

Other Anterior Pituitary Tumors

Lineage • Hormonal phenotype • Morphology • Clinical consequences

Pathology lecture

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning outcomes

- Classify the less common anterior pituitary tumors by lineage and hormone expression.
- Explain why hormonally silent tumors often present with mass effects and hypopituitarism.
- Distinguish gonadotroph, thyrotroph, plurihormonal, null-cell, metastatic tumors and pituitary blastoma.
- Apply morphology, immunophenotype, clinical features and metastatic status to diagnostic reasoning.

The entities covered in this lecture

**Gonadotroph
PitNET**

**Thyrotroph
PitNET**

**Plurihormonal
PitNET**

**Null-cell
PitNET**

Also considered separately: Metastatic PitNET and DICER1-associated pituitary blastoma.

Anterior pituitary tumor classification

- PitNETs are categorized by hormone expression and cell lineage–associated transcription factors.
- A tissue-positive hormone stain does not necessarily imply a clinically functioning tumor.
- Some tumors express multiple hormones; Genuinely null-cell tumors lack lineage and hormone markers.
- Metastatic status is a separate behavioral designation rather than another secretory lineage.

Three dimensions of every PitNET

Lineage identity
IHC transcription factors

Hormone production
Tissue and/or serum

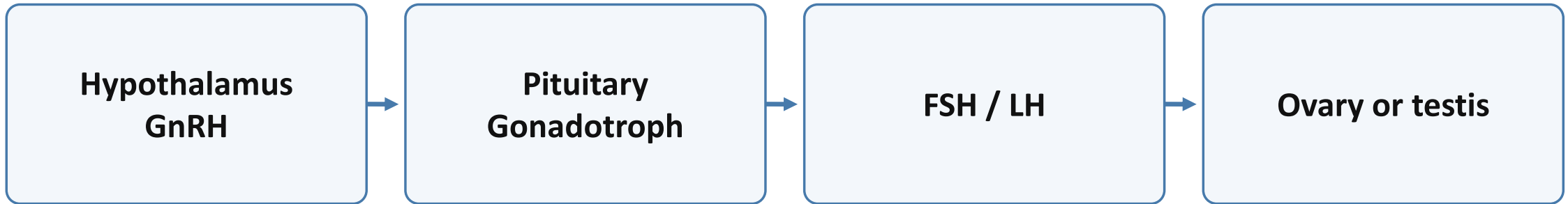
Clinical behavior
Hormone excess or mass effect

Clinical function, tissue phenotype and extent of disease must be assessed independently.

Normal anterior pituitary cell functions

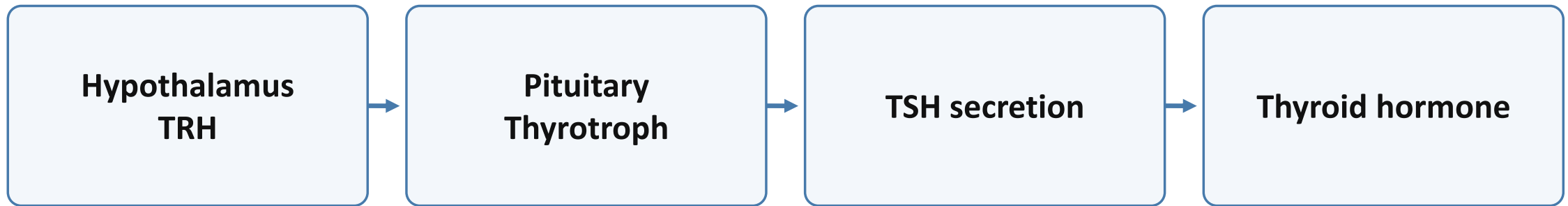
Cell lineage	Hormone(s)	Target or physiologic role
Gonadotroph	FSH, LH	Gonadal function
Thyrotroph	TSH	Thyroid hormone production
Corticotroph	ACTH	Adrenal cortex
Somatotroph	GH	Growth and IGF-1 axis
Lactotroph	PRL	Lactation

The gonadal endocrine axis



Impaired gonadotropin secretion can result in gonadal endocrine dysfunction.

The thyroid endocrine axis



A TSH-producing tumor can cause pituitary-driven hyperthyroidism.

Three routes to clinical presentation

Hormone excess	Mass effect	Hormone deficiency
A secretory tumor stimulates its target organ. Thyrotroph PitNET: Hyperthyroidism.	Expanding lesion affects optic pathways and other local structures. Headache, field loss or diplopia.	Compression compromises normal pituitary tissue. Gonadal and other target-organ dysfunction.

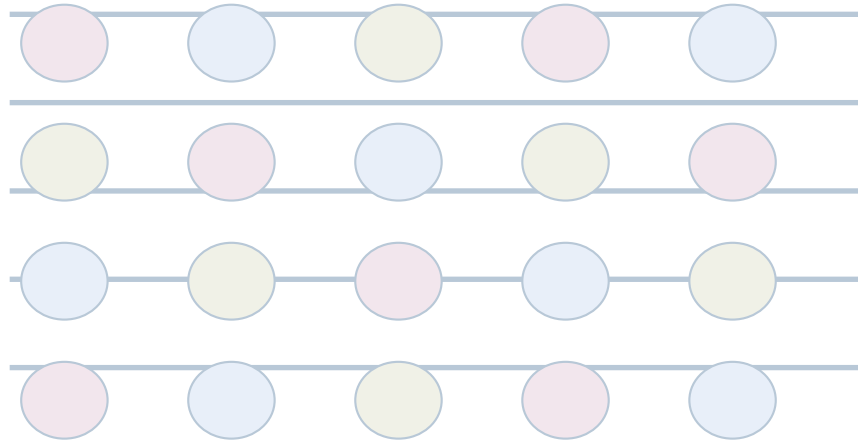
A tumor may produce more than one of these clinical consequences.

