock lactation arrest, no restoration of menstrual cycle)
3. empty sella sy → following inflammation, operation, irradiation herniation of arachnoid & CSF into the sella

Hypopituitarism - clinical symptoms

- pituitary nanism: decrease of GH → substitution
- hypogonadism (Fröhlich's sy = dystrophia adiposogenitalis) – accomp. by mental retardation namely in males
- hypothyroidism
- disorders of adrenal cortex

Posterior lobe syndrome

the cause is usually in hypothalamus, very rare

decreased ADH → diabetes insipidus (polyuria, polydypsia, dehydratation)

THYROID GLAND

regulated by adenohypophysis (TSH) and blood levels of iodine

thyroglobulin in follicular colloid → transformation to thyroxine (T4) a triiodothyronine (T3)

parafollicular C cells → calcitonin – facilitates binding of Ca^{2+} to bones and inhibits bone resorption

derived from pharyngeal epithelium – thyroglossal duct

→ persistence → thyroglossal duct cyst (median neck cyst)

→ lingual thyroid

Thyroid gland - pathology

- more frequent in females (M:F = 1:10!)
- namely enlargement - goiter
- increased secretion - hyperthyroidism, thyreotoxicosis
- decreased secretion - hypothyroidism
- hyperplasia, inflammations, tumors

Hyperthyroidism

- diffuse hyperplasia of TG (M. Graves-Basedow)
- toxic nodular goiter
- toxic adenoma
- thyroiditis
- pituitary adenoma, hypothalamic disorders

Hyperthyroidism - clinical symptoms

- increase of basal metabolism, O_2 consumption
- restlessness, emotional lability
- tremor, sweating, loss of weight, intolerance of warmth
- SOB, increased heart rate and output, palpitations congestive heart failure due to thyrotoxic cardiomyopathy (dilated type)
- exophtalmus

Hypothyroidism

- loss of parenchyma (resection, irradiation, medication)
- Hashimoto's thyroiditis
- idiopathic (autoimmune?) hypothyroidism

Hypothyroidism - clinical symptoms

IN **CHILDHOOD** - cretinism

endemic iodine deficiency in mountain regions ➡ (addition of iodine to salt)

short stature, big tongue, defective teeth, rough facial features

IN **ADULTHOOD** - myxedema

accumulation of mucopolysacharides in corium ➡ pale thick (doughlike) skin, namely in periorbital area

bradycardia, apathy, intolerance of cold, big lips and tongue

enlarged and failing heart with pericardial fluid

coronary arteriosclerosis due to

THYROIDITIS

- Hashimoto's thyroiditis
  (= H. goiter)
  most frequent inflammation, autoimmune → immune reaction against TG -up to 20× more frequent in females
  histology: replacement of parenchyma by lymphoid tissue with formation of lymph. follicles with germinal centers
  follicular cells → eosinophillic, finely granular oncocytes, goiter

- **Focal lymphocytic t.**

  very frequent, in females

  usually only subclinical manifestation (increase of TSH, normal T3, T4)

  often incidental morphological finding

- **Subacute granulomatous t. (De Quervain's)**

  viral etiol.? - fever, palp. tenderness, pain, transitory hyperfunction

  granulomas with multinucleated giant cells

  heals spontaneously, not operated

- **Fibrous goiter (Riedel's)**

  firm idiopathic fibrosis of the gland, merging into surrounding structures, extremely rare

GRAVES - BASEDOW DISEASE

= toxic goiter

most frequent cause of hyperthyroidism (diffuse hyperplasia)

- triad: hyperthyroidism
  exophthalmia (in 2/3) - edema of retrobulbar connective tissue
  ("malignant" e. – not possible to close eyelids – corneal ulcers - blindness)
  pretibial edema - (in 1/6) - mucin, lymphocytes

up to 7× more frequent in females

autoimmune mechanism (thyroid stimulating Ab., thyroid growth stimulating Ab.) – against TSH-receptors

