Gonadotroph Adenomas

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16.1 Epidemiology and Clinical Presentation

- Pituitary adenomas that hypersecrete functional follicle-stimulating hormone (FSH) and/or luteinizing hormone (LH) are extremely rare.
- Although many nonfunctioning pituitary adenomas demonstrate positive immunoreactivity for FSH and LH, the overwhelming majority of these tumors are clinically silent [1], as discussed previously in chapter 10.
- In women, functional gonadotroph adenomas may cause ovarian stimulation syndrome with enlarged ovaries, pelvic pain, galactorrhea, and/or menstrual abnormalities [2, 3]. Levels of circulating estradiol are typically elevated.
- In men, excess levels of serum testosterone with testicular enlargement have been reported.
- In boys, precocious puberty has been reported.
- Functioning gonadotroph adenomas are often plurihormonal tumors, which may co-secrete TSH, prolactin, and/or GH.
- Exacerbation of disease has been reported with administration of gonadotropin-releasing hormone agonists such as leuprolide [4].

16.2 Diagnosis

16.2.1 Imaging

- Imaging characteristics of gonadotroph adenomas are similar to those described for other functioning adenomas.

16.2.2 Histopathology

- Adenomas may demonstrate immunoreactivity for FSH, LH, or both, and invariably for the gonadotrophic transcription factor SF-1.
- Many of these adenomas will also demonstrate immunoreactivity for the alpha-subunit (Fig. 16.1) [5].
- Electron microscopy may demonstrate different structural features in the adenomas of men versus those of women. Gonadotroph adenomas in men resemble null-cell adenomas, with poorly or moderately developed cytoplasmic organelles. In women, tumors tend to be well differentiated, with distinctive vesicular dilatation of the Golgi complex ("honeycomb Golgi") [6].

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16.3 Clinical Management

- As with most functional pituitary adenomas, transsphenoidal surgical resection remains the mainstay of treatment.
- Dopamine agonist therapy (cabergoline or bromocriptine) has been reported to be an effective medical treatment for a subset of these tumors [7].
- Successful treatment with a gonadotropin-releasing hormone antagonist also has been reported [8].
- Resolution of ovarian hyperstimulation, reduction of ovary size, and successful pregnancy have been reported following effective treatment.
- Gonadotropin-releasing hormone agonists should be avoided in these patients, as they may promote tumor growth [9, 10].