Silent does not mean marker-negative

- A silent PitNET may express a pituitary hormone or lineage factor by immunohistochemistry.
- Despite this expression, the patient does not develop the expected hormone-excess syndrome.
- A null-cell PitNET has neither convincing hormonal differentiation nor lineage-marker expression.
- Both may present with headache, visual disturbance and pituitary hormone deficiencies.

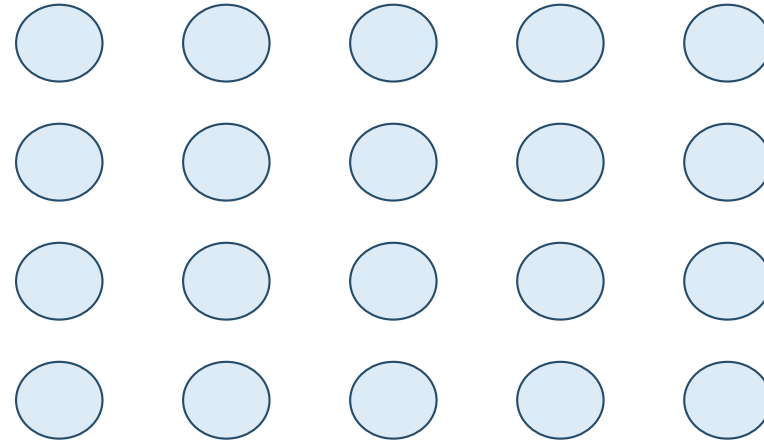
PitNET architecture is distinct from normal pituitary

Normal anterior pituitary — schematic



Mixed cell populations; Preserved stromal network

PitNET — schematic

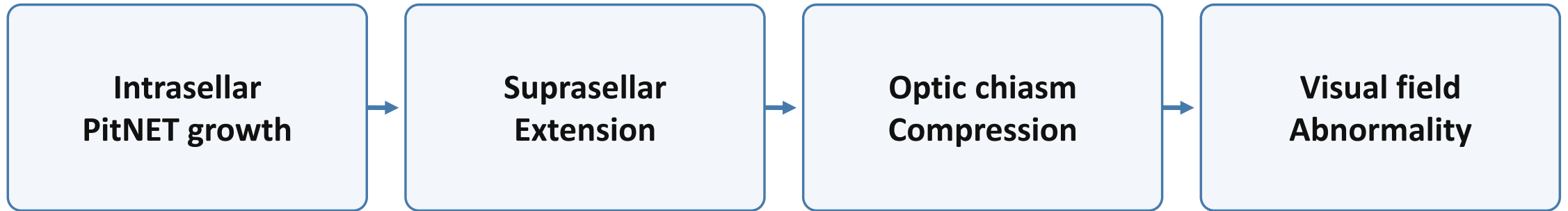


Relatively monomorphic cells; Sparse reticulin

Morphologic hallmarks of a typical PitNET

- Tumors often appear soft and well circumscribed within the sella turcica.
- Histology shows relatively uniform polygonal cells arranged in sheets or cords.
- The supporting reticulin framework is sparse compared with normal anterior pituitary.
- Immunostaining establishes hormone and transcription-factor phenotype.

Local growth can threaten visual function

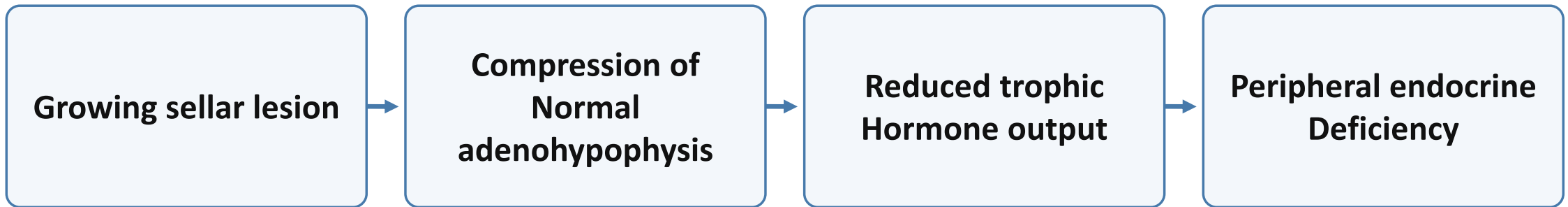


The classic chiasmal pattern is bitemporal hemianopia.

Sellar mass effects may dominate the presentation

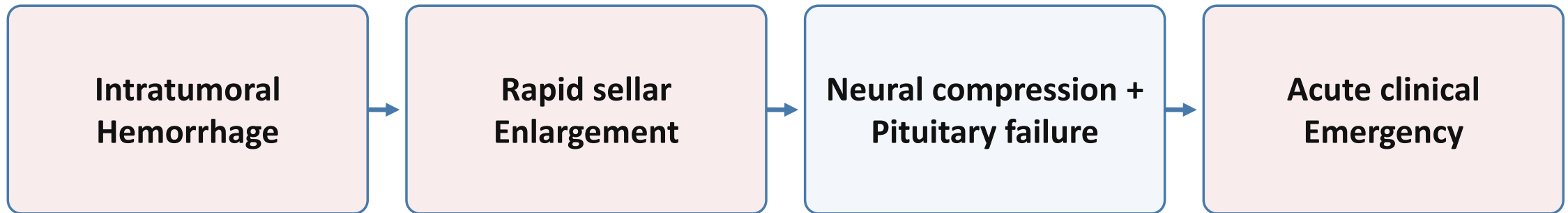
- Expansion may cause headache and compress the optic chiasm, producing temporal visual field defects.
- Invasion or extension toward adjacent structures can be accompanied by diplopia.
- Nonfunctioning tumors often enlarge before detection because endocrine symptoms are absent.
- The anatomical burden of disease may be more conspicuous than its secretory phenotype.

