Pituitary Adenoma with Granulomatous Hypophysitis: A Rare Coexistence

Dear sir,

Pituitary adenomas (PAs) are the most common neoplastic lesion seen in the sellar region.[1] Granulomatous hypophysitis is rare, which can be idiopathic/autoimmune or secondary to systemic illness or local pathology. Nonnecrotizing granulomatous inflammation within the pituitary adenoma is extremely rare, which requires additional treatment and care. Very few cases are reported in the literature with varied clinical picture. In this article, we describe the clinical and pathological features of a case with a combined pathology of GRH and PA with review of literature.[2-4]

A 35-year-old gentleman was found to have an incidental seller mass in adenohypophysis. There were no clinical features of gigantism, Cushing syndrome or autoimmune disorders and no other systemic symptoms. Laboratory evaluation showed normal levels of all pituitary hormones. Imaging revealed stalk thickening. Preoperatively, a clinical diagnosis of nonfunctioning pituitary adenoma was considered and planned for surgery. Transendoscopic excision of lesion was done and intraoperatively, the tumor appeared grayish in color and firm in consistency.

Light microscopic study of the submitted tissue revealed a microadenomatous lesion with monomorphic medium-sized round cells arranged in organoid nests, solid nodules, and sinusoidal pattern with a variably clear to pale eosinophilic to amphophilic cytoplasm and a uniform round regular nucleus with stippled chromatin and inconspicuous mitosis [Figure 1a]. Reticulin stain highlighted the loss of acinar architecture [Figure 1c]. Immunohistochemistry for pituitary hormones revealed immunoreactivity for follicular-stimulating hormone [Figure 1d] and negative for all other hormones. Amidst these neoplastic nodules are clusters of epithelioid cells forming granulomas with an occasional Langhan's type of multinucleated giant cell [Figure 1a and b]. These granulomas were surrounded by variable number of lymphoplasmacytic inflammatory infiltrate. There was no evidence of necrosis. Special stains for acid fast bacilli and fungal elements were negative. Based on these findings, a diagnosis of gonadotrophic pituitary microadenoma with coexisting granulomatous hypophysitis was offered.

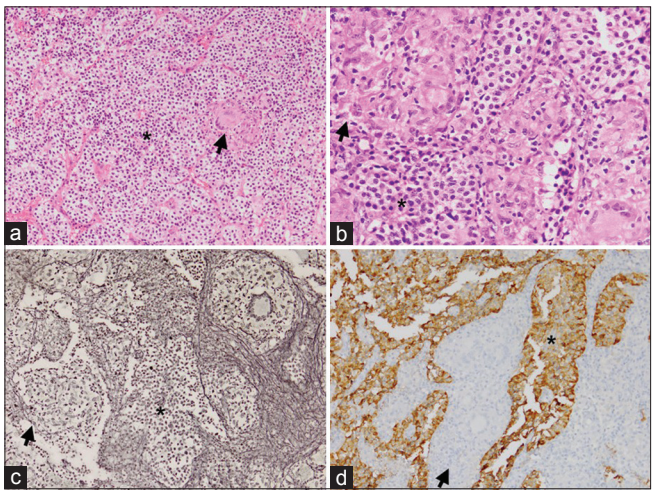

Figure 1: It shows concurrent pituitary adenoma (*) and nonnecrotizing granulomas (arrow) (a and b). The reticulin stain highlighted loss of acinar architecture (c) and immunoreactivity of FSH in adenomatous component (d). (a), (c) and (d) are magnified at 100×, and B at 200×

PA is the most common neoplasm in the sellar region. They are either functioning or nonfunctioning.[1] Functioning pituitary adenoma may require medical treatment, whereas nonfunctioning pituitary adenoma (NFPA) is generally treated by surgical resection. Hypophysitis is a rare inflammatory disorder, accounting for <1% of all pituitary lesions.[5] They most commonly affect middle age females and are broadly classified into primary and secondary hypophysitis.[5] Primary hypophysitis is proposed to be idiopathic or autoimmune disorder; which is further classified into four groups as lymphocytic hypophysitis (LYH), granulomatous hypophysitis (GRH), xanthomatous hypophysitis (XH), and necrotizing hypophysitis (NEH).[5] Secondary hypophysitis is secondary to rupture of Rathke's cleft cyst or tumors like germinoma or recurrent adenoma or systemic diseases. Hypophysitis resembles a neoplasm mimicking pituitary adenoma clinically and differentiating NFPA from hypophysitis is very difficult radiologically. Hence, histopathological diagnosis is the gold standard for differentiating these tumors.

