#▶ GROSSLY, pheochromocytoma range from

→ **small,** circumscribed lesions confined to the adrenal to

*

→ **large, hemorrhagic T** weighing **several kilograms.**

*

C/S → well-defined **yellow-tan** small tumors that compress the adjacent adrenal (F 20-43).

Larger pheochromocytomas tend to be **hemorrhagic, necrotic, cystic & typically efface the adrenal gland.

*

Incubation of the fresh tissue with potassium dichromate solution turns the tumor in to a **diagnostic dark brown color.

*

#◙ H,

composed of **polygonal to spindle-shaped chromaffin cells & their supporting cells, arranged into small "Zellballen" nests of cells , with a rich vascular network.

The cytoplasm has a finely granular appearance, due to the presence of granules containing **catecholamines (F20-44).

**The nuclei are quite pleomorphic.

**Both capsular & vascular invasion may be encountered in benign lesions(!) & the presence of mitotic figures per se does not imply malignancy. Malignancy معناها عنا Mitotic figures مش معناته انه عنا

**Therefore, the definitive diagnosis of malignancy in pheochromocytomas is based exclusively on the presence of metastases, wh ch may involve regional LN, liver, lungs, & bones.

* Metastasis : انبثاثات رموية ~~لمكان~~ عادة إلى أجزاء الاخرى للجسم الليمفاوية *

* * ملخص & عشان نحكم انه هاد Malignancy لازم يكون فيه Metastasis مشابس صورة 20-44 : capsular + vascular invasion لأنه بوضه موجود benign

* Bizzar : الغريب العجيب تشكل وبالحجم يعني endocrine anaplasia & التي وجودها لا تدل على Malignancy

Bizarre cells can be seen, even in biologically benign pheochromocytomas, & this **"endocrine anaplasia"** by itself should not be used to diagnose malignancy, which should be based, in pheochromocytoma, exclusively, on the presence of **metastases!**

* بس papillary ca of thyroid ← عشان نحكي انه صح Maliginant لازم يكون nuclear features موجودة زي "orphan eye"

NEUROBLASTOMA

The most common extra-cranial solid T of childhood, **highly malignant cancer, **with early metastases** occur during the first 5 years of life & may arise during infancy.

* خاصة إلى liver و bone * يختلف الاسم حسب المكان يلي بتروح عليه

They arise in the sympathetic nervous system (occasionally within the brain), most commonly in the abdomen; **arising in either the adrenal medulla or the retroperitoneal sympathetic ganglia. شرح وراء صفحة

* أحيانا بطلع بالجنين من هو ببطن أمه

* occasionally و هي صحيح ورم بالأعصاب ولكن نادراً ماتحدث بـ brain

* يصير غالباً بـ SNS ← Renal medulla

* Retroperitoneal sympathetic ganglia

MULTIPLE ENDOCRINE NEOPLASIA SYNDROMES

*

* المقصد تبعها MEN وهي مجموعة من المتلازمات

* ويتصيب عدد غدد أكثر من واحد * يتكون فرط نمو على شكل Hyperplasia ← ca A

▶ MEN syndromes are a group of inherited diseases, resulting in proliferative lesions (hyperplasias, benign A, & carcinomas) of multiple endocrine organs, such T have certain features that contrast with their sporadic counterparts:

* الأورام التي تصنف بـ Men syndrome عندها صفات خاصة يلي بتضليها مختلفة عن الأورام

(1) They **arise in *multiple endocrine organs,*** either *synchronously* or *metachronously.* (at the same time) (After another) يعني Sporadic (single) (Not familial)

(2) Even in one organ, the tumors are often ***multifocal.***

(3) The T are usually **preceded by an *asymptomatic stage of endocrine hyperplasia*** involving the cell of origin of the T

(1) الـ tumors الذي تظهر بهذه الغدد صماء المتعددة

* يا تظهر بنفس الوقت

* يا بالله ريح على توالي

(e.g., patients with MEN-1 syndrome develop varying degrees of pancreatic islet cell hyperplasia, some of which progress to pancreatic T).

*

هدول نقاط مهمين

(2) يعني حتى لو صار الورم بمكان واحد بغدة صماء وحدة تكون متعددة البؤر ... يعني تفتح thyroid تلاقي مو مكان واحد في Malignancy بتلاقي 5foci فيها Malignancy

(3) هذه الاورام التي تظهر بحالات MEN-syndrome يكون صار فيها مسبقاً

↳ asymptomatic Stage of hyperplasia

يعني فرط نمو في خلايا التي تكون هذا الورم ووحدة منهم

أو أكثر تتحول لسرطان

* مثلاً يلي عندهم MEN I عندهم درجات متفاوتة من :

→ pancreatic islets hyperplasia • وبعد ذلك

• بعض من مناطق فرط النمو تتحول لـ tumor → benign / malignant

عمر مبكر

(4) Occur at a *younger age* than sporadic cancers.