Destructive expansion leads to hypopituitarism



Hypopituitarism may accompany a nonfunctioning PitNET even when the tumor itself has no secretory syndrome.

Pituitary apoplexy: An acute deterioration



Sudden severe headache, visual or ocular-motor symptoms and adrenal insufficiency require urgent assessment.

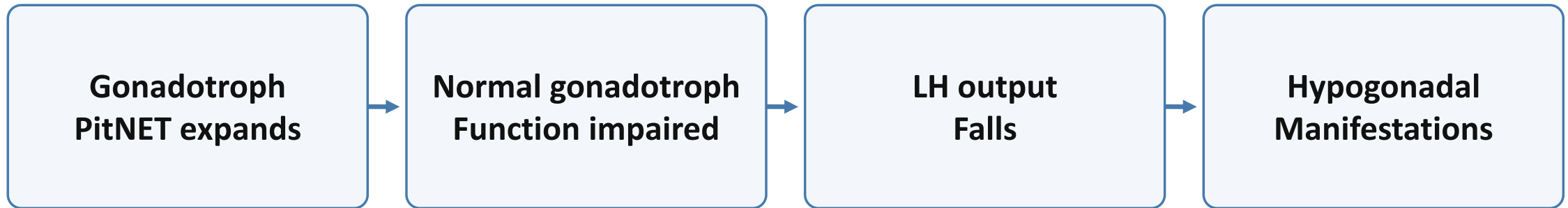
Why gonadotroph PitNETs can be overlooked

- Gonadotroph tumors synthesize gonadotropin-related proteins but usually cause no recognizable hormone-excess syndrome.
- Only small amounts of hormones may be secreted into the circulation.
- Most behave clinically as nonfunctioning lesions until local effects become apparent.
- The absence of a classic endocrine syndrome should not be mistaken for absent cell differentiation.

Gonadotroph PitNET: Usual presentation

- The typical clinical setting is a middle-aged adult with a sellar lesion.
- Visual impairment and headaches reflect an expanding mass.
- Diplopia may arise when local extension affects ocular motor pathways.
- Pituitary apoplexy can bring an otherwise unrecognized lesion to attention abruptly.

How a gonadotroph tumor causes sexual symptoms



The clinical hypogonadism can reflect reduced normal LH secretion, not an LH excess syndrome.

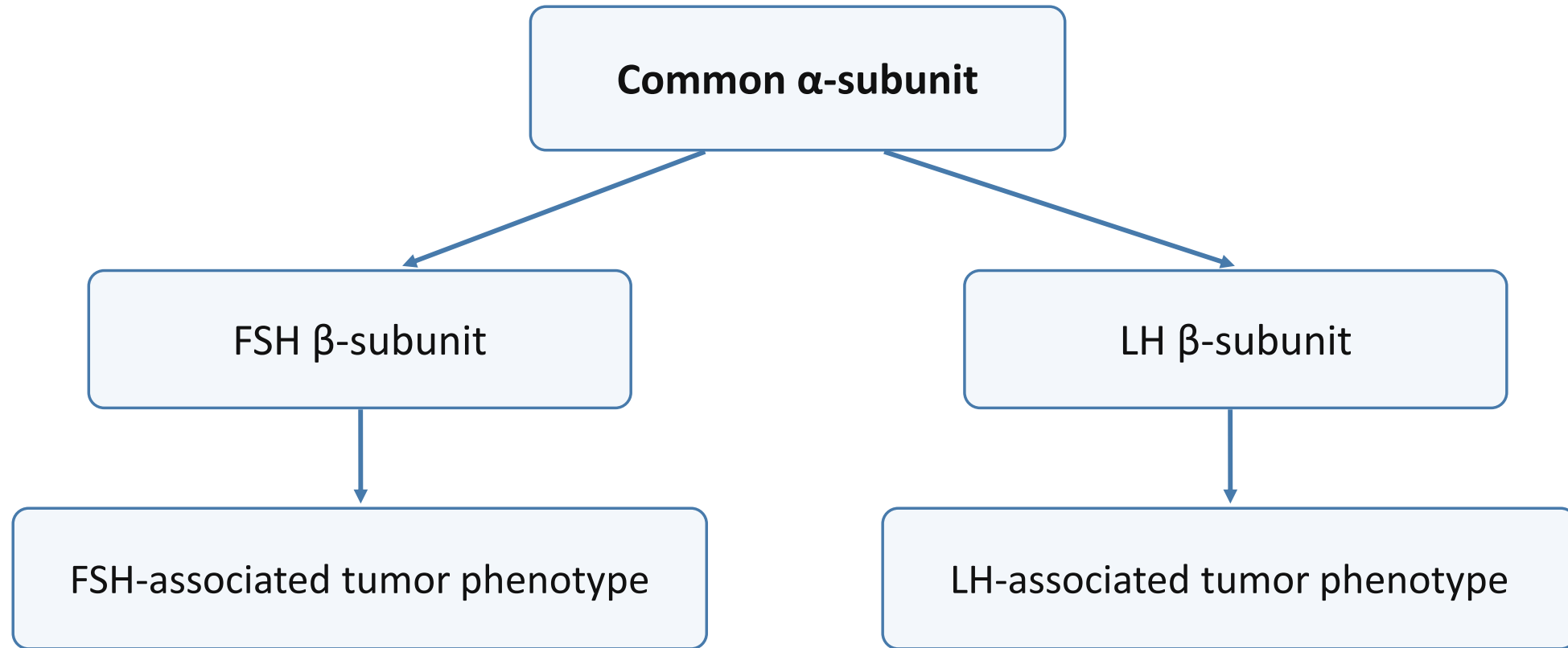
Gonadotroph tumors in men

- Compression of the nonneoplastic anterior pituitary can reduce LH secretion.
- Insufficient LH stimulation results in reduced testicular testosterone production.
- Clinical correlates in the source include decreased energy and libido.
- These findings may coexist with headache or visual field abnormalities.