GB goiter - histology

"too much epithelium, too few colloid"

epithelial cells tall, colloid pale, "watery", vacuolated (marginal usurations), stromal lymphoid infiltrates

rich vascularization

GOITER

this term doesn't say neither anything about etiology

nor about the character of the process

most often of hyperplastic origin

first diffuse, later on nodular

often accompanied by regressive changes

- Endemic goiter

by iodine deficiency decreased synthesis of hormone → compensatory increase of TSH → enlargement (hyperplasia) of the gland

- Sporadic goiter

multifactorial, i.e. iodine and goitrogenes in diet: cabbage, cauliflower, turnip, kale

females, frequently onset in puberty or pregnancy

Nodular colloidal goiter

weight 300g up to 1kg, sometimes retrosternal growth

histologically - nodules, sometimes with bleeding and/or calcifications

micro- normo- a macrofollicular (majority) - large follicles with colloid (colloidal goiter)

eufunctional g., toxic g., hypofunctional g.

cytology of cold nodes (diff. from carcinoma)

(suspicious goiters and g. with clin. symptoms are operated)

TUMORS

80% of solitary nodules are adenomas
benign, mainly solitary, spheric, encapsulated

follicular adenoma

normofollicular, macrofollicular (colloidal), microfollicular (fetal), trabecular (embryonic)
nonfunctional a. (scintigrafic) - cold nodule
functional a. – hot nodule (= toxic)

oncocytic adenoma

large eosinophillic cells

CARCINOMAS

not frequent, up to 3 × more often in females
post-irradiation- Hiroshima 7% survivors, Tschernobyl,
therapeutic irradiation (lymphomas in childhood)

- from follicular cells

  well differentiated - papillary, follicular, oncocytic
  poorly differentiated - insular
  undifferentiated - anaplastic

- from C cells

  medullary

- Papillary carcinoma

approx. 70% of all carcinomas

diagnostic feature is not presence of papillae,

but so called „ground glass nuclei"

sometimes only minute (mm) - microcarcinoma

invasion into capsule, fibrosis

psammoma bodies (concentric calcifications)

meta to LN, good prognosis - 80% 10y. survival

- **Follicular carcinoma**

  about 20% of malignancies
  difficult diff. dg. vs. adenoma - invasion through the capsule and/or vascular invasion!
  meta to bones, lungs, brain

- **Anaplastic carcinoma**

  10% of malignancies, highly agressive
  histologically – small cell, large cell, spindle cell type
  death within 2 years

- **Medullary carcinoma**

  from C cells (calcitonin!), sometimes familial occurrence
  solid foci of small cells, production of amyloid („APUD amyloid")

ADRENAL GLANDS

2 organs in 1

cortex vs. medulla

different embryogenesis

different structure & function

ADRENAL CORTEX

spongiocytes producing steroid hormones
glucocorticoids, mineralocorticoids, sex steroids
hyperfunction, hypofunction, tumors

- Hyperfunction (hypercorticism)

steroids: glucocorticoids (mainly cortisol)
→ Cushing's sy

mineralocorticoids (mainly aldosterone)
→ hyperaldosteronism (Conn's sy)

androgens → virilism (adrenogenital sy)

Cushing's sy - clinical symptoms

- obesity (so called arachnoid type)
- moon-face, neck hump, striae
- hypertension, muscle weakness
- osteoporosis, hirsutism and amenorrhea
- impaired metabolism of glucose (steroid diabetes)
- psychotic disorders

Cushing's sy - causes

- pituitary adenoma – increase → of ACTH hyperplasia of the cortex
- functioning cortical adenoma
- paraneoplastic sy - (in 10-15%) – increased ACTH produced by tumor cells (most often small cell lung cancer) → hyperplasia of the cortex
- iatrogenic – Cushing's sy caused by treatment

Cushing's sy - morphology

- cortical adenoma
  - high level of cortisol causes hyaline degeneration of B cells in hypophysis → Crooke's cells
  - atrophy of the cortex

- pituitary adenoma
  - hyperplasia of adrenal cortex - diffuse or nodular
  - bilateral