(5) Usually ***more aggressive & recur*** in a higher proportion of cases than similar sporadic endocrine tumors. * Recur : تعود مرة ثانية

MULTIPLE ENDOCRINE NEOPLASIA TYPE 1

MEN type 1 is inherited in an **autosomal dominant pattern.

The gene *(MEN1)* is located at 11q13 & is a **tumor suppressor gene; & **inactivation of both alleles of the gene** is the basis of tumorigenesis.

Commonly involved organs include "3 Ps": Parathyroid **(95%), Pancreas **(40%),** & Pituitary (**30%).** *شو راح يصير فيها ؟!

●***Parathyroid*** with primary **hyperplasia** multiglandular *:* hyperparathyroidism is the most consistent feature of MEN1.

* Multiglandular يعني أكثر من parathyroid Gland (معظم عددهم اربعة)

* هاد بصير ب 95% من حالات

40% ●***Pancreas***: **gastrinomas** associated with Zollinger-Ellison syndrome**,** & **insulinomas** causing hypoglycemia, both tumors are common, aggressive & present with metastases or multifocality, & are the leading cause of **death** in MEN-1.

* تذكر: انه insulinoma إذا كانت sporadic ب 90% ب benign

* ولكن إذا ماكانت لوحدها وكان معها gastrinoma لمريض مصاب ب MEN1 ب 90% ب Malignant عشان هيك بتكون aggressive / present with metastesis

30% ● ***Pituitary***: **prolactin-secreting A** is the most frequent pituitary T in MEN-1 patients. Some individuals develop acromegaly from **somatotrophin-secreting** T

* Prolactin الذي يؤدي إلى إفراز الحليب بالمرأة و إلى Hyperprolactinemia ب Male

MULTIPLE ENDOCRINE NEOPLASIA TYPE2

MEN type 2 is actually **two distinct groups of disorders that are **unified by the occurrence of activating mutations of the *RET* protooncogene** located at 10q11.2.

MEN-2 is inherited in an **autosomal dominant pattern.

Multiple Endocrine Neoplasia, Type 2A:

Organs commonly involved include:

- ***Thyroid:* Medullary ca:** develops in **all (100%)** of **untreated cases,** usually occur in the first 2 decades of life, T are commonly **multifocal**, & foci of **C-cell hyperplasia** can be found in the adjacent thyroid tissue.

*

- ***Adrenal medulla:* 50%** of patients develop adrenal **pheochromocytoma;** about 10% are malignant.
- ***Parathyroid:* 33%** of patients develop multiglandular **hyperplasia** with primary hyperparathyroidism

*

Multiple Endocrine Neoplasia, Type 2B

**Commonly involved organs include: the thyroid & adrenal medulla, with diseases similar to that in MEN-2A.

However, unlike *MEN-2A, patients with MEN-2B:* Do not develop primary hyperparathyroidism,

endocrine System تخيران فارج

2) **Develop **extraendocrine manifestations** :ganglioneuromas of mucosal sites (GIT, lips, tongue).

tumor of neuronal cells

* صدول الفروق عن Type 2A

**Now, routine genetic testing identifies *RET* mutation carriers earlier & more reliably in MEN-2 kindred's;

خلفة أبناء

* MEN2 Kinder's بوقت أبكر بالشخص المصاب ب RET mutations * بنقدر نكتشف

**All persons carrying germ-line RET mutations are advised to have prophylactic thyroidectomy to prevent the inevitable development of medullary carcinomas.

* * هاي نصيحة الجراحية التي تحمي المريض من سرطان خطير

* * يعني عالله بنقدر نكتشف ال RET mutation بأبناء الشخص المصاب ب MEN2 عشان

**Such surgical intervention, based on the results of a single genetic test, represents a new paradigm (prototype) in the practice of "molecular medicine."

* شي متميز * بعالم طب

الاستاج

End of Endocrine System = W120 + 42 Text figures + 20 Curran's Gross Path figures = 182 PPP @ 1-10-2017.

Dr. Mohammad Kamel Alwiswasi, MBChB, PhD, FRCPath

نشيل الغدة الدرقية للاشخاص يلي طلعهم عندهم 100% يلي بصير Medullary Ca لحتى نتجنب MEN2 حياة