Gonadotroph tumors in women

- Loss of normal pituitary LH secretion disrupts ovarian endocrine function.
- Amenorrhea is a recognized presentation in premenopausal patients.
- Visual disturbances and headaches may provide the clue to an underlying sellar lesion.
- Absence of a hypergonadotropic syndrome does not exclude a gonadotroph lineage.

Gonadotropins comprise shared and specific subunits

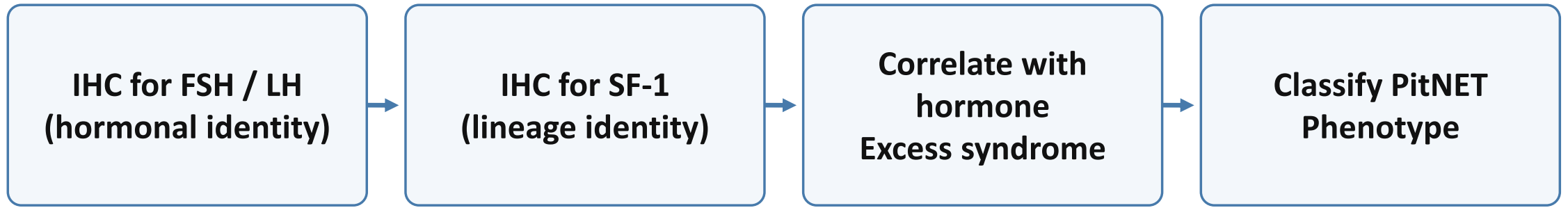


Schematic • FSH is described as the predominant secreted hormone.

Immunophenotype of gonadotroph PitNET

- Tumor cells can express the common gonadotropin α -subunit.
- Immunoreactivity for FSH- β and/or LH- β supports gonadotropin differentiation.
- Steroidogenic factor-1 (SF-1) is an important lineage-associated nuclear factor.
- Estrogen receptor α (ER α) is also associated with gonadotroph differentiation in the supplied discussion.

Diagnostic distinction: Hormone versus lineage



Lineage markers can classify a clinically silent tumor when serum hormone excess is absent.

What is and is not established by hormone staining

What it establishes	What it does not establish
Expression of a protein within neoplastic cells.	A clinically significant secretory syndrome.
Support for lineage-specific differentiation.	The degree of serum hormone elevation.
A basis for histologic classification.	That the tumor is confined or metastatic.

A nonfunctioning PitNET may be IHC-positive for a specific hormone.

Case: A hormonally silent sellar mass

Hypothetical: A middle-aged patient has progressive peripheral visual loss and reduced libido. A sellar tumor lacks a clinically recognizable hormone-excess syndrome.

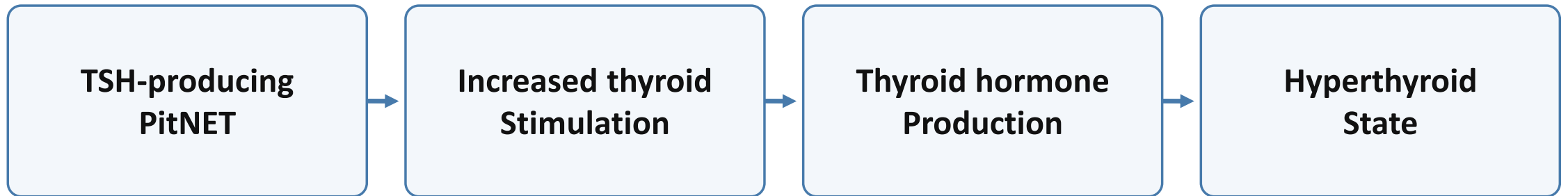
Interpretation

- Which pituitary lineage is common in this type of presentation?
- Why can libido fall when the tumor is not actively secreting excess LH?
- Which tissue markers would help establish the lineage?

Thyrotroph PitNET: A rare functional tumor

- Thyrotroph PitNETs synthesize thyroid-stimulating hormone (TSH).
- They are uncommon, accounting for approximately 1% of PitNETs in the supplied source.
- They can drive thyroid hormone overproduction and are a rare cause of hyperthyroidism.
- Their identity must be considered in the context of the normal hypothalamic–pituitary–thyroid axis.

How TSH excess produces hyperthyroidism



The initiating lesion is in the pituitary rather than in the thyroid gland.

Central versus primary thyroid pathology

- In thyrotroph PitNET, abnormal pituitary TSH secretion can stimulate the thyroid.
- The resulting hyperthyroidism does not establish an autonomous primary thyroid disorder.
- Tumor lineage, thyroid hormone findings and the direction of endocrine drive must be considered together.
- The supplied section does not specify numerical thresholds or a formal biochemical testing algorithm.

Thyrotroph lineage is shared with other PIT1 tumors

POU1F1 (PIT1)
Lineage identity

Thyrotroph
TSH

Somatotroph
GH

Lactotroph
PRL

The shared transcription-factor lineage does not make these tumors hormonally equivalent.