Hyperaldosteronism

mineralocorticoid aldosterone
regulation through renin-angiotensin system

increased excretion of K+ and retention of Na+
→ hypokalemia, hypernatremia → increased volume of extracellular fluid, blood → hypertension

muscle weakness (including myocardium)

primary aldosteronism in cortical adenoma - Conn's sy

Adrenogenital syndrome

adenoma, hyperplasia or carcinoma of the cortex

in young females masculinisation

in young males pubertas praecox

Hypofunction

primary = insufficiency due to damage of cortex

(Addison's disease)

secondary = insufficiency due to pituitary lesion

(decrease of ACTH)

Addison's disease

- Morphology

leaf-like adrenals (very thin cortex)

- Clinical symptoms

weakness, fatigue, skin and mucosa pigmentation - melanin
hypoglycemia, hypotension
diarrhea, loss of weight

stress may lead to acute crisis with coma (acute cortical insufficiency)

massive bleeding into cortex (labor trauma, venous thrombosis, meningoc. sepsis w. DIC – Waterhause-Friderichsen sy)

Tumors

- adenoma – majority non-functional, 1-2 cm incidental finding in US, CT or at autopsy histology = zona fasciculata
- carcinoma – very rare, usually non-functional
- myelolipoma - benign mesenchymal tumor histology – similar to bone marrow

ADRENAL MEDULLA

chromaffine cells producing epinephrine (adrenalin) and norepinephrine (noradrenalin)

pathology of medulla: virtually only 2 neoplasms

- Pheochromocytoma
- Neuroblastoma

Pheochromocytoma

production of adrenalin a noradrenalin
90% from medulla, 10% from sympatic ganglia (paraganglioma)

„tumor of 3× 10%": 10% bilateral
10% extraadrenal
10% malignant

grams to kg!

histology: polygonal cells, EM a immunocytoch. neuroendocrine granules

clinically: permanent or paroxysmal hypertension (tachycardia, sweating, headache)

Neuroblastoma

highly malignant tumor of children aged 5 - 15 years
from adrenal medulla and sympat. ganglia (cervical, thoracic and abdominal)
related to retinoblastoma
frequent necroses, bleeding and intratumoral calcifications (X-ray!), sometimes production of catecholamins

histology:
small cells, Homer-Wright rosettes
metastases to bones and liver
according to degree of differentiation neuroblastoma
ganglioneuroblastoma
ganglioneuroma

DIABETES MELLITUS

chronic defect of carbohydrates metabolism
affects also metabolism of lipids and
proteins insufficient production of insulin by
B-cells

- hyperglycemia
- glycosuria, polyuria (osmotic)

causes: idiopathic (genetic)
secondary (destruction of L.i. by
inflammation, surgery, tumor,
hemochromatosis)

Idiopathic DM

type I insulin-dependent, juvenile 10%

type II insulin-non-dependent, adult 90%

genetic disposition

obesity (80% DM-II pts. are obese, 60% of obese pts. have disorders of metabolism of carbohydrates)

pregnancy, stress, viral infections

7th most frequent cause of death – increasing tendency!

Pathogenesis of DM

insulin regulates: utilisation of glucosis in cells
synthesis of glycogen (liver and muscles) synthesis of triglycerides from glucose synthesis of proteins

lack of insulin → hyperglycemia →
glycosuria + ketosis + acidosis → intoxication by ketones
→ diabetic coma

DM I - insulin is missing
B cells destroyed by autoimmunity, viral infection,
??? survival - exogenous insulin (insulin-dependent DM)
DM II – mildly impaired secretion + resistance

Morphology

- **Pancreas – changes of L. islets**
  - often none
  - sometimes reduction of size and/or number
  - sometimes increase of size and/or number
    - babies of diabetic mothers
  - less frequently APUD amyloid in L.i.
  - degranulation of B cells (EM)
  - lymphocytic infiltration of L.i. („insulitis")

• Vessels

from capillary vessels to aorta

after 10-15 years since onset of DM are vascular lesions prominent!

• diabetic microangiopathy

thickening of BM and narrowing of capillaries

skin, retina, nerves, muscles, glomerules

• arteriolosclerosis

hyaline change in arterioles, identical with hypertonic

sometimes combination

• arteriosclerosis

most prominent in large arteries

➡ MI (most freq. cause of d. in diabetics) – silent !

➡ diabetic gangrene of lower extr. (10× amputations)