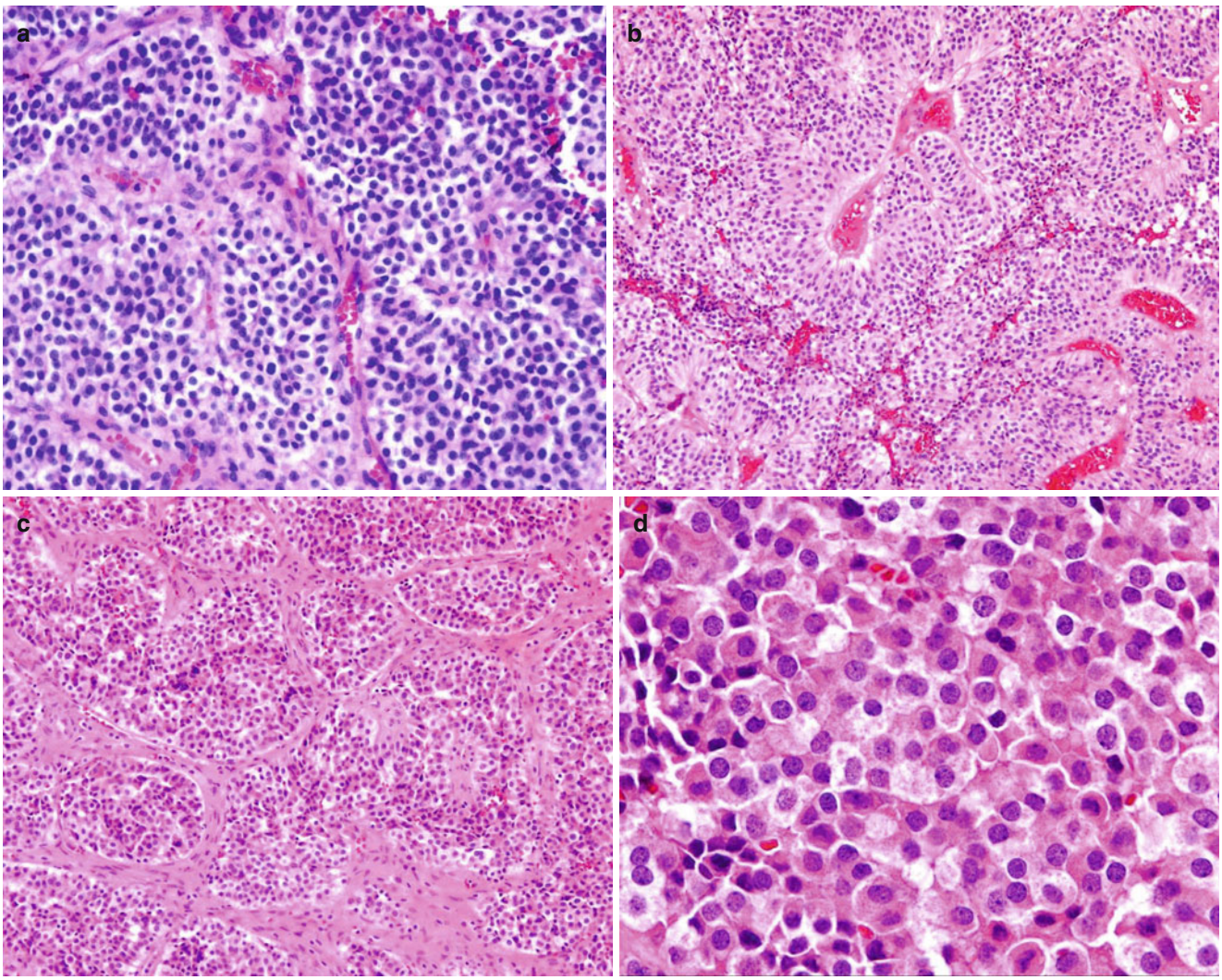

Fig. 16.1 Gonadotropin-secreting adenoma. Gonadotropin-secreting adenomas or gonadotroph cell adenomas are characteristically chromophobic tumors (**a**) with diverse histopathological arrangements. Tumors may have papillary arrangements (**b**), nested arrangements (**c**), and focal oncocytic appearance (**d**). Gonadotroph adenomas show variable immunoreactivity for follicle-stimulating hormone (FSH) (**e**), luteinizing hormone (LH) (**f**), and the alpha-subunit of glycoproteins (**g**). Gonadotroph cell adenomas are mostly composed of well-differentiated, elongated cells with a degree of cellular polarity at the ultrastructure level. Secretory granules are small and tend to be located at the periphery of the cytoplasm (**h**)

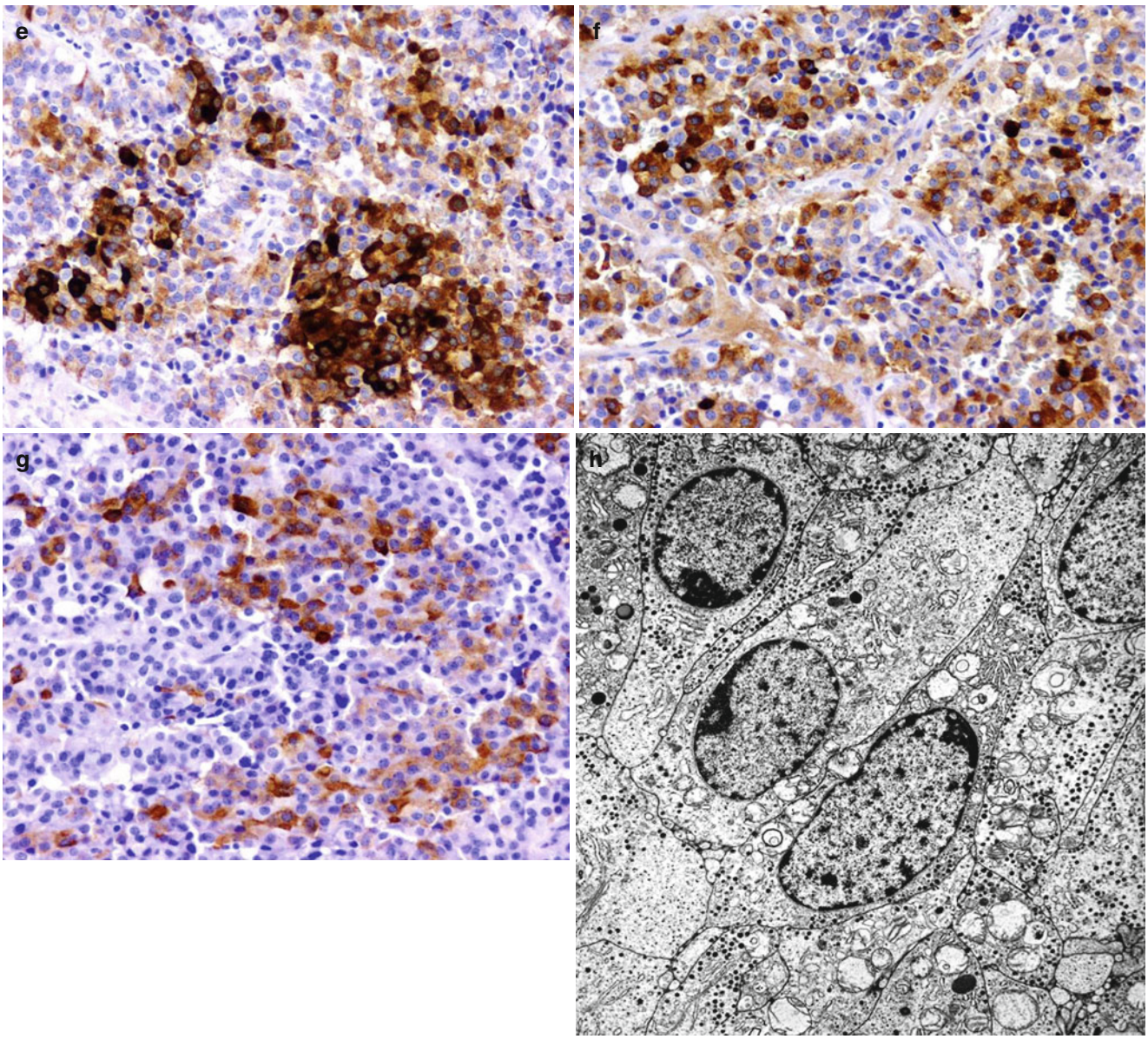

Fig. 16.1 (continued)

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