Comparison within the PIT1 lineage

Lineage phenotype	Dominant hormone	Characteristic endocrine effect
Thyrotroph PitNET	TSH	Hyperthyroidism
Somatotroph PitNET	GH	Acromegaly / gigantism
Lactotroph PitNET	PRL	Reproductive dysfunction / galactorrhea
Some plurihormonal PitNETs	GH, PRL, TSH	Multiple hormone expression

Interpreting an apparent TSH-producing lesion

- First identify the patient's endocrine phenotype and the nature of the sellar mass.
- Demonstrate TSH expression in the tumor and assess its PIT1-lineage phenotype.
- Differentiate tumor-derived hormone excess from secondary endocrine disturbances caused by tissue compression.
- Do not equate TSH immunopositivity alone with clinically manifest hyperthyroidism.

Case: Hyperthyroidism with a sellar tumor

Hypothetical: An adult presents with clinical hyperthyroidism. Imaging shows a pituitary mass, and tumor cells are immunoreactive for TSH.

Interpretation

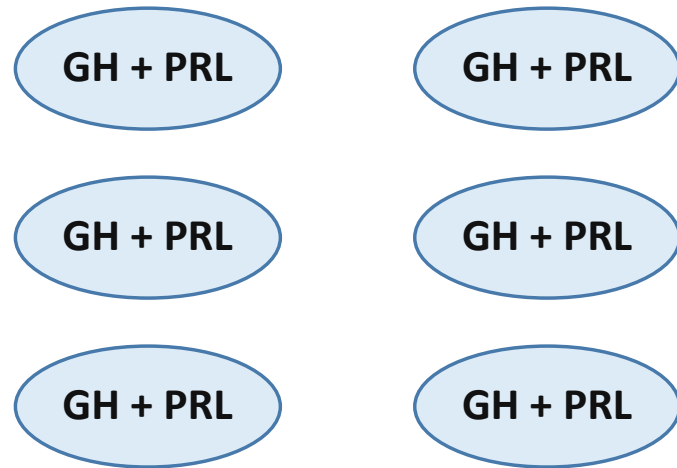
- What lineage is suggested by the tumor hormone?
- Which transcription factor family supports the lineage?
- Why must tissue hormone expression be correlated with clinical endocrine findings?

Plurihormonal PitNETs: The key distinction

- Some PitNETs express or secrete more than one pituitary hormone.
- The source highlights GH and PRL as a frequent combination in double-hormone pituitary tumors.
- Table 24.1 includes a plurihormonal phenotype with GH, PRL and TSH expression.
- Hormone multiplicity must be interpreted alongside cell-lineage and cell-distribution findings.

Two patterns of multiple-hormone expression

Bihormonal tumor cell



Same neoplastic cells express both hormones

Mixed populations



Different cell groups express different hormones

Cell-level hormone mapping matters

- A single cell that expresses GH and PRL differs conceptually from a tumor containing distinct GH-positive and PRL-positive populations.
- The adjacent somatotroph section explicitly distinguishes mammosomatotroph from mixed somatotroph–lactotroph PitNET.
- The phenotype of a plurihormonal lesion cannot always be inferred from one bulk positive stain.
- Cell distribution and lineage markers contribute to precise classification.

Behavior of plurihormonal PitNETs

- The supplied section describes plurihormonal tumors as usually aggressive.
- This is a qualitative description, not a quantified risk or an individually predictive rule.
- Aggressive local behavior must not be equated with the presence of metastasis.
- Clinical course, tissue differentiation and disease extent remain distinct assessments.

Null-cell PitNET: A stringent diagnosis

- A null-cell PitNET lacks detectable markers of pituitary hormonal differentiation.
- It also lacks convincing immunophenotypic evidence of the recognized pituitary cell lineages.
- A clinically silent tumor with demonstrable SF-1 or PIT1 expression is therefore not null by definition.
- The label should not be applied merely because endocrine symptoms are absent.