Among primary hypophysitis, LYH is relatively more common among other subvarieties of hypophysitis and involves the infundibulum and adenohypophysis. The hypophysitis is common in young women especially during pregnancy. Also, around 3% of the PA shows lymphocytic infiltration with in the tumors.[6] LYH in adjacent adenohypophysis is considered as a novel finding and is mentioned in the literature.[7] Primary GRH is very rare without systemic involvement, whereas secondary GRH can occur in the setting of autoimmune disorders like Wegener's granulomatosis, infective conditions like tuberculosis or syphilis, sarcoidosis, and foreign body reaction to cystic lesion in sella.[8] The etiology of primary GRH is unknown, but it is postulated that it is triggered by an unknown exogenous or endogenous antigen. These cases of hypophysitis are often misdiagnosed as adenoma on imaging.[9]

Table 1: Histological studies defining PA with primary hypophysitis

	Author name And year	Number of cases	Age	Sex	Clinical features	Type of adenoma	Type of hypophysitis
1	Moskowitz, *et al*.[7] 2006	1	43	F	Galactorrhea of 2 months	NFPA-Null cell	LYH Seen in adjacent adenohypophysis
2	Holck and Laursen[2] 1983	1	54	M	Headache Hyperprolactinemia	FPA Prolactinoma	GRH
3	McConnon, *et al*.[12] 1991	1	22	F	Amenorrhea and spontaneous galactorrhea	FPA Somatotroph PA	LYH
4	Cuthbertson, *et al*.[13] 2008	2	39	F	Features of Cushing syndrome History of hypothyroidism	Corticotrope adenoma	LYH
			61	M	Primary hypothyroidism Hyperprolactinemia	Prolactinoma	LYH
5	Ballian, *et al*.[14] 2007	1	38	F	Compression on adjacent structures	Null cell	LYH
6	Saeger, *et al*.[3] 2007	1	44	M		NFPA ACTH adenoma	GRH
7	Mitra and Chakraborty[4] 2017	1	59	F	Headache and visual field defects	NFPA	GRH
8	Present case 2019	1	35	M	Incidental finding	Gonadotrophic adenoma	GRH

FPA: Functioning pituitary adenoma; NFPA: Non-functioning PA; ACTH: Adrenocorticotropic hormone

The present case demonstrates two different pathologies which are coexisting. Collision tumors in pituitary are relatively common than any other areas in central nervous system. Hypophysitis in background of cystic lesion-like ruptured Rathke's cleft cyst and craniopharyngioma; and neoplasm like germinoma are described in the literature. Rarely, a great variety of lesions coexist like PA with renal cell carcinoma, schwannoma, gangliocytoma, and sarcoidosis.[10,11] However, the coexistence of PA with concurrent primary hypophysitis is very rare and till date only a few (eight) cases have been reported in the literature.[2,4,12-14] The hypophysitis is generally lymphocytic in these cases and presence of granulomatous hypophysitis in a pituitary adenoma is much rarer and only a few of cases have been reported in the literature.[2-4] Table 1 provides clinical and histopathological findings of reported cases of PA with concurrent hypophysitis.

Reports mention that GRH is idiopathic with no systemic illness. An immunological mechanism with autoantibodies against nonsecretory pituitary proteins has been considered by some.[7] The varied inflammatory process in different tumors may be due to development of different autoantibodies in the tumors or normal pituitary tissue. Development of autoantibodies in null cell adenoma has been mentioned in a couple of case reports wherein they have suggested that autoantibodies may not be due to the secretory substance. Presence of granulomas within the adenoma as in our case supports a potential interaction between pituitary adenoma and hypophysitis.[7]

To summarize, dual pathologies in pituitary are extremely rare. The present case is one such rare example occurring in a middle-aged man where in a granulomatous inflammation was observed in the adenohypophysis which harbored a gonadotrophic adenoma. The PA in these associations can have varied histological and functional profile with no characteristic clinical profile. These dual lesions especially the inflammatory component is generally not recognized preoperatively and most often considered as pituitary adenomas. The neoplasm may be incidental, and the inflammation does not warrant a surgery. Despite PA being the commonest tumors, identification of coexisting or isolated hypophysitis is important which requires medical attention to control the inflammatory/immune reaction. The present case represents an example for a rare coexistence of pathologies and attempts to create an awareness, prompting us to look for a dual pathology. Coexisting microadenomatous lesion in case of hypophysitis radiologically mistaken for adenoma or to follow-up the patient with a diagnosis of hypophysitis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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