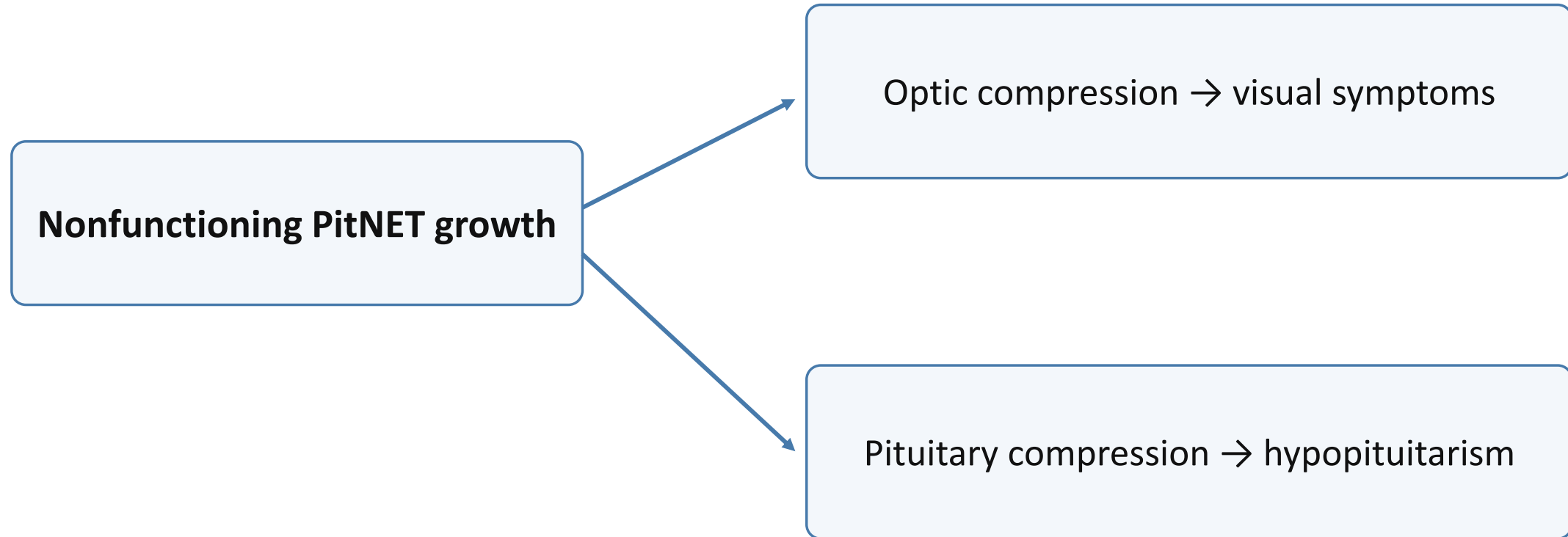
Silent PitNET versus null-cell PitNET

Diagnostic feature	Silent lineage-defined PitNET	Null-cell PitNET
Hormone-excess syndrome	Absent	Absent
Tissue hormone expression	Can be present	Absent by definition
Lineage factor	Can be present	Absent by definition
Typical clinical problem	Mass effect $\pm$ deficiency	Mass effect $\pm$ deficiency

Why null-cell tumors produce local symptoms

- A null-cell PitNET has no defining hormonal hypersecretion syndrome.
- Its expanding volume can compromise optic pathways and other local structures.
- It may also compress residual anterior pituitary and reduce normal endocrine output.
- The clinical burden reflects mass and gland destruction rather than tumor hormone secretion.

Progressive null-cell tumor: Dual consequences

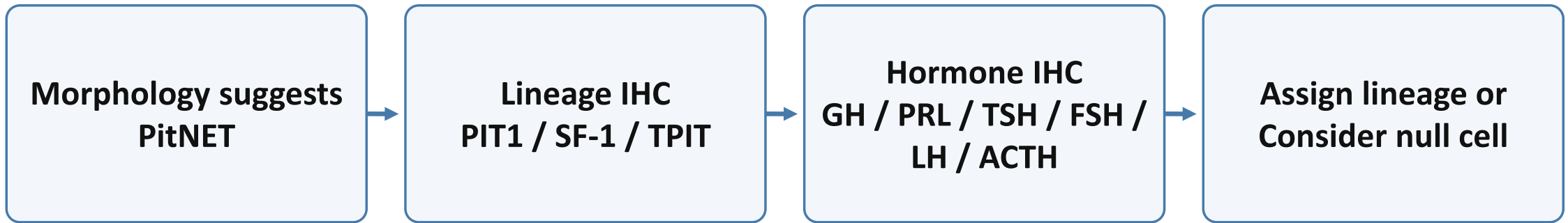


Distinct effects can coexist: Local neurologic dysfunction and trophic-hormone deficiency.

Acute versus gradual gland failure

- Gradual null-cell tumor expansion can progressively impair pituitary function.
- Hemorrhage into the tumor can produce abrupt enlargement and acute endocrine failure.
- Acute corticotropin deficiency may cause adrenal insufficiency and hemodynamic deterioration.
- Recognizing possible apoplexy matters even when a lesion has no known hormonal activity.

A tissue workup for clinically nonfunctioning PitNET



This is a conceptual classification pathway, not a complete clinical laboratory protocol.

Metastatic PitNET: Definition is anatomical

- Metastatic PitNETs were formerly called pituitary carcinomas.
- The decisive criterion is documented craniospinal or systemic metastasis.
- Invasion of nearby dura, cavernous sinus or bone alone does not satisfy this metastatic definition.
- Metastatic behavior is established by spread, not inferred solely from atypia or local size.

Local invasion is not the same as metastasis

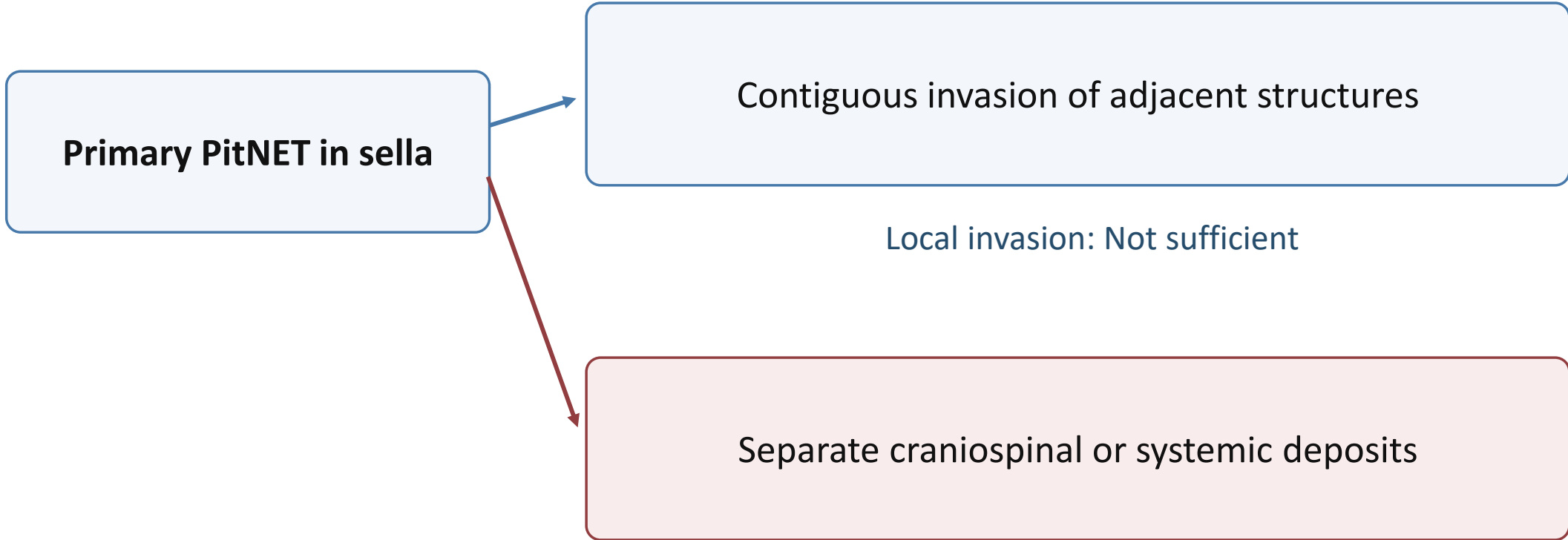
Primary PitNET in sella

Contiguous invasion of adjacent structures

Local invasion: Not sufficient

Separate craniospinal or systemic deposits

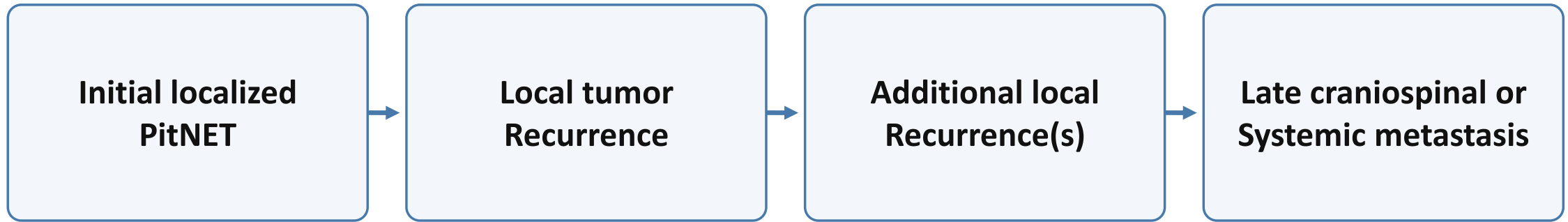
Metastatic disease: Required criterion



Metastatic PitNET: Frequency and timing

- The source reports metastatic PitNETs in fewer than 1% of pituitary tumors.
- Metastases tend to appear late in the disease course.
- Many affected patients have had multiple episodes of local tumor recurrence.
- The presence of recurrences raises concern but does not itself demonstrate metastatic spread.

A typical sequence before metastasis



Schematic represents a frequently described course, not a predetermined natural history.

Hormonal activity in metastatic PitNET

- Most metastatic PitNETs are described as hormonally functional.
- Prolactin and corticotropin are the most commonly secreted products in the source.
- Secretory phenotype and metastatic designation answer different diagnostic questions.
- Hormone staining cannot replace anatomic proof of a craniospinal or systemic metastasis.

Case: Recurrence versus metastatic disease

Hypothetical: A PitNET has recurred locally after treatment and invades an adjacent cavernous sinus. No separate lesion has been established.

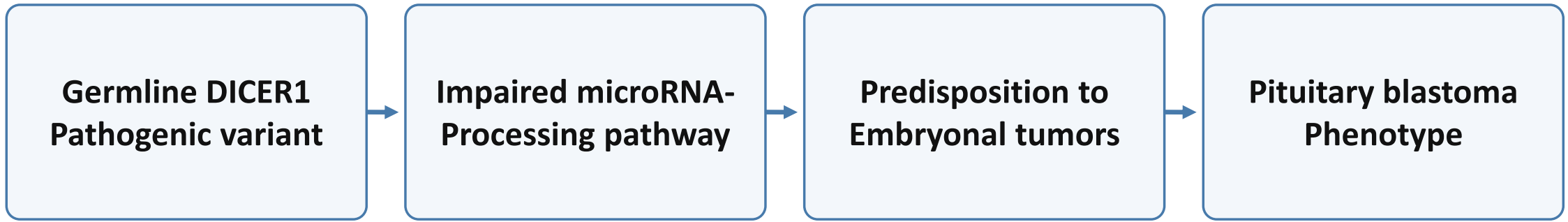
Interpretation

- Does local recurrence and invasion meet the metastatic definition?
- What new finding would change the designation to metastatic PitNET?
- Which endocrine lineages are often functioning in metastatic PitNET?

Pituitary blastoma: A distinctive pediatric entity

- Pituitary blastoma is not simply a conventional adult PitNET presenting in childhood.
- The source places typical presentation before 2 years of age.
- It is associated with germline DICER1 mutations.
- The diagnosis combines developmental-type morphology, endocrine manifestations and hereditary context.

DICER1 and microRNA biology



DICER1 links the pituitary tumor to a broader inherited tumor-predisposition context.

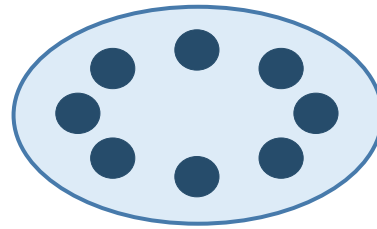
Microscopic appearance of pituitary blastoma

- The tumor contains immature blastema-like cellular components.
- These include cells described as “small round blue cells.”
- Rosette-like formations can resemble the primitive Rathke epithelium.
- The morphology suggests an embryonal developmental phenotype rather than an ordinary differentiated PitNET.

Primitive pituitary blastoma morphology — schematic

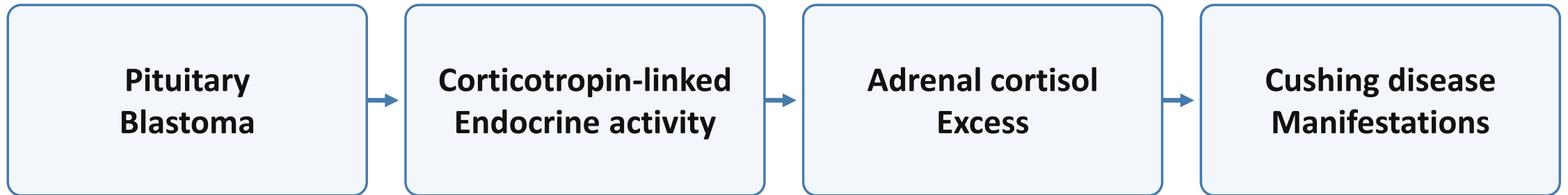
**Immature blastema-like
Cell population**

Rosette-like formations



Diagrammatic rosette motif • not a photomicrograph

Pituitary blastoma and Cushing disease



Cushing disease refers to pituitary-driven ACTH-dependent hypercortisolism.

The DICER1 tumor-predisposition context

- Pituitary blastoma is associated with a germline DICER1 alteration.
- The source highlights primitive blastema-like tumors in other organs in these children.
- Pleuropulmonary blastoma is specifically identified as a common associated neoplasm.
- The genetic association provides information beyond local pituitary morphology.

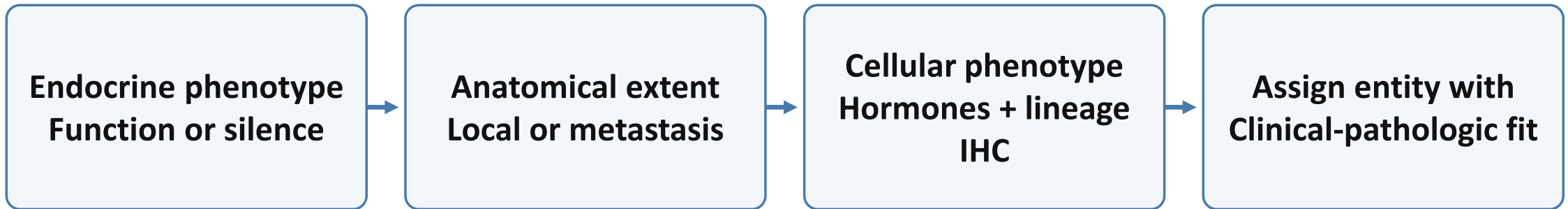
Pituitary blastoma versus conventional PitNET

Feature	Pituitary blastoma	Conventional PitNET
Usual clinical setting	Infant; often <2 years	Typically adult
Genetic association	Germline DICER1	Various somatic or inherited alterations
Morphology	Primitive blastema + rosettes	Relatively monomorphic polygonal cells
Characteristic clue	Cushing disease; associated blastomas	Hormonal phenotype or local effects

Integrated tumor classification

Entity	Phenotype or marker	Characteristic presentation
Gonadotroph	FSH / LH; SF-1	Often silent; mass effect / hypogonadism
Thyrotroph	TSH; PIT1 lineage	Hyperthyroidism
Plurihormonal	Multiple pituitary hormones	Complex hormone phenotype; aggressive course noted
Null-cell	No hormone or lineage markers	Mass effect / hypopituitarism
Metastatic PitNET	Defining distant spread	Late craniospinal / systemic metastasis
Pituitary blastoma	DICER1; primitive morphology	Infancy; Cushing disease

A practical diagnostic reasoning sequence



No single variable — hormone expression, size, or invasion — independently settles every diagnosis.

Common interpretive pitfalls

- Calling a tumor “null-cell” solely because no hormone-excess syndrome is present.
- Assuming gonadotropin positivity guarantees a clinically functioning gonadotroph lesion.
- Equating local invasion or repeated recurrence with documented metastasis.
- Mistaking pituitary blastoma for a routine PitNET without considering age and DICER1.

Synthesis case: Infantile Cushing disease

Hypothetical: An infant has signs of Cushing disease and a primitive pituitary lesion with small blue cells and rosette-like arrangements.

Interpretation

- What tumor entity best integrates age, endocrine phenotype and morphology?
- Which inherited genetic alteration is associated with it?
- Which extracranial tumor association is identified in the source?

Four concepts to retain

- Hormone expression, clinically functioning status and tumor lineage are related but not synonymous.
- Gonadotroph and null-cell PitNETs commonly enter care through mass effects and pituitary insufficiency.
- The definition of metastatic PitNET requires anatomically separate spread.
- Pituitary blastoma is an infantile, DICER1-associated embryonal tumor with Cushing disease presentation.

Suggested pathology reporting framework

- Record tumor morphology and any available reticulin or architectural observations.
- Specify hormone immunostains and pituitary lineage-associated transcription factors.
- Correlate immunophenotype with the clinical secretory syndrome or hormonally silent presentation.
- Document local invasion and any proven craniospinal or systemic metastasis separately.

Reference and source boundary

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th edition (2026), Chapter 24: The Endocrine System.
- Primary section: “Other Anterior Pituitary Tumors,” page 976; adjacent pituitary sections and Tables 24.1–24.2 for context.
- For tumor lineage classification, review the pituitary hormone/transcription-factor comparison in Table 24.1.
- For pituitary genetic associations, review the related molecular summary in Table 24.2.